GENETIC DATABASES AND THE FUTURE OF MEDICINE: CAN LAW AND ETHICS KEEP UP? PERSPECTIVES AND ANALYSIS OF A CONFERENCE

*Robert I. Field, Ethan Dombroski, Mary Kate McDevitt & Whitney A. Petrie**

ABSTRACT

Genetic science and its clinical applications are advancing at an accelerating pace. However, they bring new ethical concerns over privacy along with practical concerns over the use and interpretation of genetic information. A conference held at Drexel University's Thomas R. Kline School of Law in March 2020 explored the intersection of genetic science, law, and ethics to seek insights across disciplines on ways to balance scientific progress with these concerns. Experts in each of these fields focused on the distinctive benefits and risks of large genomic databases that provide powerful tools for advancing research and treatment but pose growing threats to the privacy of individuals whose genetic information they store. While genetic databases are helping clinicians to understand and treat a growing number of serious genetic conditions, they present risks of unauthorized disclosures of highly personal information. Their use in clinical care also raises practical concerns in the interpretation of ambiguous findings, the handling of unanticipated incidental findings, and the communication to patients of risks and uncertainties. Existing legal guidance and protections are woefully inadequate and in urgent need of updating. Within a week of this conference, COVID-19 was declared a global pandemic by the World Health Organization, and researchers began to explore genetic correlates of disease susceptibility. Should such correlates be identified, their application to treatment and prevention will raise

* Robert I. Field is professor of law at the Thomas R. Kline School of Law and professor of health management and policy at the Dornsife School of Public Health at Drexel University. Ethan Dombroski, Mary Kate McDevitt, and Whitney A. Petrie are third-year law students at the Thomas R. Kline School of Law.

especially sensitive privacy and practical concerns and the need for legal reforms will be become even more acute.

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INTRODUCTION

The chemical structure of deoxyribonucleic acid (DNA), the molecular foundation of genetics, was decoded almost seventy years ago in 1953,[1] and the secrets of how it controls cell functions have emerged gradually ever since. Recently, however, the pace of discovery has accelerated considerably, and new findings have started to emerge with astonishing speed.[2] Scientists have been able to harness these findings to diagnose and treat an array of diseases[3] and, in the process, are transforming medical care[4] in ways that had been unimaginable. However, at the same time, we are learning that medicine's new world has a treacherous side with new and unanticipated social threats that raise new legal and ethical dilemmas.[5]

The first foray into harnessing genetics for practical uses involved engineering the DNA of microorganisms, such as bacteria, to perform new functions.[6] Scientists learned how to design these manipulated lifeforms to serve a range of purposes from manufacturing pharmaceuticals to digesting oil spills.[7]

1. Howard Markel, *The Day Scientists Discovered the "Secret of Life,"* PBS NEWSHOUR (Feb. 28, 2013, 10:40 AM), https://www.pbs.org/newshour/health/the-pub-where-the-secret-of-life-was-first-announced.

2. *See The Human Genome Project Timeline of Events*, NIH: NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/human-genome-project/Timeline-of-Events (Sept. 21, 2020).

3. *Id.* (describing how the Human Genome Project will impact the diagnosis and treatment of disease).

4. *See What Is the Human Genome Project?*, NIH: NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/human-genome-project/What (last visited Jan. 9, 2021).

5. *See infra* Part II.

6. *Haemophilus Influenzae Becomes First Bacterium Genome Sequenced*, GENOME: UNLOCKING LIFE'S CODE, https://unlockinglifescode.org/timeline/1995-haemophilus-influenzae-becomes-first-bacterium-genome-sequenced (last visited Jan. 9, 2021) ("Sequencing the genome of bacterium *Haemophilus influenzae*, reported in May 1995, demonstrated for the first time that random 'shotgun' sequencing could be applied to whole genomes with speed and accuracy. . . . Within months after completion of the *H. influenzae project*, the same method was successfully applied to another bacterium, *Mycoplasma genitalium*. Since then, this method has been used to sequence the genomes of many organisms.").

7. *See* David Biello, *Scientists Break Down Oil-Eating Microbe*, SCI. AM. (July 31, 2006), https://www.scientificamerican.com/article/scientists-break-down-oil/; *see also* Drew Smith, *Medicines from Engineered Bacteria Offer Promise—and Pitfalls*, STAT (Feb. 6, 2018), https://www.statnews

The technology was initially developed in the 1970s, but it did not take off as a commercial enterprise until 1980, when the Supreme Court ruled that bioengineered organisms can be subject to patents,[8] which created a path to profitability that attracted investment.[9]

The biotechnology industry brought hundreds of drugs and other pharmaceutical products to market over the decades that followed,[10] but the greatest potential of genetic science lay in harnessing the genome of humans. Discerning the molecular blueprint that guides human biological functions could reveal the cellular basis of our physiology and many of our pathologies, including the causes of many uncurable diseases.[11] The possibilities for diagnoses, treatments, and even cures seemed immeasurable.

The human genome, however, is vastly more complex than that of bacteria. Since 1953, scientists have known that DNA is composed of chains of four chemical bases—adenine, cytosine, guanine and thymine—and that the human complement of it resides in twenty-three chromosomes.[12] They also knew that discrete segments of the chains constitute individual genes that control cellular function.[13] What scientists did not know was which segments correspond to which functions.[14] Figuring it out was like looking for needles in haystacks, and a massive effort was needed to conduct the search.

.com/2018/02/06/engineered-bacteria-medicine/ (describing the development of therapies derived from genetically engineered bacteria).

8. Diamond v. Chakrabarty, 447 U.S. 303, 318 (1980). Thirty-three years later, the Supreme Court ruled that human genes cannot be patented, as they are a "product of nature." Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 580 (2013).

9. *See* Harriet A. Washington, *Gene Patenting Produces Profits, Not Cures*, HUFFPOST, https://www.huffpost.com/entry/gene-patenting-produces-p_b_645862 (May 25, 2011).

10. Ronald Evens & Kenneth Kaitin, *The Evolution of Biotechnology and Its Impact on Health Care*, 34 HEALTH AFFS. 210, 210 (2015).

11. *Id.*

12. *DNA Is a Structure That Encodes Biological Information*, SCITABLE BY NATURE EDUC., https://www.nature.com/scitable/topicpage/dna-is-a-structure-that-encodes-biological-6493050/ (last visited Jan. 9. 2021).

13. *Id.*

14. *See What Is the Human Genome Project?*, *supra* note 4.

That effort took the form of the Human Genome Project (HGP), launched by the federal government in 1990 within the National Institutes of Health (NIH) in collaboration with the Department of Energy (DOE).[15] A little more than a decade later, in 2003, the HGP announced the completion of a map showing the position of each base on each chromosome, three billion in all.[16] However, as formidable as this accomplishment was, it did not on its own permit practical applications, as the order of base pairs does not by itself indicate which sets of them represent actual genes. The next task for scientists was to read the map so it could be put to use.[17]

The work of identifying individual genes began even before the HGP's map was complete.[18] It has led to techniques for diagnosing many conditions based on genetic markers and opened paths for treating many of them.[19] Scientists are now beginning to take that knowledge one step further by altering the composition of individual genes to prevent or cure genetically based conditions with a technology known as CRISPR.[20] Such advances are becoming so important to medical practice that some health systems are making genetic profiles of patients a standard component of medical records.[21]

15. *See id.*

16. *See id.*

17. *See generally* Richard A. Gibbs, Comment, *The Human Genome Project Changed Everything*, 21 NATURE REVS. GENETICS 575 (Oct. 2020), https://www.nature.com/articles/s41576-020-0275-3 (reflecting on the trials and advancements of the HGP over the past twenty years).

18. For example, the BRCA1 gene, which is associated with breast cancer, was discovered in 1994. Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 HEALTH L.J. 123, 131 (2002).

19. *See id.* at 133.

20. CRISPR, first discovered in 1987, permits the base pairs in genes to be edited and is increasingly being used in clinical settings. *See* Yoshizumi Ishino, Mart Krupovic & Patrick Forterre, *History of CRISPR-Cas from Encounter with a Mysterious Repeated Sequence to Genome Editing Technology*, 200 J. BACTERIOLOGY, no. 7, Apr. 2018, at 1, 5, https://jb.asm.org/content/200/7/e00580-17; Carl Zimmer, *Breakthrough DNA Editor Born of Bacteria*, QUANTA MAG. (Feb. 6, 2015), https://www.quantamagazine.org/crispr-natural-history-in-bacteria-20150206/.

21. *See* Jennifer Kulynych & Henry T. Greely, *Clinical Genomics, Big Data, and Electronic Medical Records: Reconciling Patient Rights with Research When Privacy and Science Collide*, 4 J.L. & BIOSCI. 94, 102–05 (2017).

As knowledge of human genetics has advanced, so too has the sophistication of information technologies available to store and analyze genetic data.[22] Millions of data points can be centrally stored and probed for correlations between genetic traits and clinical manifestations.[23] This is a powerful tool for finding the needles in the haystack. Over the past decade, the number and variety of genetic databases has grown steadily.[24] Some large health systems are creating databases based on the genetic profiles they have incorporated into patient records.[25] Various research organizations around the world, including the NIH, are populating these databases with data contributed by volunteers.[26] Private companies are amassing the largest databases with information on millions of individuals who provide their data in return for analyses of their genetic heritage.[27] These resources hold tremendous promise for further accelerating the pace of discoveries, but they also come with tremendous uncertainties and risks.

As the architects of human physiology, genes contain intimate information about our make-up, including details of many of our physical and psychological traits and indicators of

22. *See* Jeffrey Bonadio, *Gene Therapy: Reinventing the Wheel or Useful Adjunct to Existing Paradigms?*, *in* CONVERGING TECHNOLOGIES FOR IMPROVING HUMAN PERFORMANCE: NANOTECHNOLOGY, BIOTECHNOLOGY, INFORMATION TECHNOLOGY AND COGNITIVE SCIENCE 194, 195 (Mihail C. Roco & William Sims Bainbridge eds., 2002).

23. *See* William W. Lowrance, *The Promise of Human Genetic Databases: High Ethical As Well As Scientific Standards Are Needed*, 322 BRIT. MED. J. 1009, 1010 (2001).

24. *See* JERZY K. KULSKI, NEXT-GENERATION SEQUENCING—AN OVERVIEW OF THE HISTORY, TOOLS, AND "OMIC" APPLICATIONS 24–25 (2016), https://www.intechopen.com/books/next-generation-sequencing-advances-applications-and-challenges/next-generation-sequencing-an-overview-of-the-history-tools-and-omic-applications.

25. *See* Lowrance, *supra* note 23, at 1010.

26. *See, e.g.*, *NIH-Funded Study To Recruit Thousands of Participants To Reveal Exercise Impact at the Molecular Level*, NAT'L INST. HEALTH (June 25, 2020), https://www.nih.gov/news-events/news-releases/nih-funded-study-recruit-thousands-participants-reveal-exercise-impact-molecular-level.

27. *See, e.g.*, *AncestryDNA Research and Collaboration*, ANCESTRY, https://www.ancestry.com/cs/collaborations (last visited Jan. 9, 2021); *see also* Charles Seife, *23andMe Is Terrifying, but Not for the Reasons the FDA Thinks*, SCI. AM. (Nov. 27, 2013), https://www.scientificamerican.com/article/23andme-is-terrifying-but-not-for-the-reasons-the-fda-thinks/ ("[23andMe] isn't primarily intended to be a medical device. It is a mechanism meant to be a front end for a massive information-gathering operation against an unwitting public.").

susceptibility to a range of diseases. They also include information about our genetic heritage and the identities of relatives—even distant ones. This is highly personal information that many people would prefer to keep confidential. Disclosure could cause embarrassment and possibly social stigma. It could also invite discrimination in a range of spheres, such as insurance, employment, and housing.[28]

All of the major federal laws that offer protection against privacy violations and genetic discrimination were enacted at least a decade ago, in some cases several.[29] With the rapid pace of technological advance, these laws are showing their age, leaving gaps their drafters could not have anticipated. The considerations that went into constructing these laws reflect technologies of an earlier age and a different set of practical and ethical concerns.

In March 2020, experts in genetic science, law, and ethics considered these issues at a conference called *My Data, Myself* that was held at Drexel University's Thomas R. Kline School of Law.[30] The focus was cross-disciplinary development of public policies that balance advancing genetic science and protection of individual privacy. This Article presents key points presented by those experts and considers their application going forward. Notably, the conference took place as COVID-19 was emerging as a global threat, and nations were beginning to implement social distancing measures in response, such as school and business closures and stay-at-home orders.[31] Several

28. *See Genetic Discrimination*, NIH: NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/about-genomics/policy-issues/Genetic-Discrimination (Sept. 16, 2020) (explaining that GINA covers health insurance and employment discrimination but not housing).

29. See *infra* Part III.

30. *See generally* Drexel University Thomas R. Kline School of Law, *My Data, Myself: Conference on the Science, Law and Ethics of Genetic Databases*, DREXEL STREAMS (Mar. 6, 2020) [hereinafter *My Data, Myself*], https://tinyurl.com/yxezagmw (presentation slides on file with *Drexel Law Review*).

31. *See, e.g.*, Sheri Fink & Mike Baker, *Coronavirus May Have Spread in U.S. for Weeks, Gene Sequencing Suggests*, N.Y. TIMES, https://nyti.ms/39cz3S1 (Mar. 9, 2020); Lisa Schnirring, *Italy*

states began imposing such measures within the week following the conference.[32] This Article also considers the implications of issues raised at the conference for genetic research in relation to challenges posed by COVID-19.

Part I of this Article details current and emerging clinical opportunities that research with genetic databases create and their limitations. Part II explains significant ethical issues related to them. Part III analyzes the primary laws that protect subjects of genetic testing and their shortcomings. Part IV presents an analysis of new conflicts raised by the spread of COVID-19.

I. OPPORTUNITIES OF GENETICS AND THEIR LIMITATIONS

A. *The Need and the Promise*

Individuals differ in their susceptibility to many diseases and in their responses to treatments. Until recently, many of these differences were attributed to random variations that were difficult to systematically explain.[33] Without explanations, techniques to manage such variations were clinically difficult or impossible to develop.[34]

Genetic science is revealing the mechanisms behind much of the seeming randomness.[35] Variations in genes are now known to underlie aspects of susceptibility to many diseases, including

Expands COVID-19 Lockdown to Whole Country, CIDRAP (Mar. 9, 2020), https://www.cidrap.umn.edu/news-perspective/2020/03/italy-expands-covid-19-lockdown-whole-country.

32. Charles Courtemanche, Joseph Garuccio, Anh Le, Joshua Pinkston & Aaron Yelowitz, *Strong Social Distancing Measures in the United States Reduced the COVID-19 Growth Rate*, 39 HEALTH AFFS. 1237, 1240 (2020); Jiachuan Wu, Savannah Smith, Mansee Khurana, Corky Siemaszko & Brianna DeJesus-Banos, *Stay-at-Home Orders Across the Country*, NBC NEWS, https://www.nbcnews.com/health/health-news/here-are-stay-home-orders-across-country-n1168736 (Apr. 29, 2020).

