

Ethical Issues in Contemporary Clinical Genetics

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Abstract

As genetic sequencing capabilities become more powerful and costs decline, the reach of genomics is expanding beyond research laboratories to the wards, outpatient clinics, and, with the marketing of direct-to-consumer testing services, patients' homes. Increasingly, patients receiving various diagnoses—from cancer to cardiomyopathy—can reasonably expect to have conversations with their providers about indications for genetic testing. In this dynamic context, a grasp of the ethical principles and history underlying clinical genetics will provide clinicians with the tools to guide their practice and help patients navigate complex medical-psychosocial terrain. This article provides an overview of the salient ethical concerns pertaining to clinical genetics. The subject is approached with an emphasis on clinical practice, but consideration is also given to research. The review is organized around the temporal and informational sequence of issues commonly arising during the course of pretesting, testing, and posttesting phases of patient care. Drawing from medical, legal, and historical perspectives, this review covers the following topics: (1) informed consent, (2) return of results, and (3) privacy and confidentiality, and intends to equip readers with an appropriate foundation to apply ethical principles to genetic testing paradigms with an understanding of the contextual landscape against which these situations occur.

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In April 2017, the US Food and Drug Administration (FDA) announced that it would allow the genomics company 23andMe to market direct-to-consumer (DTC) genetic health risk tests for 10 medical conditions.¹ One year later, the FDA permitted the expansion of 23andMe's reach by allowing the company to market testing for selected BRCA1/BRCA2 variants, which confer risk for breast and ovarian cancer.² Although the FDA maintains that such tests should not be used for diagnostic or treatment purposes and that consumers should consult health care professionals with questions or concerns about results, such decisions represent a sharp departure from its 2013 warning to the company to "immediately discontinue marketing."³ The agency's reversal—and suggestion that other DTC technologies may enjoy expeditious approval—places it at odds with the current recommendations of the American College of Medical Genetics and Genomics (ACMG) regarding the assessment of an individual's genetic risk.⁴ In the setting of this

discrepancy between professional society guidelines and market realities, the trend toward broader access to personal genetic information raises difficult questions for clinicians; chief among them: what are the specific ethical and legal obligations of physicians to their patients when genetic information is concerned?

The rise of DTC and genomic testing more broadly has occurred in a technological landscape undergoing tremendous flux. As genetic sequencing capabilities become more powerful and costs decline, the reach of genomics is expanding beyond research laboratories to the wards, outpatient clinics, and patients' homes. Increasingly, patients receiving various common diagnoses—ranging from cancer to cardiomyopathy or autism—can reasonably expect to have conversations with their providers about indications for genetic testing, and as such, medical practitioners will face heightened need for genetics literacy.

As the universe of biomedical knowledge and technology rapidly expands, it is imperative that clinicians and researchers be



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equipped with sound ethical reasoning skills to guide their practice. To that end, this article is intended to provide an overview of salient issues in ethics as they pertain to clinical genetics. At the nexus of these fields lie several topics, to be reviewed in this article from medical, legal, and historical perspectives: (1) informed consent, (2) return of results, and (3) privacy and confidentiality. Furnished with this background, clinicians will be able to stay current as new developments shape the field, all the while guiding their patients through complex, dynamic medical and psychosocial terrains.

INFORMED CONSENT AND PREDICTIVE TESTING

Informed Consent

Informed consent is both an ethical and legal doctrine. Its formal origins can be traced to the 1947 Nuremberg Code that was drafted in the wake of the “Doctors’ Trial,” which scrutinized the human experimentation conducted under the Nazi regime.⁵ The code sought to establish a set of conditions defining ethical human subjects research, and included voluntary consent as 1 of its 10 critical points.⁵ In the United States, after revelations of egregious misconduct in the 40-year Tuskegee Syphilis Study,⁶ the National Commission for the Protection of Human Services of Biomedical and Behavioral Research was established and in 1979 published its first set of principles and guidelines to protect the rights of research subjects. Known as the Belmont Report, the document outlines 3 basic tenets in the conduct of ethical research: respect for persons, beneficence, and justice. The Belmont Report elaborates practices to safeguard these principles: informed consent, risk/benefit assessments, and the selection of subjects, respectively. *Informed consent* in research is defined as the right of subjects to decide whether to participate in research, provided they are furnished with adequate information, possess full comprehension, and enjoy voluntariness of decision.

Postwar ethical violations in the research arena brought informed consent into sharp focus, but within the clinical landscape, the concept took root more slowly and less formally. The belief that provider and patient share in a

decision-making partnership—requiring physician disclosure and patient consent—began to take hold in American medical practice through developments in case law during the 1950s and 1960s.⁷ Clinically, the conditions of informed consent are similar to those outlined in the Belmont Report for research purposes: the patient must be apprised of all relevant information, have the capacity to reason soundly, and have the ability to exercise decision making freely. Only when disclosure, capacity, and voluntariness are present can informed consent be obtained.⁸

A consideration of informed consent in clinical genetics practice begs the question: to what exactly are patients consenting when they agree to undergo genomic tests? Although patients may fully expect the return of primary results, they may not anticipate the trove of genetic data generated by testing and the fact that many detected variants have uncertain significance.

Although this information may be harmless, the possibility exists that the genetic testing could reveal embarrassing, stigmatizing, or deeply upsetting medical information. Furthermore, the test may reveal results with incomplete certainty, leading to misunderstanding and unnecessary concern for the recipient.

Predictive Testing of Minors

It is within this context that predictive testing of minors for genetic conditions has raised substantive ethical questions. Although minors are legally presumed to lack capacity—and thus are unable to grant consent—the legal threshold of majority is considered arbitrary by many ethicists, psychologists, and developmental specialists.⁹ Nevertheless, under current law, clinicians are required to secure parental consent for medical treatment of patients younger than 18 years, with the exception of the “mature minor” common law precedents that apply to reproductive health care.

Predictive testing is defined as genetic testing of a presymptomatic individual. Members of the ethics and genetics communities broadly support predictive testing of adults for adult-onset diseases and minors for childhood-