33. Stephen J. Chapman & Adrian V. S. Hill, *Human Genetic Susceptibility to Infectious Disease*, 13 NATURE REVS. GENETICS 175, 175 (2012).

34. *Id.* at 175–76.

35. *See, e.g.*, Fabio Coppedè, Angela Lopomo, Roberto Spisni & Lucia Migliore, *Genetic and Epigenetic Biomarkers for Diagnosis, Prognosis and Treatment of Colorectal Cancer*, 20 WORLD J. GASTROENTEROLOGY 943, 943–44 (2014).

several that are caused by infections, such as: HIV, hepatitis B and C, dengue, malaria, tuberculosis, leprosy, meningococcal disease, and prion disease.[36] Genetic variations also cause differences among patients in responses to drugs and other treatments.[37] Building on these discoveries, a new approach to medical care has emerged in which treatments are customized for each patient based on their genetic makeup[38]—an approach known as precision medicine.[39] It has proved to be particularly valuable in treating various forms of cancer.[40]

Researchers, including the conference's first speaker, Hakon Hakonarson, MD, Director of the Center for Applied Genetics at the Children's Hospital of Philadelphia (CHOP), are finding large databases of human genomes tremendously valuable in expanding precision medicine's reach.[41] A prime example is in pediatric oncology, which now commonly involves genotyping tumors, which contain genetic features distinct from those of the patient.[42] Analysis of tumor genetics allows treatments to be tailored to individual patients.[43] It has also led to the discovery that tumors in different organs may share genetic profiles, suggesting that the genetic profile of a tumor, rather than its location in the body, may be the most effective way to

36. Chapman & Hill, *supra* note 33, at 175–77.

37. Dan M. Roden, Russell A. Wilke, Heyo K. Kroemer & C. Michael Stein, *Pharmacogenomics: The Genetics of Variable Drug Responses*, 15 CIRCULATION 1661, 1661 (2011) (explaining that pharmacogenomics has been used to "transmit the idea that variable drug response may reflect sets of variants within an individual or across a population").

38. Euan A. Ashley, *Towards Precision Medicine*, 17 NATURE REVS. GENETICS 507, 507 (2016).

39. *Id.* ("Understanding the genetic basis of disease was naturally expected to lead to better targeted therapies. Indeed, the steep decline in the cost of sequencing . . . facilitated the discovery of many more causative genes and, more recently, application to individual patients, including several widely reported examples of genome-driven medical decision making.").

40. *See generally* Paulina Krzyszczyk, Alison Acevedo, Erika J. Davidoff, Lauren M. Timmins, Ileana Marrero-Berrios, Misaal Patel, Corina White, Christopher Lowe, Joseph J. Sherba, Clara Hartmanshenn, Kate M. O'Neill, Max L. Balter, Zachary R. Fritz, Ioannis P. Androulakis, Rene S. Schloss & Martin L. Yarmush, *The Growing Role of Precision and Personalized Medicine for Cancer Treatment*, TECH., Sept. & Dec. 2018, at 79, 79 (describing how cancer treatments based in precision medicine have resulted in great benefits to patients).

41. *See generally* Hakon Hakonarson, Dir., Ctr. for Applied Genetics at CHOP, Presentation at *My Data, Myself*, *supra* note 30 [hereinafter Hakonarson, *My Data, Myself*].

42. *Id.*

43. *Id.*

distinguish between different types of cancer.[44] This has important implications for diagnosis and treatment.[45]

A second example of a new use of genetics in pediatric care is in the treatment of infections.[46] The genotypes of pathogens can reveal key features relevant to their infectiousness, such as their origin and route of transmission.[47] It can also indicate which treatments are most likely to be effective against them. The genotype of a patient can help to predict how susceptible the patient is to different pathogens and responsiveness to different treatments.[48] Taken together, this information can significantly improve the effectiveness of care.

A third example is the dosing of medications.[49] Traditionally, physicians have used a patient's height and weight as the primary factors in determining the correct dose.[50] This is a crude measure, but it is often the only way to predict how much of a medication is optimal for an individual patient.[51] Clinicians are now discovering that responses to drugs are also influenced by genetic mechanisms that affect the body's ability to absorb and metabolize different compounds.[52] This has led to increasing

44. *Id.*

45. *Id.*

46. *See, e.g.*, Hector R. Wong, *Genetics and Genomics in Pediatric Septic Shock*, 40 CRITICAL CARE MED. 1618, 1622 (2012) (concluding that scientists' and doctors' approach to treating pediatric sepsis and septic shock have the potential to be enhanced by utilizing genetic and genomic approaches).

47. *See id.* at 1619 (discussing how the presence of a certain genotype in a patient has shown to be associated with mortality in children with meningococcemia).

48. GENES, BEHAVIOR, AND THE SOCIAL ENVIRONMENT: MOVING BEYOND THE NATURE/NURTURE DEBATE 57–58 (Lyla A. Hernandez & Dan G. Blazer, eds., 2006).

49. *See Pharmacogenomics: Drug-Gene Testing*, MAYO CLINIC: CTR. INDIVID. MED., https://www.mayo.edu/research/centers-programs/center-individualized-medicine/patient-care/pharmacogenomics/drug-gene-testing (last visited Jan. 9, 2021) (describing how pharmacogenomics, i.e., drug-gene testing, is a tool that can assist physicians in determining not only the best medication for patients, but which dosage is the most appropriate for a particular patient).

50. Hakonarson, *My Data, Myself*, *supra* note 41. *See also* Sheng-dong Pan, Ling-Ling Zhu, Meng Chen, Ping Xia & Quan Zhou, *Weight-Based Dosing in Medication Use: What Should We Know?*, 10 PATIENT PREFERENCE & ADHERENCE 549, 549–50 (2016).

51. Pan et al., *supra* note 50, at 549–50.

52. Hakonarson, *My Data, Myself*, *supra* note 41; GENES, BEHAVIOR, AND THE SOCIAL ENVIRONMENT, *supra* note 48, at 58.

use of genetic analyses to more accurately predict a patient's response to a prescribed medication, which enables more accurate dosing.[53]

These examples are just a few of the applications of precision medicine that have been developed so far to create vastly more effective and safer treatments. As research proceeds, more will undoubtedly join them. However, Dr. Hakonarson sees a challenge in implementation that may be even greater than that of advancing the underlying science.[54] Discoveries are emerging so quickly that it is difficult for practicing physicians to keep up.[55] Medical expertise in genetics can become obsolete almost overnight.[56] To most effectively harness new knowledge to benefit patients, better techniques will be needed to disseminate and manage it.

B. *Database Examples and Their Uses*

Large databases are central to the research that drives precision medicine. While data on individual patients can guide treatment, data on populations is needed to advance understanding of underlying genetic mechanisms.[57] As samples from more individuals are added to these databases, they contain information on a greater diversity of genetic traits, and their utility expands.[58]

53. Hakonarson, *My Data, Myself*, *supra* note 41. *See also* Aneesh T P, Sonal Sekhar M, Asha Jose, Lekshmi Chandran & Subin Mary Zachariah, *Pharmacogenomics: The Right Drug to the Right Person*, 1 J. CLINICAL MED. RSCH. 191, 192 (2009) (describing the importance and benefits of pharmacogenomics in relation to accurate dosing).

54. *See* Hakonarson, *My Data, Myself*, *supra* note 41.

55. *Id.*

56. *See, e.g.*, Hakonarson, *My Data, Myself*, *supra* note 41; *What It's Like to Specialize in Medical Genetics: Shadowing Dr. Abbott,* AM. MED. ASS'N. (Nov. 28, 2018), https://www.ama-assn.org/residents-students/specialty-profiles/what-it-s-specialize-medical-genetics-shadowing-dr-abbott.

57. *See* Hakonarson, *My Data, Myself*, *supra* note 41.

58. *Id.*

1. *deCODE: The first large-scale database*

The first attempt to create a large-scale genetic database began in 1998 in Dr. Hakonarson's native Iceland, and at the conference he presented his perspective as one of the early participants in that effort.[59] The goal was to amass data on the genomes of every citizen in the country.[60] The database was managed by a company known as deCODE, which received a license to create the database from the Icelandic government.[61] Iceland is a perfect location to launch such an initiative for several reasons. Its population of about 288,000 is small enough that a nationwide database is feasible.[62] It has been settled by humans for just over a thousand years and thorough records have been kept of inhabitants, making it relatively easy to construct genealogies.[63] It has also experienced little immigration since its settlement, so the population is thought to be genetically homogeneous, which can help in spotting mutations associated with specific genetic traits.[64]

deCODE began compiling its database with lofty ambitions of solving numerous genetic riddles. It was initially built with information extracted from physicians' medical records, which was matched with patients' genetic profiles.[65] However, this

59. *Id.* deCODE Genetics led this effort, gathering genotypic and medical data from 160,000 native Icelandic people. *See Science*, DECODE GENETICS, https://www.decode.com/research/ (last visited Jan. 9, 2021).

60. *See* Hakonarson, *My Data, Myself*, *supra* note 41; *Science*, DECODE GENETICS, *supra* note 59.

61. Renate Gertz, *An Analysis of the Icelandic Supreme Court Judgment on the Health Sector Database Act*, 1 SCRIPT-ED 241, 242 (2004), https://script-ed.org/wp-content/uploads/2016/07/1-2-Gertz.pdf.

62. *Id.* at 243.

63. *See* Olga Khazan, *How Iceland's Genealogy Obsession Leads to Scientific Breakthroughs*, ATLANTIC (Oct. 7, 2014), https://www.theatlantic.com/health/archive/2014/10/how-icelands-genealogy-obsession-leads-to-scientific-breakthroughs/381097/.

64. *See* Gertz, *supra* note 61, at 243 (discussing how the Health Sector Database Act provided for the Icelandic Population to be used in an "easily manageable" GeneBank due to the homogeneity of the Icelandic population).

65. *See id.*

method soon raised legal and ethical concerns.[66] deCODE had obtained samples from medical records based on presumed consent—the assumption that data subjects have consented to inclusion of their information unless they have affirmatively opted out.[67] That did not sit well with Iceland's Data Protection Authority and Bioethics Committee, which objected to further collection of data on that basis.[68] Subsequently, Iceland's Supreme Court prohibited deCODE from including the genomes of people who are deceased to protect the privacy of their descendants, which posed another obstacle to data collection.[69] However, the amount of information deCODE had already collected was enough to permit a number of important studies to proceed.[70] That made the database extremely valuable, and in 2012, the company sold exclusive rights to use it to the American corporation, Amgen, Inc.[71]

Dr. Hakonarson founded the Center for Applied Genomics (CAG) at CHOP in 2006.[72] CAG has created its own biobank that contains genotypes of over 100,000 patients and their family members, as well as data from deCODE.[73] In addition to

66. *See, e.g.*, Alison Abbott, *Icelandic Database Shelved as Court Judges Privacy in Peril*, 429 NATURE, May 2004, at 118, 118.

67. Andy Coghlan, *Warn People of Genetic Health Risks, Says deCODE Boss*, NEW SCIENTIST (Mar. 25, 2015), https://www.newscientist.com/article/dn27242-warn-people-of-genetic-health-risks-says-decode-boss/. Over 20,000 people opted out of the database. Abbott, *supra* note 66, at 118.

68. Abbott, *supra* note 66, at 118.

69. Michelle Meyer, Comparative Law, *Genetic Privacy—Icelandic Supreme Court Holds that Inclusion of an Individual's Genetic Information in a National Database Infringes on the Privacy Interests of His Child*, 118 HARV. L. REV. 810, 810 (2004) (citing Guðmundsdóttir v. Iceland, No. 151/2003, at Part II (Nov. 27, 2003) (Ice.)).

70. Abbott, *supra* note 66, at 118.

71. Ben Hirschler, *Amgen Buys Icelandic Gene Hunter [deCODE] for $415 Million*, REUTERS (Dec. 10, 2012, 8:30 AM), https://www.reuters.com/article/us-amgen-decode/amgen-buys-icelandic-gene-hunter-decode-for-415-million-idUSBRE8B90IU20121210. Amgen, Inc. is a U.S. biotechnology group, and the transaction did not require regulatory approval. *Id.*

72. *CHOP Genomics Expert To Speak at Inaugural Precision Health Conference*, CHOP NEWS (Sept. 7, 2016), https://www.chop.edu/news/chop-genomics-expert-speak-inaugural-precision-health-conference; Hakonarson, *My Data, Myself*, *supra* note 41.

73. *Center for Applied Genomics Laboratory*, CHOP, https://www.research.chop.edu/center-for-applied-genomics-laboratory (last visited Jan. 9, 2021); Hakonarson, *My Data, Myself*, *supra*

searching for genetic correlates of diseases, it is using novel gene editing technologies, such as CRISPR, to develop treatments.[74] CAG's database has identified thirty million genetic variants that may be linked to disease and has helped in the treatment of more than 450,000 patients.[75] Among the conditions for which applications have been developed are neuroblastoma, inflammatory bowel disease, hereditary cystatin-c amyloid Angiopathy and generalized lymphatic anomalies.[76] Its findings have been applied in a range of clinical functions, including medication prescribing and cancer care.[77]

2. *Health system databases*

As the utility of genetic databases has grown, other hospitals and health systems around the United States have developed their own, often in partnership with private companies.[78] A goal of many of these databases is to integrate genetic information with clinical data contained in electronic health records to facilitate wider use of precision medicine.[79] Some of them also include relevant information that had been historically

note 41. Genome-Wide Association Studies have been performed on approximately 100,000 children and 150,000 parents/adults. John J. Connolly, Joseph T. Glessner, Dong Li, Patrick M.A. Sleiman & Hakon Hakonarson, *The Center for Applied Genomics at the Children's Hospital of Philadelphia—Pediatric Perspectives on Genomic Medicine*, J. PRECISION MED., Mar. 2020, at 46, 51.

74. *See* Connolly et al., *supra* note 73.

75. Hakonarson, *My Data, Myself*, *supra* note 41.

76. *Id.*

77. *Id.*

78. *See, e.g.*, Alia Paavola, *6 Genetic Databases and Their Drug Industry Partners*, BECKER'S HOSP. REV. (July 23, 2019), https://www.beckershospitalreview.com/pharmacy/6-genetic-databases-and-their-drug-industry-partners.html.

79. *See, e.g.*, David Raths, *Initiative Offers Free Whole Genome Sequencing to All UCSF Health Patients*, HEALTHCARE INNOVATION (Sept. 9, 2020), https://www.hcinnovationgroup.com/clinical-it/genomics-precision-medicine/news/21153529/initiative-offers-free-whole-genome-sequencing-to-all-ucsf-health-patients; Jessica Kent, *UPMC, UPitt Launch Genome Sequencing Center for Medical Research*, HEALTHIT ANALYTICS (July 2, 2018), https://healthitanalytics.com/news/upmc-upitt-launch-genome-sequencing-center-for-medical-research.

overlooked, such as family histories and social determinants of health.[80]

Some of these initiatives have produced important findings. Among the first health systems to launch a genetics initiative was Geisinger Health System in central Pennsylvania, which created a database to conduct research focusing on autism and other developmental disorders.[81] In 2016, Geisinger published research identifying seventeen genes related to such conditions.[82] In collaboration with Regeneron Genetics Center, it developed a database of almost 100,000 genomes that matches genetic data with de-identified electronic health records to speed drug development.[83]

In 2018, Intermountain Healthcare in Salt Lake City, Utah announced the creation of a global DNA database for research.[84] Known as the GeneRosity Registry, it solicits contributions of genetic test results from patients along with electronic health histories, with a research focus on cardiac health.[85] Intermountain Healthcare works in partnership with deCODE.[86] By including genetic analyses of patients from

80. *See* Raths, *supra* note 79; Laura Dyrda, *Genomics in Healthcare: How Systems Are Using the Data and Whether There Is a Cause for Concern*, BECKER'S HOSP. REV. (Jan. 22, 2020), https://www.beckershospitalreview.com/data-analytics/genomics-in-healthcare-how-systems-are-using-the-data-and-whether-there-is-a-cause-for-concern.html.

81. *Genomic Medicine Institute*, GEISINGER, https://www.geisinger.edu/research/departments-and-centers/gmi (last visited Jan. 9, 2021).

82. Andrea J. Gonzalez-Mantilla, Andres Moreno-De-Luca, David H. Ledbetter & Christa Lese Martin, *A Cross-Disorder Method to Identify Novel Candidate Genes for Developmental Brain Disorders*, 73 JAMA PSYCHIATRY 275, 278 (2016) ("[O]ur multilevel data-integration approach identified 7 novel high-confidence DBD candidate genes (tier 2) and provided evidence of 10 novel putative candidate genes (tiers 3 and 4), which were not previously considered to act as mendelian genes with high penetrance and large effect size in any brain disorder . . . .").

83. *The DiscovEHR Collaboration with the Regeneron Genetics Center*, GEISINGER, https://www.geisinger.org/precision-health/mycode/discovehr-project (last visited Jan. 9, 2021).

84. *Intermountain Healthcare Building New Global DNA Database for Future Genetic Discoveries*, INTERMOUNTAIN HEALTHCARE (Mar. 1, 2018), https://intermountainhealthcare.org/news/2018/02/intermountain-healthcare-building-new-global-dna-database-for-future-genetic-discoveries/.

85. *Id.*

86. *See* Emily Havens, *Largest DNA Mapping Project in U.S. History Launched by Utah's Intermountain Healthcare*, SPECTRUM (June 12, 2019, 11:42 AM), https://www.thespectrum.com/story/news/2019/06/12/utah-intermountain-healthcare-starts-u-s-largest-dna-mapping-project/1431525001/.

commercial testing companies, its creators hope to create the largest genetic mapping project in the United States with samples from 500,000 people.[87]

Other examples include the Mayo Clinic, which has entered into a partnership with Helix, a private genomic company, to compile genetic data on 100,000 patients.[88] The Mayo Clinic and Helix focus on eleven genes related to diseases including breast and ovarian cancer, familial hypercholesterolemia, and Lynch syndrome.[89] NorthShore University Health System in Evanston, Illinois has also partnered with Helix to compile data on 10,000 patients to improve care and conduct health risk assessments.[90] The University of Pittsburgh Medical Center (UPMC) and the University of Pittsburgh have launched the UPMC Genome Center to work with UPMC's Institute for Precision Medicine.[91]

Further examples of the routine use of genetic analyses in clinical care were described at the conference by Reed E. Pyeritz, MD, PhD, William Smilow Professor at the University of Pennsylvania Perelman School of Medicine.[92] Dr. Pyeritz elaborated on how these analyses are particularly helpful in assessing the level of risk posed by variants of uncertain significance (VUS),[93] which are variations in the base pairs in a gene whose clinical effects have not yet been determined. The University of Pennsylvania Health System also developed a

87. *Id.*

88. Dyrda, *supra* note 80.

89. *Id.*

90. Erin Dietsche, *Through Partnership with Color, 10K NorthShore Patients Will Get Whole Genome Sequencing*, MEDCITY NEWS (Jan. 10, 2019, 9:07 PM), https://medcitynews.com/2019/01/color-northshore/.

91. Jessica Kent, *$3.7M Grant Supports Precision Medicine, Genomics Database*, HEALTHIT ANALYTICS (Oct. 17, 2019), https://healthitanalytics.com/news/3.7m-grant-supports-precision-medicine-genomics-database.

92. *See generally* Reed E. Pyeritz, William Smilow Professor Univ. Pa. Sch. Med., *My Data, Myself*, *supra* note 30 [hereinafter Pyeritz, *My Data, Myself*].

93. *Id.*

biobank to study pathogenic variants of the FBN1 gene, which is suspected of increasing the risk of aortic harm.[94]

3. *Databases designed for specific needs*

Databases created by hospitals and health systems primarily contain information on their own patients.[95] This may limit the range of genetic diversity they represent, which can constrain their utility for research. To expand the diversity of genomes available for study, the NIH is compiling a database to include a sample of contributors from a range of backgrounds in a research initiative known as *All of Us*.[96] As described at the conference by Michelle Holko, PhD, MS, Presidential Innovation Fellow with NIH, this initiative plans to gather data from at least one million people living in the United States.[97] Upon its completion, projected in 2025,[98] *All of Us* will provide a resource for studying the ways in which individual differences in lifestyle, environment, and biological makeup influence health and disease.[99] So far, more than 271,000 participants have contributed biospecimens, answered surveys,

94. *See id.* Research on the FBN1 gene involved sequencing the genomes of 12,000 subjects for twelve variants of the gene, which was compared with information in their medical records. Of seventy subjects who had the gene, one-third were found to have aortic pathology compared with 9% of controls. *Id.*

95. *See* Dyrda, *supra* note 80.

96. *Core Values*, NAT'L INST. HEALTH: ALL OF US RSCH. PROGRAM, https://allofus.nih.gov/about/core-values (last visited Jan. 9, 2021) ("To develop individualized plans for disease prevention and treatment, researchers need more data about the differences that make each of us unique. Having a diverse group of participants can lead to important breakthroughs. These discoveries may help make health care better for everyone.").

97. Michelle Holko, Presidential Innovation Fellow with NIH, *My Data, Myself*, *supra* note 30 [hereinafter Holko, *My Data, Myself*].

98. *See Research Priorities Workshop: Summary of Plenary Sessions*, NAT'L INST. HEALTH: ALL OF US RSCH. PROGRAM, (Workshop: Mar. 21–23, 2018) [hereinafter *All of Us Research Priorities Workshop*], https://www.researchallofus.org/researcher-workshops-and-public-input/ (scroll down to "Related Links," and click "View PDF") ("The goal is to genotype all participants by 2023 and to do whole genome sequencing on all participants by 2025.").

99. Holko, *My Data, Myself*, *supra* note 97; *Protocol v1 Summary*, NAT'L INST. HEALTH: ALL OF US RSCH. PROGRAM, https://allofus.nih.gov/about/all-us-research-program-protocol (scroll down to "Downloads," and click on "Summary of the Operational Protocol") (Dec. 19, 2018).

and agreed to share their electronic health records.[100] About "80% of them are from groups that have been historically underrepresented in biomedical research."[101] The NIH sees their representation as important to advancing precision medicine.[102]

Numerous other smaller research databases also exist to facilitate specific kinds of studies.[103] They include two that focus on genetic variants, ClinVar maintained by the National Center for Biotechnology Information, and the Leiden Open Variant Database.[104] A third, BRCA Share, focuses on variants of the BRCA1 and BRCA2 genes, which are associated with increased risk for breast and ovarian cancer.[105] A similar database, the Universal Mutation Database, is maintained by the French National Institute of Health and Medical Research.[106] All of these are accessible by outside researchers.[107]

4. *Commercial databases*

An even more valuable resource may lie in the largest compilations of human genomes—the databases of private companies that offer customers genetic analysis for a fee. One of the largest of these, 23andMe, has over ten million customers.[108] As described at the conference by Sierra Luther, associate privacy counsel for 23andMe, the company requires

100. *All of Us Research Program at UW-Madison Joins the Fight Against COVID-19*, UW HEALTH (July 17, 2020), https://www.uwhealth.org/news/all-of-us-research-program-at-uw-madison-joins-the-fight-against-covid-19/53437.

101. *Leaders of NIH's All of Us Research Program Recap Progress and Next Steps*, NAT'L INST. HEALTH (Aug. 14, 2019), https://www.nih.gov/news-events/news-releases/leaders-nihs-all-us-research-program-recap-progress-next-steps.

102. *See All of Us Research Priorities Workshop*, *supra* note 98.

103. Charles M. Strom, Opinion, *Not All Genetic Databases Are Equal*, SCIENTIST (Nov. 30, 2016), https://www.the-scientist.com/critic-at-large/opinion-not-all-genetic-databases-are-equal-32439.

104. *Id.*

105. *Id.*

106. *Id.*

107. *Id.*

108. *About Us*, 23ANDMe, https://mediacenter.23andme.com/company/about-us/ (last visited Jan. 9, 2021).

consent for use of customer data in research,[109] which more than 80% of its customers have granted.[110] The focus of the company's research based on customer genomes and self-reported health outcomes has been quite broad.[111] One analysis found that 27% of men in their thirties who reported being in good health also reported experiencing depression.[112]

23andMe has historically entered into research partnerships with two pharmaceutical companies, Genentech and Pfizer, and has launched its own drug-discovery laboratory known as 23andMe Therapeutics.[113] It has also collaborated with several hospitals and research institutes on studies of specific conditions.[114] For example, 23andMe works with Boston's Brigham and Women's Hospital to study age-related hearing impairment, Vanderbilt University to study the genetics of musical rhythm, and the Psychiatric Genomics Consortium on a global, multi-ethnic genome-wide study of major depressive disorders.[115]

Other commercial database companies have also launched research initiatives. A prominent example is Ancestry.com, which compiles data in its Ancestry Human Diversity Project from customers who have consented to having their information used.[116] Data are made available to investigators in academic institutions, government agencies, for-profit businesses and nonprofit organizations.[117] Its projects focus on human ancestry and build on early ties with the Mormon

109. *Id.*; Sierra Luther, Contracts Associate, Respecting Your Privacy at 23andMe, *My Data, Myself*, *supra* note 30 [hereinafter Luther, *My Data, Myself*].

110. *23andMe Research Innovation Collaborations Program*, 23ANDME, https://research.23andme.com/research-innovation-collaborations/ (last visited Jan. 9, 2021).

111. Luther, *My Data, Myself*, *supra* note 109.

112. *Id.*

113. Daniela Hernandez, *Ancestry.com Is Quietly Transforming Itself into a Medical Research Juggernaut*, SPLINTER NEWS (Apr. 3, 2015, 11:27 AM), https://splinternews.com/ancestry-com-is-quietly-transforming-itself-into-a-medi-1793846838.

114. *23andMe Research Innovation Collaborations Program*, *supra* note 110.

115. *Id.*

116. *AncestryDNA Research and Collaboration*, *supra* note 27.

117. *Id.*

Church.[118] Examples include investigations of migration patterns and of genetic variation in human lifespans.[119] The company has also entered into a partnership with the Commonwealth of Pennsylvania to digitize family history records in the state's archives[120] and into similar partnerships with repositories in New York.[121]

II. ETHICAL CONCERNS

While the fruits of genetic research have been bountiful, and many more undoubtedly lie ahead, practical and ethical issues abound. Dr. Pyeritz described such concerns as unavoidable in the process of testing for genetic traits and in its clinical application.[122] As techniques evolve and more is learned about genetic mechanisms, new procedures will be adopted, which will in turn generate new questions. For example: can genetic companies and geneticists reanalyze patient data after its initial use and, if so, how often? Who bears the responsibility of contacting the patients when interpretations change? How should incidental findings be handled? How should relatives be informed when they may have a similar susceptibility to a disease? Who should decide what information is shared and with whom?

In pursuing answers, the clinical geneticist must remain mindful to respect the personal and civil rights of data subjects as well as those of any relatives who may be impacted by the findings.[123] In a field that promises so much growth and further discovery, it is foreseeable that ethical dilemmas may be pushed

118. *See id.*; Hernandez, *supra* note 113.

119. *See AncestryDNA Research and Collaboration*, *supra* note 27.

120. *Ancestry Pennsylvania*, PA. HIST. & MUSEUM COMM'N, https://www.phmc.pa.gov:443/Archives/Research-Online/Pages/Ancestry-PA.aspx (last visited Jan. 9, 2021).

121. *How To Use Ancestry.com New York*, N.Y. ST. ARCHIVES, http://www.archives.nysed.gov/research/how-to-video-ancestry (last visited Jan. 9, 2021).

122. *See* Pyeritz, *My Data, Myself*, *supra* note 92.

123. *See* Louis J. Elsas II, *A Clinical Approach to Legal and Ethical Problems in Human Genetics*, 39 EMORY L.J. 811, 819 (1990).

aside for the sake of scientific progress. However, they must eventually be answered.

A. *Guiding Ethical Principles*

Bioethics recognizes basic principles that drive ethical analysis, which are especially important in analyzing situations where goals conflict.[124] The goals of genetic researchers and physicians in advancing genetic technologies may not align with those of individuals whose data are being analyzed or of their family members who may be impacted. Several bioethical principles are relevant to reconciling these goals, in particular: beneficence, nonmaleficence, autonomy, and utilitarianism, as well as their consequences in terms of privacy and proportionality.[125]

1. *Beneficence*

Beneficence is the imperative to protect and prevent harm to those who are vulnerable.[126] In the clinical context, providers are bound by a fiduciary duty to "pursue the best interests of their patients."[127] In research, the principle of beneficence creates an obligation to minimize harms and risks to subjects while keeping in mind the broader goals and implications of the research.[128]

The application of beneficence to genetic care can lead to conflicting conclusions. For example, a physician may be

124. *See* Peter Schröder-Bäck, Peter Duncan, William Sherlaw, Caroline Brall & Katarzyna Czabanowska, *Teaching Seven Principles for Public Health Ethics: Towards a Curriculum for a Short Course on Ethics in Public Health Programmes*, 15 BMC MED. ETHICS, no. 73, Oct. 7, 2014, at 1, 2, https://bmcmedethics.biomedcentral.com/articles/10.1186/1472-6939-15-73.

125. *See generally id.* (applying "seven mid-level principles . . . non-maleficence, beneficence, health maximisation, efficiency, respect for autonomy, justice, proportionality . . . . " to cases).

126. *See id.* at 3.

127. Yvonne Bombard, Kyle B. Brothers, Sara Fitzgerald-Butt, Nanibaa' A. Garrison, Leila Jamal, Cynthia A. James, Gail P. Jarvik, Jennifer B. McCormick, Tanya N. Nelson, Kelly E. Ormond, Heidi L. Rehm, Julie Richer, Emmanuelle Souzeau, Jason L. Vassy, Jennifer K. Wagner & Howard P. Levy, *The Responsibility To Recontact Research Participants After Reinterpretation of Genetic and Genomic Research Results*, 104 AM. J. HUM. GENETICS 578, 582 (2019).

128. *Id.*

presented with the dilemma of whether to breach the duty of confidentiality to a patient in order to alert genetic relatives of their possible susceptibility to a hereditary disorder.[129] The American Medical Association (AMA) Code of Medical Ethics states that physicians have an obligation to safeguard the confidentiality of patient genetic information.[130] It directs that information shall not be revealed without patients' consent or over their objections.[131] Beneficence, however, would also impose an obligation to make such a notification to relatives when doing so could prevent harm to them or potentially save their lives.[132] Should beneficence prevail with regard to genetic relatives, or should it apply only to minimizing harms and risks for the patient whose genetic data are being analyzed?

2. *Nonmaleficence*

The principle of nonmaleficence calls for avoiding actions that may cause harm.[133] For health care professionals, it applies even if a patient requests an action that will prove to be harmful.[134] With regard to disclosure of genetic information, this can present the clinician with a difficult choice. Does a clinician who discloses sensitive information about an individual's potential susceptibility to a disease "do harm"? Is it better for the individual to be informed of risks even if that knowledge may lead to a negative psychological impact? When genetic analysis produces uncertain results or presents incidental findings unrelated to its original purpose, how should the clinician balance the risk of harm in informing the

129. *See* Samuel D. Hodge, Jr., *Does a Physician Have a Duty To Inform At-Risk Relatives of a Positive Genetic Test When the Patient Refuses To Allow That Disclosure?*, 16 J. HEALTH & BIOMED. L. 127, 134–52 (2020).

130. AMA Council on Ethical & Jud. Affairs, *AMA* Code of Medical Ethics' *Opinions on Genetic Testing*, 11 AM. MED. ASSOC. J. ETHICS 683, 683 (2009).

131. *See* Hodge, Jr., *supra* note 129, at 137.

132. *See* Warren T. Jahn, *The 4 Basic Ethical Principles That Apply to Forensic Activities Are Respect for Autonomy, Beneficence, Nonmaleficence, and Justice*, 10 J. CHIROPRACTIC MED. 225, 225 (2011).

133. Schröder-Bäck et al., *supra* note 124, at 3.

134. *See id.*

patient against the risk of harm in keeping them ignorant of the possibility of susceptibility to a genetic disease?

3. *Autonomy and privacy*

The concept of autonomy and its application to privacy of the individual dictates that patients should be allowed to make decisions regarding their own care free of coercion.[135] This principle holds it as paramount that the individual patient retains the ability to act on his or her own accord, and this is achievable only when the individual remains "free from both controlling interferences by others and personal limitations, such as inadequate understanding, that prevent meaningful choice."[136] The principle of autonomy raises difficult questions when pathology is discovered in someone who has not asked to be screened for it or when a discovery may have a downstream impact on another.[137] Autonomy calls for respecting privacy, which may be violated if a clinician discloses the results of a patient's medical test to others whom those results may affect. With regard to genetics, other interested people primarily include genetic relatives.

Patient education and genetic counseling are fundamental to upholding this bioethical principle. Joann Bodurtha, MD, MPH, professor in the departments of genetic medicine, pediatrics, and oncology at the Johns Hopkins University School of Medicine, described at the conference how it is important for providers to recognize that patients and their family members vary in their levels of literacy and understanding, which is particularly the case with their tolerance of uncertainty or

135. *Id.* at 7.

136. Elsas II, *supra* note 123, at 815 (quoting TOM L. BEAUCHAMP & JAMES F. CHILDRESS, PRINCIPLES OF BIOMED. ETHICS 68 (3d ed. 1989)).

137. J. Illes, A. C. Rosen, L. Huang, R. A. Goldstein, T. A. Raffin, G. Swan & S. W. Atlas, *Ethical Consideration of Incidental Findings on Adult Brain MRI in Research*, 62 NEUROLOGY 888, 888–890 (2004).

ambiguity, and understanding of privacy.[138] The AMA Code of Medical Ethics mandates that pre- and post-test counseling include a conversation about the repercussions of genetic findings for the patients' biological relatives.[139] Further, at the time of pre-test counseling, the AMA recommends that physicians discuss potential situations where the patient may be expected to tell their relatives of the availability of information pertaining to the risks of a disease in the family.[140] However, the breadth and complexity of information and the abundance of potential consequences resulting from genetic interpretation can make this information difficult for the lay person to comprehend.[141] Findings that result from genetic analyses involve an individual's uniquely personal and intimate features. In a society that emphasizes protecting confidentiality of such information, should the choice of whether or not to disclose it ultimately lie with individuals in recognition of their autonomy, even if this decision may have a harmful impact on others?

4. *Proportionality and utilitarianism*

Proportionality dictates that individual freedom and larger social goals be balanced and weighed proportionately.[142] This balance is related to the ethical principle of utilitarianism, which calls for acting in a way that will do the "greatest good for the greatest number of people."[143] In applying this principle in clinical settings, scholars have explained that it "is essential to show that the probable public health benefits outweigh the

138. Joann Bodurtha, MD, MPH, Professor in the Dep'ts of Genetic Med., Pediatrics & Oncology, Johns Hopkins Univ. Sch. of Med., *My Data, Myself*, *supra* note 30 [hereinafter Bodurtha, *My Data, Myself*].

139. AMA Council on Ethical & Jud. Affairs, *supra* note 130, at 683.

140. *Id.*

141. *See* Angela D. Lanie, Toby Epstein Jayaratne, Jane P. Sheldon, Sharon L. R. Kardia, Elizabeth S. Anderson, Merle Feldbaum & Elizabeth M. Petty, *Exploring the Public Understanding of Basic Genetic Concepts*, 13 J. GENETIC COUNSELING 305, 315–16 (2004).

142. Schröder-Bäck et al., *supra* note 124.

143. *See* DEAN M. HARRIS, ETHICS IN HEALTH SERVICES AND POLICY: A GLOBAL APPROACH 5 (2011).

infringed general moral considerations . . . . All of the positive features and benefits must be balanced against the negative features and effects . . . ."[144] When genetics are applied in medical care, clinical geneticists must assume this difficult balancing act. It is important that clinicians consider the individual's concerns even when genetic analysis may present potential utility for the general public.

B. *Clinical Dilemmas*

1. *Uncertain findings*

Genetic analysis can lead to five different kinds of conclusions for an individual patient: that a finding is pathogenic, benign, likely pathogenic, likely benign, or a VUS.[145] While the first four categories rely on statistical support, a VUS leaves the researcher or clinician with little to go on because there is not enough information to make a reliable determination of risk.[146]

The evidence that can be used to interpret genetic findings is continuously evolving, and the understanding of a VUS's clinical significance may change with it.[147] To apply new information to a finding, a clinician must reinterpret the original genetic data.[148] This raises a number of issues, both financial and ethical. At the conference, Dr. Pyeritz warned that an obligation to reinterpret data may impose a heavy cost on laboratories that could be financially ruinous for some of them.[149] Beyond financial concerns, it must also be determined who should be responsible for initiating a reinterpretation.[150]

144. James F. Childress, Ruth R. Faden, Ruth D. Gaare, Lawrence O. Gostin, Jeffrey Kahn, Richard J. Bonnie, Nancy E. Kass, Anna C. Mastroianni, Jonathan D. Moreno & Phillip Nieburg, *Public Health Ethics: Mapping the Terrain*, 30 J. L. MED. & ETHICS 170, 173 (2002).

145. *See* Pyeritz, *My Data, Myself*, *supra* note 92.

146. *Id.* There are various factors that account for uncertainty, such as genes that have yet to be identified or different predictions about pathogenicity from different programs. *Id.*

147. Bombard et al., *supra* note 127, at 578.

148. *See id.*

149. *See* Pyeritz, *My Data, Myself*, *supra* note 92.

150. *Id.*

Should the patient have to request it, or should laboratories be responsible for developing protocols to reinterpret data proactively when new scientific evidence emerges? If there is a reinterpretation, should only the finding that was initially categorized as a VUS be reinterpreted? If reanalysis produces a conclusion that is different from the original one, should the patient always be made aware of it? Dr. Pyeritz argued that because of questions like these, health care professionals and geneticists have an obligation to take the initiative through genetic counseling to inform patients that changes in diagnoses are a realistic possibility.[151]

2. *Duty to recontact*

Recontacting patients highlights the tension between the duty to keep them as informed as possible and the costs and practical challenges of doing so.[152] There are varying benefits and harms in recontacting patients, and the considerations involved are medical and scientific , as well as personal and psychological.[153] A range of players, including clinicians, researchers, physicians, patients, and research participants all have roles to play in this process.[154]

Nearly two decades ago, the American College of Medical Genetics (now the American College of Medical Genetics and Genomics) issued a policy statement highlighting the increasingly complicated nature of patient recontacting.[155] The

151. *Id. See also, e.g.*, Julia El Mecky, Lennart Johansson, Mirjam Plantinga, Angela Fenwick, Anneke Lucassen, Trijnie Dijkhuizen, Annemieke van der Hout, Kate Lyle & Irene van Langen, *Reinterpretation, Reclassification, and Its Downstream Effects: Challenges for Clinical Laboratory Geneticists*, 12 BMC MED. GENOMICS, no. 170, Nov. 29, 2019, at 1, 5, https://bmcmedgenomics.biomedcentral.com/articles/10.1186/s12920-019-0612-6.

152. *See* Pyeritz, *My Data, Myself*, *supra* note 92.

153. *Id.*

154. Karen L. David, Robert G. Best, Leslie Manace Brenman, Lynn Bush, Joshua L. Deignan, David Flannery, Jodi D. Hoffman, Ingrid Holm, David T. Miller, James O'Leary & Reed E. Pyeritz, *Patient Re-Contact After Revision of Genomic Test Results: Points to Consider—A Statement of the American College of Medical Genetics and Genomics (ACMG)*, 21 GENETICS MED. 769, 770 (2019), https://www.nature.com/articles/s41436-018-0391-z.pdf.

155. *Id.* at 769–70.

evolution of genetic testing has permitted ever larger amounts of data to be collected on each patient sample, with a corresponding increase in the complexity of the results. Whenever a new relationship is discovered between a disease and a genetic variant, the need to revisit initial results must be considered.[156] An ethical obligation based on the principle of beneficence requires at least attempting to recontact the patient in circumstances that may meaningfully alter medical care.[157] However, the principle of nonmaleficence dictates that care should be used in deciding whether to recontact the patient to avoid the risk of psychological harm, especially when he or she has indicated a preference not to be recontacted.[158]

Recontacting patients has become less of a logistical burden with the growth of electronic communication, electronic health records, and the ability of patients to access results from testing laboratories through online portals.[159] While there is currently no legal requirement to recontact in order to deliver updated results, it is possible that this will change as the logistical burden is reduced and the potential resulting injury or missed opportunity for clinical benefit from failure to recontact is better understood.[160] Recontacting was described by Dr. Pyeritz as an intrinsically shared responsibility among all involved, including the patient, who bears responsibility for providing up-to-date contact information so that any updated results can be effectively delivered.[161]

3. *Incidental and secondary findings*

Because genomic sequencing is such an extensive process involving thousands of pieces of data, the potential for

156. *Id.* at 769.

157. *Id.* at 770.

158. *See* Colin Mitchell, Corrette Ploem, Valesca Retèl, Sjef Gevers & Raoul Hennekam, *Experts Reflecting on the Duty To Recontact Patients and Research Participants; Why Professionals Should Take the Lead in Developing Guidelines*, 63 EUR. J. MED. GENETICS 1, 5 (2020).

159. David et al., *supra* note 154, at 770.

160. *Id.*

161. Pyeritz, *My Data, Myself*, *supra* note 92.

discovering a variant that is not directly related to the original purpose of the analysis is ever-present.[162] These discoveries are known as secondary or incidental findings and may indicate that a genetic variant predisposes carriers to a disease.[163] Because such findings go beyond the original aims of an analysis, they are difficult to plan for or anticipate.[164] A physician or researcher must balance the benefits of disclosing such findings against the anxiety that disclosure may cause.[165]

As Dr. Bodurtha explained, there is a range in terms of people who want predictive information and those who do not want it, but generally what people are looking for is some "optimism and reassurance that things aren't going to get worse, and if there are ways to prevent or head off bad things from happening," though this is not always possible based on genotype information alone.[166] She warned that insufficient guidelines for obtaining consent, integrating direct-to-consumer and patient-driven research testing, and communicating findings can strain the doctor-patient relationship.[167] "How do we [clinicians] deal with what [is] the relatively established land of developing trust as a health provider [when] the terms of service that are out there are twenty-three pages long?" she wondered.[168]

Should concern with incidental findings be limited to those that are likely to be of clinical significance? Adhering to the bioethical principle of nonmaleficence, Dr. Pyeritz suggested that only those of direct clinical importance, for which ignorance could have adverse consequences, should be disclosed.[169] However, the number of variants found to have

162. David et al., *supra* note 154, at 769.

163. Meredith C. Meacham, Helene Starks, Wylie Burke & Kelly Edwards, *Researcher Perspectives on Disclosure of Incidental Findings in Genetic Research*, 5 J. EMPIRICAL RSCH. ON HUM. RSCH. ETHICS 31, 31 (2010).

164. *Id.*

165. *Id.*; Pyeritz, *My Data, Myself*, *supra* note 92.

166. Bodurtha, *My Data, Myself*, *supra* note 138.

167. *Id.*

168. *Id.*

169. *See Pyeritz, My Data, Myself*, *supra* note 92.

clinical implications is growing rapidly; so even with such a limitation, the duty to disclose may become unmanageable.[170] Dr. Pyeritz emphasized that it is important for clinicians and genetic researchers to try to anticipate potential incidental findings and have a plan for dealing with them.[171] For example, clinicians and researchers should generate more thorough informed consent documents that would make all potential implications clearer and describe the actions that would be taken in response to any incidental findings.[172]

However, Dr. Pyeritz believes that an approach grounded solely in what a clinician would find useful would not be appropriate.[173] Physicians and researchers must keep in mind that the clinical utility or personal meaning of medical or genetic information may be assessed differently by the patient or research subject than by clinicians or the research team.[174] Since all conceivable interests of the data subject cannot be considered when deciding which information to disclose, information that directly concerns health and well-being should be prioritized.[175] This determination may be subjective, and it should be guided by input from the patient or research subject at the time of consent.[176]

4. *Informing relatives*

Clinicians and researchers may also face the dilemma of whether to contact relatives concerning incidental findings.[177] Traditionally, there has been no obligation to warn family members of a genetic trait, unless a patient expressly consents, because relatives are third parties to the physician-patient

170. *Id.*; David et al., *supra* note 154, at 769.
171. *See* Pyeritz, *My Data, Myself*, *supra* note 92; *accord* Meacham et al., *supra* note 163, at 38.
172. *See* Pyeritz, *My Data, Myself*, *supra* note 92; *accord* Meacham et al., *supra* note 163, at 38.
173. *See* Pyeritz, *My Data, Myself*, *supra* note 92.
174. *Id.*; Meacham et al., *supra* note 163, at 38.
175. *See* Pyeritz, *My Data, Myself*, *supra* note 92; Meacham et al., *supra* note 163, at 38.
176. Meacham et al., *supra* note 163, at 34.
177. Hodge, Jr., *supra* note 129, at 135.

relationship.[178] There is generally no duty at all for researchers.[179] The lack of an obligation is premised on respect for patient autonomy in controlling their own medical information.[180] However, failure to disclose findings to relatives may directly conflict with the principle of utilitarianism and its manifestation in proportionality, if the results are likely to have an impact on the health and well-being of a substantial number of people. As possibilities for incidental findings expand, the dilemma will become more challenging.

C. *Turning Ethical Considerations into Legal Policy*

Several federal statutes regulate aspects of these conflicts. They reflect judgments on whom to protect, which harms to protect them from, and how stringent the protections should be.[181] However, all of these laws were enacted at least a decade ago, before current genetic technologies had advanced to their present state and before some genetic discoveries had even been anticipated.[182] In the face of recent scientific and clinical advances, these laws have begun to show their age. They leave a growing number of risks unaddressed, providing clinicians and researchers with limited or ambiguous legal guidance in managing them.

178. *Id.* (explaining how doctors have no obligation to warn relatives because the doctor's relationship is directly with the patient).

179. Emmanuelle Souzeau, Kathryn P. Burdon, David A. Mackey, Alex W. Hewitt, Ravi Savarirayan, Margaret Otlowski & Jamie E. Craig, *Ethical Considerations for the Return of Incidental Findings in Ophthalmic Genomic Research*, 5 TRANSLATIONAL VISION SCI. & TECH. 1, 6 (2016) (demonstrating that researchers are generally in favor of returning clinically actionable results of incidental findings, though they believe it will pose an undue burden on researchers).

180. *Id.*

181. *See infra* Part III.

182. *See* Carolyn Riley Chapman, Kripa Sanjay Mehta, Brendan Parent & Arthur L. Caplan, *Genetic Discrimination: Emerging Ethical Challenges in the Context of Advancing Technology*, J.L. BIOSCI. 1, 10 (2019).

III. CURRENT SOURCES OF LAW AND THEIR LIMITATIONS

Four federal laws and regulations provide the basic legal framework for oversight of genetic research and clinical care in the United States: the Federal Policy for the Protection of Human Subjects (known as the Common Rule),[183] the Americans with Disabilities Act (ADA),[184] the Health Insurance Portability and Accountability Act (HIPAA)[185] and the Standards for Privacy of Individually Identifiable Health Information (Privacy Rule)[186] issued pursuant to it, and the Genetic Information Nondiscrimination Act (GINA).[187] In addition, the European Union's General Data Protection Regulation (GDPR) imposes obligations on companies that store or process European Union citizens' personal data.[188] Similarly, a statute in California offers its residents rights similar to those in the GDPR, although with weaker enforcement provisions.[189] According to two conference speakers, Holly Fernandez Lynch[190] and Mark A. Rothstein,[191] the protections afforded by these pieces of legislation are

183. 82 Fed. Reg. 7149 (Jan. 19, 2017).

184. 42 U.S.C. §§ 12101–12213.

185. Pub. L. No. 104–191, 110 Stat. 1936 (1996).

186. 45 C.F.R. pts. 160, 164 (2021).

187. Pub. L. No. 110–233, 122 Stat. 881 (2008).

188. Commission Regulation 2016/679, 2016 O.J. (L 119) 1 (EU) [hereinafter GDPR]. The GDPR applies regardless of the location of a company's headquarters.

189. *See* California Consumer Privacy Act, CAL. CIV. CODE §§ 1798.100–99 (Deering 2020); DATAGUIDANCE & FUTURE PRIV. F., COMPARING PRIVACY LAWS: GDPR V. CCPA 5 (2019), https://fpf.org/wp-content/uploads/2018/11/GDPR_CCPA_Comparison-Guide.pdf.

190. Holly Fernandez Lynch is the John Russell Dickson, MD Presidential Assistant Professor of Medical Ethics and Health Policy at the University of Pennsylvania Perelman School of Medicine. *Holly Fernandez Lynch, JD, MBe,* PENN MED. ETHICS & HEALTH POL'Y, https://medicalethicshealthpolicy.med.upenn.edu/faculty-all/holly-fernandez-lynch (last visited Jan. 10, 2021).

191. Mark A. Rothstein is the Herbert F. Boehl Chair of Law and Medicine and founding director of the Institute for Bioethics, Health Policy, and Law at the University of Louisville. *Mark A. Rothstein,* UNIV. LOUISVILLE, https://louisville.edu/bioethics/directory/mark-a.-rothstein (last visited Jan. 10, 2021).

inadequate or even illusory.[192] A proposal for a new regulatory mechanism to fill some oversight gaps by creating review boards for data sharing by commercial genetic testing companies was described by Robert I. Field, one of the authors of this Article, at the conference.[193] Beyond legislative and regulatory remedies, plaintiffs may be able to sue for negligence in the collection and storage of their genetic information, and they may have rights under the terms of service of commercial genetic testing companies, although these tend to be limited.[194]

A. *The Common Rule and Institutional Review Boards*

Genetic database research presents a particular risk to privacy, as it involves intimate details of subjects, pertains to traits that are immutable, and may permit identification of relatives who have not consented to storage or use of their data.[195] In addition to the potential harm to individuals, failure to maintain a proper level of privacy could engender public distrust, which could suppress participation in research.[196]

The Common Rule was originally enacted in 1991 and has been adopted by the Department of Health and Human Services (DHHS) and nineteen other federal departments and agencies.[197] The rule acts as a baseline set of guidelines for researchers insofar as biomedical and behavioral research

192. Mark A. Rothstein, Herbert F. Boehl Chair L. & Med., Dir., Inst. for Bioethics, Health Pol'y & L., Univ. Louisville Sch. Med., Keynote Address: Law, Privacy, & Genetic Information, *My Data, Myself*, *supra* note 30 [hereinafter Rothstein, *My Data, Myself*]; Holly Fernandez Lynch, John Russell Dickson, MD Presidential Assistant Professor Med. Ethics, Perelman Sch. of Med, Univ. Pa., Genetic Databases & Priv.: Where Should the Law Go Next?, *My Data, Myself*, *supra* note 30 [hereinafter Lynch, *My Data, Myself*].

193. Robert I. Field, Professor L. & Professor Health Mgmt. & Pol'y, Dir., Joint JD/MPH Program, Drexel Univ., Genetic Databases & Priv.: Where Should the Law Go Next?, *My Data, Myself*, *supra* note 30 [hereinafter Field, *My Data, Myself*].

194. *See infra* Section III.F.

195. *Id.*

196. *Id.*

197. Protection of Human Subjects, 45 C.F.R. pt. 46 (2021); *Federal Policy for the Protection of Human Subjects ('Common Rule')*, U.S. DEP'T HEALTH & HUM. SERVS., https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html (Mar. 18, 2016).

involves human subjects.[198] Under the rule, Internal Review Boards (IRBs) provide the first line of defense against privacy threats to subjects of research.[199] An IRB is a "board, committee, or other group formally designated by an institution to review research involving humans as subjects."[200] It reviews protocols for studies that are conducted or funded by the federal government. A similar set of rules applies to studies that are used to support applications to the Food and Drug Administration (FDA) to market new drugs.[201] After conducting a review, an IRB can approve a protocol, reject it, or require modifications.[202]

In conducting their reviews, IRBs are directed to ensure that studies include "adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data."[203] One way they do this is by accessing data sharing plans.[204] Under revisions to the Common Rule implemented in 2018, these plans must require that the research subjects consent to the collection of their data and that they must be told whether their information might be used for future research without additional consent.[205] Subjects must also be informed whether

198. *Federal Policy for the Protection of Human Subjects ('Common Rule')*, *supra* note 197.

199. U.S. DEP'T HEALTH & HUM. SERVS., NAT'L INST. HEALTH, INSTITUTIONAL REVIEW BOARDS AND THE HIPAA PRIVACY RULE (2003) [hereinafter IRBS AND THE PRIVACY RULE], https://privacyruleandresearch.nih.gov/pdf/IRB_Factsheet.pdf.

200. *Id.*

201. *Institutional Review Boards Frequently Asked Questions: Guidance for Institutional Review Boards & Clinical Investigators*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/regulatory-information/search-fda-guidance-documents/institutional-review-boards-frequently-asked-questions (Apr. 18, 2019).

202. IRBS AND THE PRIVACY RULE, *supra* note 199.

203. 45 C.F.R. § 46.111(a)(7) (2021).

204. *See* Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7151 (Jan. 19, 2017).

205. Lynch, *My Data, Myself*, *supra* note 192. This is referred to as "broad consent," which the revised Rule provides is "an optional alternative that an investigator may choose instead of, for example, conducting the research on nonidentified information and nonidentified biospecimens, having an institutional review board (IRB) waive the requirement for informed consent, or obtaining consent for a specific study." Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7150 (Jan. 19, 2017). Broad consent is meant to strike a "balance between participant rights to determine the future use of their research data and the scientific

the research will include sequencing of their genome and whether specimens may be used in profit-making ventures with or without identifiers.[206]

As described by Professor Fernandez Lynch, the revised Common Rule continues to limit required IRB oversight in many respects.[207] The Common Rule does not apply to research with human subjects conducted without federal funding, although many research institutions and academic journals nonetheless require IRB review and approval.[208] It also does not offer standardized privacy safeguards for identifiable information and identifiable biospecimens, although other federal provisions address related privacy issues.[209] The Common Rule applies only to research, so that non-research uses of data, such as for health care quality improvement and clinical care, are not required to undergo IRB review.[210] In addition, the Common Rule currently excludes secondary research with deidentified data and specimens from the definition of human subjects research and exempts several types of research from its requirements. Given the Common Rule's scope, it does not apply to privately funded studies conducted by commercial database companies such as 23andMe, although, as noted, IRB review can be pursued voluntarily by these companies.[211]

benefits that may accrue when such use involves unspecified investigators and research aims." Celia B. Fisher & Deborah M. Layman, *Genomics, Big Data, and Broad Consent: A New Ethics Frontier for Prevention Science*, 19 PREVENTION SCI. 871, 874 (2018).

206. Federal Policy for the Protection of Human Subjects, 82 Fed. Reg. 7149, 7266 (Jan. 19, 2017).

207. Lynch, *My Data, Myself*, *supra* note 192; *accord* GARY L. CHADWICK, CITI PROG., FINAL RULE MATERIAL: OVERVIEW OF THE FINAL RULE REVISIONS 2 (2017), https://about.citiprogram.org/wp-content/uploads/2019/08/Final-Rule-Material-Overview-of-the-Final-Rule-Revisions.pdf.

208. Lynch, *My Data, Myself*, *supra* note 192.

209. *Id.*

210. *Id.*

211. *Id.* Sierra Luther noted that 23andMe does, of its own accord, constitute IRBs to review research that it conducts. Luther, *My Data, Myself*, *supra* note 109; *accord* Research Participation, 23ANDME, https://www.23andme.com/research/?mkbanner=true (scroll to "How It Works" and click "Learn More") (last visited Jan. 10, 2021).

Another limitation of IRBs is in the composition of their membership.[212] Expertise can vary widely; consequently, the ability of members to understand privacy risks for different types of data, for different uses of data, and for information on different populations can vary considerably.[213] IRBs can also be slow to act, which often presents an impediment to the timely implementation of studies.[214] To supplement IRB review, the Council for International Organizations of Medical Sciences (CIOMS) has advised research organizations to create separate governance systems to review data collection and storage practices,[215] in the form of Data Access Committees (DACs).[216] These bodies focus specifically on data privacy; however, they face many of the same issues as IRBs, especially with regard to inconsistency in expertise and administration.[217] Use of DACs is entirely voluntary and best practices for their operation have not been established.[218]

In the view of Professor Fernandez Lynch, IRBs are not currently situated to effectively manage the many uses for research and other purposes.[219] More aggressive expert oversight of data sharing and privacy protections is needed.[220] Moreover, such oversight must be more uniform than it

212. Lynch, *My Data, Myself*, *supra* note 192.

213. CHADWICK, *supra* note 207, at 2.

214. Field, *My Data, Myself*, *supra* note 193.

215. *See* CIOMS, INTERNATIONAL ETHICAL GUIDELINES FOR HEALTH-RELATED RESEARCH INVOLVING HUMANS 87 (2016), https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf. CIOMS's Guideline 23 provides that "[r]esearch ethics committees must provide independent ethical opinions." *Id.* at 89.

216. Lynch, *My Data, Myself*, *supra* note 192; *see also* Phaik Yeong Cheah & Jan Piasecki, *Data Access Committees*, 21 BMC MED. ETHICS, no. 12, Feb. 2020, at 1, 2, https://bmcmedethics.biomedcentral.com/articles/10.1186/s12910-020-0453-z ("[O]ne way to promote potential benefits of data sharing and ameliorate its potential harms would be through the adoption of a managed access approach where requests are channeled through a Data Access Committee . . . .").

217. Lynch, *My Data, Myself*, *supra* note 192.

218. Cheah & Piasecki, *supra* note 216, at 2 ("Many group, consortia, institutional and independent DACs have been set up but there is currently no widely accepted framework under which DACs operate.").

219. Lynch, My Data, Myself, *supra* note 192.

220. *See id.*

currently is to effectively protect the sensitive genetic information of millions of people.[221]

Professor Field's proposal would add a layer of review to data sharing arrangements involving commercial testing companies, which are exempt from mandatory IRB review.[222] The review would be conducted by bodies known as Data Protection Review Boards.[223] Incorporating features of IRBs and DACs, these boards would include experts in science, business, ethics, and law, and would consider arrangements through which a company shares its data with business partners for any purpose, including research, drug development, and marketing.[224] The boards would be empowered to require additional privacy safeguards beyond those already in place or to block arrangements altogether. Professor Field explained the proposal as a first step in taming this growing and thus far unregulated segment of the genetic research enterprise.[225]

B. *Americans with Disabilities Act*

The ADA was enacted in 1990 "to provide a clear and comprehensive national mandate for the elimination of discrimination against individuals with disabilities . . . ."[226] Title I of the Act prohibits discrimination against those with disabilities by private employers with fifteen or more employees, state and local government employers, employment agencies, and labor unions.[227] Titles II and III prohibit discrimination in public services broadly, which are referred to as "public accommodations."[228] The ADA defines a

221. *See id*.

222. Field, *My Data, Myself*, *supra* note 193; Robert I. Field, Anthony W. Orlando & Arnold J. Rosoff, *Am I My Cousin's Keeper? A Proposal to Protect Relatives of Commercial Databases Subjects*, 18 IND. HEALTH L. REV. (2021).

223. Field, *My Data, Myself*, *supra* note 193.

224. *Id.*; Field, Orlando & Rosoff, *supra* note 222.

225. Field, *My Data, Myself*, *supra* note 193; Field, Orlando & Rosoff, *supra* note 222.

226. Americans with Disabilities Act of 1990, 42 U.S.C. § 12101(b)(1).

227. § 12111–12117.

228. § 12131–12189.

disability as "a physical or mental impairment that substantially limits one or more major life activities," "a record of such an impairment," or "being regarded as having such an impairment."[229]

Unlike GINA, the ADA was not enacted with the specific intent to prohibit genetic discrimination.[230] It does not even mention genetic information.[231] Nevertheless, in 1995 the Equal Employment Opportunity Commission (EEOC), which enforces the ADA, issued a non-binding guidance that interpreted the act as prohibiting "discrimination based on genetic information relating to illness, disease, or other disorders."[232] Amendments that passed in 2008, the ADA Amendments Act of 2008,[233] did not change this interpretation.[234] While the ADA would, therefore, offer protection concerning the use of genetic information once disabling symptoms of a genetic condition appear, the Seventh, Eighth, and Eleventh Circuit Courts of Appeals have ruled that it does not apply to those whose genetic information merely indicates a potential future impairment.[235] As a result, the

229. § 12102(1).

230. The ADA was enacted as a "comprehensive law prohibiting disability-based discrimination in employment, public services, public accommodations, and telecommunications." MARK A. ROTHSTEIN ET AL., EMPLOYMENT LAW CASES AND MATERIALS 397 (8th ed. 2015).

231. *See* § 12101–12213 (wherein there is no mention of one's genetic information).

232. *Genetic Discrimination*, NIH: NAT'L HUM. GENOME RSCH. INST., https://www.genome.gov/about-genomics/policy-issues/Genetic-Discrimination (last visited Jan. 10, 2021). EEOC guidance documents are non-binding on courts. *What You Should Know: EEOC Regulations, Subregulatory Guidance and Other Resource Documents*, U.S. EQUAL EMP. OPPORTUNITY COMM'N (May 5, 2016), https://www.eeoc.gov/laws/guidance/what-you-should-know-eeoc-regulations-subregulatory-guidance-and-other-resource.

233. ADA Amendments Act of 2008, Pub. L. No. 110–325, 122 Stat. 3553.

234. Mark A. Rothstein, *GINA, the ADA, and Genetic Discrimination in Employment*, 36 J. L. MED. & ETHICS 837, 837–38 (2008). Rothstein also notes that perhaps because GINA was passed that same year, the drafters of the ADA Amendments Act did not think it was necessary to incorporate discrimination on the basis of genetic information. *Id.* at 838.

235. Shell v. Burlington N. Santa Fe Ry., 941 F.3d 331, 336 (7th Cir. 2019) ("The ADA's . . . text plainly encompasses only current impairments, not future ones."); Morriss v. BNSF Ry. Co., 817 F.3d 1104, 1113 (8th Cir. 2016) ("[T]he ADA does not prohibit an employer from acting on . . . its assessment that although no physical impairment currently exists, there is an

ADA's protections only extend to those with currently manifested disabilities.[236] Nevertheless, the law fills an important gap left by GINA,[237] which does not apply once a genetic condition has manifested itself.[238]

C. *Health Insurance Portability and Accountability Act and the Standards for Privacy of Individually Identifiable Health Information*

Together, HIPAA and the Privacy Rule issued under it restrict the disclosure of patient medical data without consent.[239] HIPAA was enacted in 1996, though patient privacy was not its primary purpose.[240] Indeed, the main goal of HIPAA was to reduce the problem of "job lock," through which employees were unable to change jobs because subsequent employers may have denied coverage for their (or their family members') preexisting medical conditions.[241] As the bill moved

unacceptable risk of a future physical impairment."); EEOC v. STME, LLC, 938 F.3d 1305, 1311 (11th Cir. 2019) ("[T]he ADA protect[s] persons who experience discrimination because of a current, past, or perceived disability—not because of a potential future disability that a healthy person may experience later.").

236. *See* Harris Mufson, Laura Fant & Jacob L. Hirsch, *Emerging Trend: ADA Does Not Cover Potential Future Disabilities*, PROSKAUER: L. & WORKPLACE (Nov. 13, 2019), https://www.lawandtheworkplace.com/2019/11/emerging-trend-ada-does-not-cover-potential-future-disabilities/.

237. *See, e.g.*, Ellen Wright Clayton, Opinion, *Why the Americans With Disabilities Act Matters for Genetics*, 313 JAMA 2225, 2225–26 (2015). See *infra* Section III.D for a discussion of GINA and its limitations.

238. Rothstein, *My Data, Myself*, *supra* note 192.

239. Health Insurance Portability and Accountability Act of 1996 (HIPAA), Pub. L. No. 104–191, 110 Stat. 1936; Standards for Privacy of Individually Identifiable Health Information (Privacy Rule) 45 C.F.R. pts. 160, 164 (2021).

240. *See* U.S. DEP'T HEALTH & HUM. SERVS., OFFICE C. R., SUMMARY OF THE HIPAA PRIVACY RULE 1–2 (2003) [hereinafter SUMMARY OF THE HIPAA PRIVACY RULE] ("HIPAA required the Secretary to issue privacy regulations governing individually identifiable health information, if Congress did not enact privacy legislation within three years of the passage of HIPAA. Because Congress did not enact privacy legislation, HHS developed a proposed rule and released it for public comment on November 3, 1999. The Department received over 52,000 public comments. The final regulation, the Privacy Rule, was published December 28, 2000."), https://www.hhs.gov/sites/default/files/privacysummary.pdf.

241. Rothstein, *My Data, Myself*, *supra* note 192; Rebecca Lewin, *Job Lock: Will HIPAA Solve the Job Mobility Problem?*, 2 U. PA. J. LAB. & EMP. L. 507, 508 (2000); Ellen Wright Clayton, Barbara J. Evans, James W. Hazel & Mark A. Rothstein, *The Law of Genetic Privacy: Applications,*

through Congress, insurance companies lobbied for the inclusion of a provision to create a standard format for the electronic submission of health care providers' claims.[242] Claims data include confidential patient medical information, which raised concerns about leaks, so this provision was coupled with one that authorized DHHS to develop regulations to safeguard data from unauthorized disclosure.[243] Those regulations were issued in 2003 as the Privacy Rule.[244]

The Privacy Rule is limited in scope, which is due, in part, to this history. It only applies to three kinds of individuals and organizations that hold patient data, which are known as "covered entities," which are health care providers, payers that cover a patient's care, and health data clearinghouses that centrally maintain claims information on a national basis.[245] These entities must also ensure that organizations with whom they do business and have access to patient data, known as "business associates," abide by the same restrictions.[246] The law does not apply to others, such as employers, life insurance companies, and members of the general public.[247] Additionally,

Implications, and Limitations, 6 J. L. BIOSCI., no. 1, May 2019, at 1, 10, https://academic.oup.com/jlb/article/6/1/1/5489401.

242. Rothstein, *My Data, Myself*, *supra* note 192; *see also* T. Mills Fleming, *The Final HIPAA Rules*, 49 PRAC. LAW. 29, 33 (2003) (discussing the HIPAA requirement that covered entities use special codes when performing certain health care transactions); Wright Clayton et al., *supra* note 241, at 10 (noting that "Congress added 'Administrative Simplification' provisions to HIPAA during the legislative process to mandate the use of standard electronic formats in the submission of health insurance claims . . . .").

243. SUMMARY OF THE HIPAA PRIVACY RULE, *supra* note 240, at 1–2.

244. Standards for Privacy of Individually Identifiable Health Information (Privacy Rule), 45 C.F.R. pts. 160, 164 (2021).

245. SUMMARY OF THE HIPAA PRIVACY RULE, *supra* note 240, at 2–3 ("The Privacy Rule . . . appl[ies] to health plans, health care clearinghouses, and to any health care provider who transmits health information in electronic form in connection with transactions for which the Secretary of HHS has adopted standards under HIPAA (the 'covered entities').").

246. *Id.* at 3.

247. *See* Wright Clayton et al., *supra* note 241, at 10 ("[T]he HIPAA statute gave the US Department of Health and Human Services (HHS) the jurisdiction to regulate entities that provide healthcare or pay for it (such as insurers) but gave HHS no jurisdiction to regulate the multitude of other private companies and institutions (e.g. drug manufacturers, research institutions that provide no health care services, companies that sell fitness tracking devices, DTC genetic testing services, and many others) that—in our current times—use and store people's health and genetic data in ways that affect their privacy.").

it contains several broadly worded exceptions that allow providers to disclose, without a patient's knowledge or consent, health information in individually identifiable form.[248] These exceptions include sharing with other providers involved in a patient's care, sharing with entities paying for that care, use in the administration of a health care organization, reporting to public health authorities, and disclosure in response to a court order.[249] Data may also be disclosed in deidentified form for research.[250]

The Privacy Rule is the primary tool for protecting patient data contained in clinical databases.[251] Nevertheless, this decades-old law has several limitations as applied to genetic privacy.[252] Most notably, while data that are shared for research must be deidentified through the removal of various data elements, reidentification of genetic data is becoming increasingly easy.[253] Alarmingly, data sharing for health care administration opens the door to access by a range of third parties,[254] and there is no prior notice or consent required before disclosing patient health information to a business associate.[255]

248. *Exceptions to the Privacy Rule*, HEALTHCARE COMPLIANCE PROS (July 17, 2013, 12:00 AM), https://www.healthcarecompliancepros.com/blog/exceptions-to-the-privacy-rule.

249. *Id.*

250. *See* Lisa Bari & Daniel P. O'Neill, *Rethinking Patient Data Privacy in the Era of Digital Health*, HEALTH AFFS.: BLOG (Dec. 12, 2019), https://www.healthaffairs.org/do/10.1377/hblog20191210.216658/full/.

251. *See* Field, *My Data, Myself*, *supra* note 193.

252. *See, e.g.*, Wright Clayton et al., *supra* note 241, at 11–12 (noting that the HIPAA Privacy Rule "was never intended to be a comprehensive health policy regulation," and that the rule "has glaring gaps in its framework for keeping people informed about who has access to their genetic information.").

253. *See* Erika Check Hayden, *Privacy Protections: The Genome Hacker*, NATURE (May 8, 2013), https://www.nature.com/news/privacy-protections-the-genome-hacker-1.12940; Megan Molteni, *Genome Hackers Show No One's DNA Is Anonymous Anymore*, WIRED (Oct. 11, 2018, 2:04 PM), https://www.wired.com/story/genome-hackers-show-no-ones-dna-is-anonymous-anymore/.

254. Bari & O'Neill, *supra* note 250.

255. *See* Luther, *My Data, Myself*, *supra* note 109. By way of example, Google recently announced a partnership with Ascension Healthcare through which it will analyze identified patient information. Tariq Shaukat, *Our Partnership with Ascension*, GOOGLE CLOUD: BLOG, https://cloud.google.com/blog/topics/inside-google-cloud/our-partnership-with-ascension (Nov. 12, 2019).

Several scholars have concluded that it is time for HIPAA and the Privacy Rule to be modified to apply to the modern era to ensure the privacy of genetic data.[256]

D. *Genetic Information and Nondiscrimination Act*

The Privacy Rule and Common Rule address access to sensitive health data. A different set of protections apply to uses of data once they have been disclosed. The law most directly applicable to genetic information is GINA, which was enacted in 2008.[257] It was intended to allay fears regarding potential discrimination based on genetic traits, which could discourage participation in genetic testing.[258] It does so by prohibiting discrimination in health insurance and employment based on the results of such tests.[259]

Title I of GINA prohibits genetic discrimination in health insurance.[260] However, this protection was rendered irrelevant by the Affordable Care Act, enacted in 2010, which prohibits the use of medical information in underwriting for individual policies.[261] GINA does not apply to other forms of health-related coverage, such as life, disability, or long-term care insurance, or to the use of genetic information in other contexts, such as education, housing, and lending.[262] As noted, it also does not

256. *See, e.g.*, Bari & O'Neill, *supra* note 250 (describing a proposal for Congress to enact "incremental reforms to ensure the privacy of health data").

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

258. *Id.* § 2(5) ("Congress has collected substantial evidence that the American public and the medical community find the existing patchwork of State and Federal laws to be confusing and inadequate to protect them from discrimination. Therefore, Federal legislation establishing a national and uniform basic standard is necessary to fully protect the public from discrimination and allay their concerns about the potential for discrimination, thereby allowing individuals to take advantage of genetic testing, technologies, research, and new therapies.").

259. *See* Mark A. Rothstein, *GINA's Beauty Is Only Skin Deep*, 22 GENEWATCH, no. 2, Apr.–May 2009, at 9, 9 ("The real reason for enacting GINA was to assure people that they could undergo genetic testing without fear of genetic discrimination.").

260. GINA §§ 101–06.

261. Mark A. Rothstein, *GINA at Ten and the Future of Genetic Nondiscrimination Law*, 2018 HASTINGS CTR. REP. 3, 5 (2018).

262. *Id.*

apply once a genetic condition has become manifested.[263] Title II prohibits genetic discrimination in employment.[264] It bars employers from requesting, requiring, or purchasing genetic information about employees, applicants, or their family members.[265] However, there are several exceptions, which include: inadvertent requests for family medical histories, optional health or genetic services offered as part of an employer's wellness program, requests for family medical history to comply with the documentation requirements of the Family Medical Leave Act, and optional genetic monitoring for the effects of occupational exposures.[266]

GINA defines "genetic information" as "information about . . . [an] individual's genetic tests, the genetic tests of family members of such individual and the manifestation of a disease or disorder in a family members of such individual."[267] Professor Rothstein remarked that this definition is "locked in time" and has not kept up with advances since the law's passage.[268] For example, it does not apply to changes in gene expression not caused by alterations of the DNA sequence, known as epigenetics, because GINA defines genetic tests as involving DNA.[269] Similarly, the definition of genetic information excludes findings related to the genomes of microorganisms, known as microbiomics, because such findings do not involve human DNA.[270]

In addition to these shortcomings, GINA includes provisions that can make the pursuit of claims for employment discrimination based on genetics difficult. Most notably,

263. *Id.* at 6.

264. GINA § 202.

265. § 202(b).

266. *See* Roy Maurer, *Family Medical History Queries Violate GINA*, SHRM (Dec. 22, 2015), https://www.shrm.org/resourcesandtools/hr-topics/talent-acquisition/pages/family-medical-history-violate-gina.aspx.

267. § 201(4).

268. Rothstein, *My Data, Myself*, *supra* note 192.

269. *Id.*

270. *Id.*

plaintiffs bear the burden of proving motive.[271] They must show that an employer's action resulted from an intent to discriminate on the basis of genetic information and not from another other reason.[272] Similarly, while GINA requires that employers ensure that "reasonable measures within its control" are taken to protect the confidentiality of genetic information obtained through medical examinations, the determination of what is reasonable is subjective and fact-specific.[273] Moreover, if a plaintiff were to litigate the issue, his or her information would have already been compromised and the damage to privacy done.

In the view of Professor Rothstein, GINA and the Privacy Rule are widely misunderstood, which may have led to a false sense of security for patients and commercial testing customers.[274] "We have no privacy. We may *think* we do, but there is no privacy of health information," he cautioned.[275] Specifically, he mentioned that the Privacy Rule has numerous, broadly worded exceptions. In addition, each year individuals are compelled to sign at least twenty-five million authorizations disclosing their health information in applying for employment, insurance, government benefits, and other important matters.[276] As these various shortcomings reflect, the law is limited in scope and in need of updating.

E. *General Data Protection Regulation*

In addition to these American laws, in 2018, the European Union enacted the GDPR to enhance privacy protection for data

271. Field, *My Data, Myself*, *supra* note 193.

272. *Id. See* Ortiz v. City of San Antonio Fire Dep't, 806 F.3d 822, 827 (5th Cir. 2015) (denying employee's discrimination claim on the basis of genetic information because the employer's actions were motivated, in part, by nondiscriminatory reasons).

273. Christine Watts Johnston & Mark D. Pomfret, *Evolving Genetic Science Spurs Legal Protections: A GINA Primer*, 24 BENEFITS L.J., no. 2, Summer 2011, at 59, 64 (2011) (quoting 29 C.F.R. § 1635.8(d)).

274. *See* Rothstein, *My Data, Myself*, *supra* note 192.

275. *Id.*

276. *See* Mark A. Rothstein & Meghan K. Talbott, *Compelled Disclosures of Health Records: Updated Estimates,* 45 J.L. MED. & ETHICS 149, 149 (2017).

stored online.[277] While that law applies only in the European Union, American companies collecting personal data on European Union citizens must comply with it.[278] The GDPR provides data subjects the right to access, correct, and have deleted upon request any personal information,[279] which is defined as "any information relating to an identified or identifiable natural person ('data subject')."[280] Among the ways in which a person may be identified is through genetic data.[281] However, because the law "does not distinguish between *anonymous* and *anonymized* data," it does not protect those whose data was collected in an identifiable manner but is later anonymized.[282] In this case, genetic data is considered "non-personal."[283]

Unlike HIPAA, the GDPR applies broadly to storage and processing of all personal data, not just to those collected in health care.[284] As a result, in the view of one observer, "[i]ts provisions apply almost completely across the genomic research process—from the moment of collection of biological samples and associated data up until the production of research results."[285] This engenders a common criticism of the law—that it is extremely complex and at the same time ambiguous in some respects.[286] The resulting uncertainty can be burdensome

277. GDPR, *supra* note 188, at 1–2, 32.

278. *See* Field, *My Data, Myself*, *supra* note 193. While there is no United States federal equivalent to the GDPR, California enacted the California Consumer Privacy Act in 2018, which is comparable to the GDPR, albeit on a smaller scale, and is only applicable to California residents. *Compare* CAL CIV. CODE § 1798.100 (Deering 2020) *with* GDPR, *supra* 188, at 1–2.

279. *See* GDPR, *supra* note 188, at 33.

280. Mahsa Shabani & Pascal Borry, *Rules for Processing Genetic Data for Research Purposes in View of the New EU General Data Protection Regulation*, 26 EUR. J. HUM. GENETICS 149, 150 (2018).

281. *See id.* at 149.

282. *Id.* at 150.

283. *Id.* at 150–51.

284. *See* GDPR, *supra* note 188, at 32–33.

285. Dara Hallinan, *Broad Consent Under the GDPR: An Optimistic Perspective on a Bright Future*, 16 LIFE SCIS., SOC'Y & POL'Y, no. 1, Jan. 6, 2020, at 1, 1, https://lsspjournal.biomedcentral.com/articles/10.1186/s40504-019-0096-3.

286. *See* Alison Cool, Opinion, *Europe's Data Protection Law Is a Big, Confusing Mess*, N.Y. TIMES (May 15, 2018), https://www.nytimes.com/2018/05/15/opinion/gdpr-europe-data-protection.html.

for companies and researchers trying to comply with it. As an example, genomics researchers have been grappling with the question of whether the GDPR allows the use of broad consent for subsequent uses of data.[287] While its text seems to allow it, guidance from the regulatory body that interprets the law, the Article 29 Working Party, suggests that it does not.[288]

The California Consumer Privacy Protection Act, which became effective on January 1, 2020, grants customers similar rights to know what data have been collected on them and to demand deletion.[289] However, it applies only to for-profit companies, not to universities and nonprofit research organizations, and only to data collected during the previous year.[290] Moreover, penalties for noncompliance are much milder than under the GDPR.[291]

F. *Liability for Damages*

Entities that collect and store genetic data may be liable in tort for harm caused by negligent use or disclosure.[292] However, claims along these lines face several obstacles. When genetic data are used in clinical settings, the roles and duties of clinicians and laboratories may be difficult to disentangle.[293] A

287. Hallinan, *supra* note 285, at 2. Broad consent has been defined as "consent for an unspecified range of future research subject to a few content and/or process restrictions. Broad consent is less specific than consent for each use, but more narrow than open-ended permission without any limitations (i.e. 'blanket consent')." Christine Grady, Lisa Eckstein, Ben Berkman, Dan Brock, Robert Cook-Deegan, Stephanie M. Fullerton, Hank Greely, Mats G. Hansson, Sara Hull, Scott Kim, Bernie Lo, Rebecca Pentz, Laura Rodriguez, Carol Weil, Benjamin S. Wilfond & David Wendler, *Broad Consent for Research with Biological Samples: Workshop Conclusions*, 15 AM. J. BIOETHICS, no. 9, Aug. 25, 2015, at 34, 35.

288. Hallinan, *supra* note 285, at 2. The Article 29 Working Party is similar in function to the United States' EEOC for the ADA; it is the European body tasked with interpreting the GDPR. *See id.*

289. CAL. CIVIL CODE §§ 1798.100, 1798.105 (Deering 2020).

290. §§ 1798.130, 1798.140.

291. *Compare* § 1798.155 *with* GDPR, *supra* note 188, at 80–83.

292. *See* Adrian Thorogood, Robert Cook-Deegan & Bartha Maria Knoppers, *Public Variant Databases: Liability?*, 19 GENETICS MED. 838, 839 (2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5527130/ (describing a wrongful death suit where plaintiff alleged that the defendant negligently interpreted genetic material).

293. *Id.* at 839–40.

plaintiff must determine whether fault for a breach lies in the processing of a test sample by a laboratory or the receipt and interpretation of results by a physician.[294] Laboratories are required by federal regulations to "ensure that reports of test results include pertinent information required for interpretation."[295] This provides little protection for privacy breaches. They are also subject to guidelines on analytic procedures issued by the American College of Medical Genetics and Genomics (ACMG).[296] However, the ACMG guidelines are voluntary.[297] A court may use them as the basis for establishing the standard of care, but it would not be bound to do so.[298]

The interpretation of test results raises particularly difficult issues regarding causation when medical care is involved.[299] When can a failure to effectively communicate findings be considered the actual cause of harm from a genetic trait? The answer is especially difficult when a test yields uncertain results.[300] Even if it can be shown that a physician breached a duty, the chain of causation breaks down when a course of

294. *See id.* at 839 (discussing how the "division of responsibility between physicians and laboratories has increasingly blurred in the genomics age").

295. 42 C.F.R. § 493.1445(e)(8) (2021).

296. Sue Richards, Nazneen Aziz, Sherri Bale, David Bick, Soma Das, Julie Gastier-Foster, Wayne W. Grody, Madhuri Hegde, Elaine Lyon, Elaine Spector, Karl Voelkerding & Heidi L. Rehm, *Standards and Guidelines for the Interpretation of Sequence Variants: A Joint Consensus Recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology*, 17 GENETICS MED. 405, 405 (2015), https://doi.org/10.1038/gim.2015.30.

297. Molika Ashford, *Labs Confront Legal Risks Posed by Genetic Variant Classification, Reporting*, GENOMEWEB (Nov. 27, 2017), https://www.genomeweb.com/molecular-diagnostics/labs-confront-legal-risks-posed-genetic-variant-classification-reporting.

298. *See* Thorogood et al., *supra* note 292, at 839. A plaintiff similarly may wish to reference the ACMG guidelines in a case regarding a laboratory's or clinician's liability, but because the court is not bound to follow those guidelines, would be well-advised to include multiple potential bases for liability. For example, in *Williams v. Quest Diagnostics*, where the plaintiff sued a laboratory for the alleged misreading of her child's genetic mutation leading to a seizure disorder and death, the plaintiff did not solely rely on the ACMG Guidelines in establishing a duty of care, but also alleged that the defendant laboratory had failed to follow its own protocol and procedure. *See* Complaint at 6–11, Williams v. Quest Diagnostics, 353 F. Supp. 3d 432 (D.S.C. 2018) (No. 3:16-cv-00972); Thorogood et al., *supra* note 292, at 839.

299. Thorogood et al., *supra* note 292, at 839.

300. *Id.*; *see* Turna Ray, *Mother's Negligence Suit Against Quest's Athena Could Broadly Impact Genetic Testing Labs*, GENOMEWEB (Mar. 14, 2016), https://www.genomeweb.com/molecular-diagnostics/mothers-negligence-suit-against-quests-athena-could-broadly-impact-genetic.

treatment is prescribed by a different physician.[301] The plaintiff must prove that the other physician would have changed the treatment in response to a test result and that such a change would have actually prevented the harm.[302]

Moreover, legal duties differ between clinicians and researchers, and they are guided by different professional standards and guidelines. When considering liability, courts must balance different policy goals regarding each—minimizing harm to patients in the case of physicians, and promoting scientific innovation in the case of researchers.[303] In terms of duties, clinicians are obliged to consider the needs of the patient first, while researchers have a responsibility to focus on the needs of the study.[304] Expectations of patients and research subjects can be guided with warnings and clear consent agreements to make them aware in advance of the responsibilities of those who will be collecting and using their genetic data. However, these documents may have to explain technical information, which may be difficult for lay people to understand.[305]

Nevertheless, clear liability standards could create incentives to make interpretations of test results more consistent. They could also promote refinements in testing methods, lessening of delays, and reduction of errors in diagnosis.[306] This would help to guide physicians and laboratories in best practices while promoting public trust in their work.

301. Thorogood et al., *supra* note 292, at 839. *See* Turna Ray, *Quest, Athena Make Moves in Wrongful Death Lawsuit*, GENOMEWEB (Apr. 1, 2016), https://www.genomeweb.com/molecular-diagnostics/quest-athena-make-moves-wrongful-death-lawsuit.

302. *See* Thorogood et al., *supra* note 292, at 839.

303. *See* Carl H. Coleman, *Duties to Subjects in Clinical Research*, 58 VAND. L. REV. 387, 388 (2005).

304. *Id.*

305. Erin E. Donovan, *Patients Are Signing Consent Forms They Don't Understand. We Can Do Better.*, NAT'L COMMC'N ASS'N (June 1, 2014), https://www.natcom.org/communication-currents/patients-are-signing-consent-forms-they-don't-understand-we-can-do-better.

306. *See* Richards et al., *supra* note 296, at 840; SOBIA RAZA, ALISON HALL, CHRIS RANDS, SANDI DEANS, DOMINIC MCMULLAN & MARK KROESE, PHG FOUND., DATA SHARING TO SUPPORT UK CLINICAL GENETICS AND GENOMIC SERVICES 6 (2015), https://www.phgfoundation.org/report/data-sharing-to-support-uk-clinical-genetics-and-genomics-services.

G. *Commercial Database Terms of Service*

For data collected by commercial genetic testing companies, none of the privacy protections contained in the statutes discussed above apply. Their customers are protected only by their terms of service and privacy policies, which are voluntary and created at the companies' discretion.[307] They are also highly variable across organizations.[308] Some companies have no privacy policy at all, and others have policies that are changeable on 30-days' notice.[309] Enforcement of terms may also be difficult for customers, as it involves complex issues of contract interpretation.[310]

Professor Field warned about risks to unsuspecting relatives of those who voluntarily contribute their genetic data to such databases.[311] They are not parties to the transaction between the customer and the testing company, and so they do not enjoy even the limited protection of the terms of service.[312] To illustrate the point, he wondered "I'm sure I have third cousins twice removed walking around out there somewhere, and I would bet anything that at least one of them has donated a sample to a commercial or research database. Does that mean that it will implicate me at some point?"[313]

IV. GENETIC RESEARCH AND COVID-19

The *My Data, Myself* conference took place soon after the global spread of COVID-19 had begun to accelerate. The

307. *See* Field, *My Data, Myself*, *supra* note 193.

308. *Id.*

309. *Id.*

310. *Id.*

311. *Id.*

312. *Id.* Terms of service and privacy policies have their own limitations: companies are not mandated to enact them; they are variable and subject to change; enforcement is often unclear; and because the database is a corporate asset, terms of service provide little protection during corporate restructuring such as mergers, acquisitions, and bankruptcy. *Id.* Importantly, none of the terms of service or privacy policies protect relatives—they only protect the patient or consumer. *Id.*

313. *Id.*

following week, the World Health Organization declared it a pandemic,[314] and within two weeks, many countries and most states in the United States had issued business closure and stay-at-home orders.[315] Priorities for medical care and public health shifted rapidly.

A distinctive feature of COVID-19 is the variability of its course between patients. Some remain asymptomatic, some experience mild symptoms and some experience severe symptoms that can lead to death.[316] Explanations for this variability have focused on a number of factors, including age, sex, presence of underlying health conditions, and viral load.[317] Research findings have also suggested that genetic factors may play a role.[318]

Research into genetic determinants of COVID-19 susceptibility could help to elucidate the cellular mechanisms behind progression of the disease and could enable clinicians to

314. *See generally* Domenico Cucinotta & Maurizio Vanelli, *WHO Declares COVID-19 a Pandemic*, 91 ACTA BIOMEDICA, no. 91, Mar. 19, 2020, at 157, 157 (2020), https://pubmed.ncbi.nlm.nih.gov/32191675/ (describing the World Health Organization's March 11, 2020 declaration that COVID-19 was a global pandemic and detailing the events leading up to that decision).

315. *See* Daniel Dunford, Becky Dale, Nassos Stylianou, Ed Lowther, Maryam Ahmed & Irene de la Torre Arenas, *Coronavirus: The World in Lockdown in Maps and Charts*, BBC (Apr. 7, 2020), https://www.bbc.com/news/world-52103747; Jennifer Kates, Josh Michaud & Jennifer Tolbert, *Stay-At-Home Orders To Fight COVID-19 in the United States: The Risks of a Scattershot Approach*, KAISER FAM. FOUND. (Apr. 5, 2020), https://www.kff.org/policy-watch/stay-at-home-orders-to-fight-covid19/.

316. *See* Yufang Shi, Ying Wang, Changshun Shao, Jianan Huang, Jianhe Gan, Xiaoping Huang, Enrico Bucci, Mauo Piacentini, Giuseppe Ippolito & Gerry Melino, Editorial, *COVID-19 Infection: The Perspectives on Immune Responses*, 27 CELL DEATH & DIFFERENTIATION 1451, 1451 (2020), https://www.nature.com/articles/s41418-020-0530-3.

317. *See* Brian Resnick, *Scientists Are Trying To Figure Out Why Covid-19 Hits Some Young, Healthy People Hard*, VOX (Apr. 8, 2020), https://www.vox.com/science-and-health/2020/4/8/21207269/covid-19-coronavirus-risk-factors.

318. For example, a possible correlation has been noted between disease severity and blood type. *See* Joacim Rocklöv & Paul Franks, *'Immunological Dark Matter': Is This Why Some People Have a Pre-Existing Immunity to COVID-19?*, GENETIC LITERACY PROJ. (Aug. 7, 2020), https://geneticliteracyproject.org/2020/08/07/immunological-dark-matter-is-this-why-some-people-have-a-pre-existing-immunity-to-covid-19/. Interest has also focused on the role of ACE2, an enzyme that sits on the surface of the host's cells and helps the virus to penetrate them. *Id.*

predict the risk of serious outcomes for individual patients.[319] This could translate into better tools for prevention and treatment. If genetic markers for susceptibility were identified, those at heightened risk could be counseled to take extra precautions, such as being especially scrupulous about social distancing.[320] They might also be advised to avoid jobs that involve frequent contact with infected individuals, for example in health care or retail customer service. If they develop symptoms, they might be triaged for a more intensive level of care or monitored more closely as symptoms develop.[321] They might also be prioritized for contact tracing,[322] if someone who tests positive for the virus reports having come into contact with them. Conversely, the presence of genetic markers associated with resistance to the virus might allow individuals to take exposure-prone jobs with less concern.

However, many of the practical challenges involved in other forms of genetically guided care would likely apply. In particular, markers for susceptibility to COVID-19 might not be clear-cut, and findings of VUS might be common.[323] In this case, medical advice would require subjective judgments of risk, leaving patients and clinicians without clear direction. Competent genetic counseling would be essential. As data accumulate, the interpretation of VUS for COVID-19 genes

319. Robert I. Field, Anthony W. Orlando & Arnold J. Rosoff, *Genetics and COVID-19: How To Protect the Susceptible*, TRENDS GENETICS (Aug. 29, 2020), https://www.cell.com/trends/genetics/fulltext/S0168-9525(20)30233-X.

320. *See* Yuan Hou, Junfei Zhao, William Martin, Asha Kallianpur, Mina K. Chung, Lara Jehi, Nima Sharifi, Serpil Erzurum, Charis Eng & Feixiong Cheng, *New Insights into Genetic Susceptibility of COVID-19: An ACE2 and TMPRSS2 Polymorphism Analysis*, 18 BMC MED. no. 216, July 15, 2020, at 1, 7 (2020), https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-020-01673-z.

321. *See e.g.*, Nat'l Ctr. Immunization & Respiratory Diseases (NCIRD), Div. Viral Diseases, *Standard Operating Procedure (SOP) for Triage of Suspected COVID-19 Patients in Non-US Healthcare Settings: Early Identification and Prevention of Transmission During Triage*, CTRS. DISEASE CONTROL & PREVENTION (Sept. 11, 2020), https://www.cdc.gov/coronavirus/2019-ncov/hcp/non-us-settings/sop-triage-prevent-transmission.html.

322. *See e.g.*, *id.*

323. *See* discussion *supra* Section II.B.

would likely change, and standards would be necessary for determining when and how to recontact test subjects.[324]

Testing for genetic markers for increased susceptibility to COVID-19 may also produce incidental findings. Standards would be needed for determining the responsibilities of clinicians and laboratories to inform patients should they occur. While such concerns arise with regard to genetic tests for other conditions, in the case of COVID-19, addressing them would be more urgent.[325] Patients who may have been exposed to the virus would need to know as quickly as possible whether a genetic susceptibility puts them at heightened risk.[326] This would leave less time for meaningful counseling.

COVID-19 testing also raises distinctive privacy concerns in the reporting of findings to public health authorities.[327] Since the disease is highly contagious, genetic data on individual susceptibility would be especially important in understanding and controlling risk at a population level.[328] It could also help in understanding factors, such as environmental and social influences, that affect disease spread.[329] However, to be most useful, genetic test results would have to be linked to individuals so that public health officials could most effectively

324. *Id.*

325. *See* Hou et al., *supra* note 320, at 1 (suggesting that COVID-19 is more impactful and global than past coronaviruses, like SARS and MERS).

326. *See generally id.* (suggesting that genetics may affect susceptibility, severity, and clinical outcomes in patients with COVID-19).

327. *See, e.g.*, Off. C.R., U.S. Dep't Health & Hum. Servs., Bulletin: HIPAA Privacy and Novel Coronavirus (Feb. 3, 2020), https://www.hhs.gov/sites/default/files/february-2020-hipaa-and-novel-coronavirus.pdf (providing guidance on how HIPAA covered entities may disclose protected health information related to COVID); Off. C.R., U.S. Dep't Health & Hum. Servs., COVID-19 and HIPAA: Disclosures to Law Enforcement, Paramedics, Other First Responders and Public Health Authorities (Oct. 2, 2020), https://www.hhs.gov/sites/default/files/covid-19-hipaa-and-first-responders-508.pdf (updating guidance).

328. *See* Field, Orlando & Rosoff, *supra* note 319 (discussing government proposals for "genetic passports" and "immunity passports" which would allow for limited lockdowns); *see also* Hou et al., *supra* note 320 (recognizing importance of genetic markers in paving way for precision medicine and personalized treatment strategies in combating COVID-19).

329. Rocklöv & Franks, *supra* note 318.

target protection efforts. This presents the obvious risk of inadvertent disclosure.[330]

Reporting identifiable medical data to public health authorities is not new. It even has its own explicit exception to the disclosure limitations in the Privacy Rule.[331] It is central to tracking the incidence and prevalence of a range of diseases, such as cancer and diabetes, and public health agencies are accustomed to the need to safeguard its confidentiality.[332] However, COVID-19 data raise especially challenging concerns. Efforts to mitigate the spread of an infectious disease may require a focus on susceptible individuals, and their identities might be difficult to conceal.[333] Given the urgency of COVID-19 mitigation, the balance between public health protection and privacy safeguards is likely to tip against the latter, which presents the risk that some people might be dissuaded from submitting to genetic testing related to the disease.[334]

Genetic testing for susceptibility to COVID-19 also raises broader ethical issues, some of which are similar to those raised by other kinds of genetic analyses. As with medical testing in general, the principle of autonomy dictates that those who submit to genetic tests provide consent based on an informed

330. *See* ASSESSING GENETIC RISKS: IMPLICATIONS FOR HEALTH AND SOCIAL POLICY 267–68 (Lori B. Andrews, Jane E. Fullarton, Neil A. Holtzman & Arno G. Motulsky eds., 1994) (discussing concerns regarding confidentiality and genetic testing).

331. 45 C.F.R. § 164.512(b) (2021).

332. As an example, most states maintain Immunization Information Systems that contain information on immunization doses administered by participating providers in specified geographical areas. *See About Immunization Information Systems (IIS)*, CTRS DISEASE CONTROL & PREVENTION, https://www.cdc.gov/vaccines/programs/iis/about.html (June 7, 2019).

333. Field, Orlando & Rosoff, *supra* note 319.

334. *See* Cynthia Cole, Brooke Chatterton & Natalie Sanders, *The Safety of Privacy: Increased Privacy Concerns May Prevent Effective Adoption of Contact Tracing Apps*, LAW.COM: LEGALTECH NEWS (Aug. 18, 2020, 7:00 AM), https://www.law.com/legaltechnews/2020/08/18/the-safety-of-privacy-increased-privacy-concerns-may-prevent-effective-adoption-of-contact-tracing-apps/ ("[M]any Americans are increasingly wary of being traced just when public safety is at heightened concern. As a result, contact tracing apps may not be fully successful in the United States until Americans trust that their privacy is protected."). Genetic markers raise even greater concern, as they are immutable. Field, Orlando & Rosoff, *supra* note 319.

understanding of the risks.[335] These risks include the concerns of unauthorized disclosure of results and the discovery of incidental findings.[336] Respect for autonomy also requires that test subjects be able to decide whether they would like to be recontacted concerning incidental or other findings that result from reanalysis of their samples at a later time.[337] They must also be informed that the results may indicate VUS, which would force them to confront continued uncertainty.[338]

There is also an important ethical concern posed by COVID-19 genetic testing that is specific to that condition. That is the nature of discrimination that the results could engender.[339] Until a vaccine or effective treatment is widely available, those found to be genetically susceptible might be considered ill-suited by employers for exposure-prone jobs and summarily rejected or terminated.[340] Similar discrimination might also occur in other spheres, such as disability and life insurance because of a heightened risk of filing claims, apartment rentals because of the risk of transmission to other tenants, nursing homes placements because of the risk of transmission to other residents, and bank loans because of the risk that unemployment due to disability from the disease would make repayment difficult.[341] Conversely, those found to have genetic resistance may be preferred in these spheres. Governments might also face incentives to favor those with genetic resistance to COVID-19 in disease mitigation strategies.[342] For example, to limit the extent of social distancing restrictions, which can cause widespread economic harm, they might consider issuing "genetic passports" to those who can safely risk contact with

335. ASSESSING GENETIC RISKS, *supra* note 330, at 248.

336. *See* Meacham et al., *supra* note 163, at 31–33.

337. *See* discussion *supra* Section II.B.

338. *Id.*

339. Field, Orlando & Rosoff, *supra* note 319.

340. *Id.*

341. *Id.*

342. *Id.*

others.[343] By the same token, for those with genetic markers for susceptibility, they might consider stronger restrictions.[344]

Current legal protections against these risks are as porous for any COVID-19-related traits that may be found as they are for other genetic characteristics. The exceptions to the HIPAA Privacy Rule for disclosure without patient consent include the broad categories of health care operations and public health reporting through which genetic findings could leak out.[345] The Common Rule permits sharing of deidentified genetic data for research,[346] even though genomes can be reidentified with increasing ease.[347] GINA does not apply to disability or life insurance.[348]

However, individuals found to have COVID-19 susceptibility might enjoy stronger legal protection under the ADA than those with genetic susceptibilities to other conditions.[349] COVID-19 susceptibility, even without actual exposure or symptoms, could produce an immediate limitation in the need for stricter social distancing. This would restrict the ability to engage in the major life activity of socializing, which could arguably qualify it as a disability under the law.[350] Nevertheless, while the ADA may protect susceptible individuals against overt discrimination, it would be of little help with regard to discriminatory public health regulations or social ostracism.

343. *Id.*

344. *Id.*

345. 45 C.F.R. § 164.512 (2021).

346. 45 C.F.R. § 164.514 (2021).

347. Mark A. Rothstein, *Is Deidentification Sufficient to Protect Health Privacy in Research?*, 10 AM. J. BIOETHICS, no. 9, Sept. 1, 2010, at 3, 5, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3032399/.

348. *See* Lauren Elizabeth Nuffort, *The Genetic Information Nondiscrimination Act of 2008: Raising a Shield to Genetic Discrimination in Employment and Health Insurance*, 21 ABA: HEALTH LAW, no. 5, June 2009, at 1, 1, 16 (2009).

349. 42 U.S.C. § 12102.

350. Amendments to the ADA passed in 2008 substantially expanded the range of qualifying disabilities and made it easier for social disabilities to come within the law's protections. *See* Susan D. Carle, *Analyzing Social Impairments Under Title I of the Americans with Disabilities Act*, 50 U.C. DAVIS L. REV. 1109, 1131–32 (2017).

Balanced against these concerns is the pressing need for research to better understand the nature of COVID-19. Overly restrictive regulation could impede investigations that might prevent untold suffering and save countless lives. Achieving a balance between advancing knowledge and protecting subjects is important in all genetic research, and investigations related to COVID-19 are no different. However, for research to help mitigate a raging pandemic, speed is especially critical.

CONCLUSION

The *My Data, Myself* conference highlighted both dramatic medical breakthroughs that have resulted from research using genetic databases and social risks and ethical conflicts that this research engenders. Scientists are on the cusp of transforming health care with new technologies, such as precision medicine, gene editing, and gene therapy, however the accumulation of data that lies behind these advances poses a serious and growing threat to privacy. Existing legal protections are inadequate to balance the prospect of these unprecedented medical advances against the novel personal threats they pose.[351] A new legal framework grounded in new forms of ethical analysis is needed.

Defining an ethical balance is essential as a first step, but that will be easier said than done. In addition to personal threats, genomic medicine presents a host of challenges in its practical application that cry out for ethical guidance. These include defining the parameters for counseling patients on the meaning of results, for advising them when results are ambiguous, for communicating incidental findings, and for recontacting them when new findings emerge based on their samples. As technology advances, the number of such issues is certain to multiply.

Ethical guidance on issues such as these will be necessary in updating current legal protections, which are increasingly

351. *See* Field, Orlando & Rosoff, *supra* note 319.

obsolete. HIPAA was enacted at a time when fax machines were in common use and the Internet was in its infancy. The Common Rule was written and revised when it could be assumed that anonymized genetic data would stay that way.[352] GINA was written to exempt disability and life insurance from its protections before the complexity of many genetic markers was fully understood.[353] The ADA did not anticipate the impairment of social isolation that might by implicated by a genetic finding of susceptibility to an infectious disease such as COVID-19.[354]

Reassessment of all of these regulatory schemes is urgently needed. It can begin with a ramping up of debate among scientists, clinicians, lawyers, and ethicists. The sooner this takes place, the better. If legal oversight does not get out in front of scientific advances, it may be difficult to catch up.

352. *See* Lynch, *My Data Myself*, *supra* note 192.

353. *See* Rothstein, *My Data, Myself*, *supra* note 192.

354. *See* Mufson, Fant & Hirsch, *supra* note 236.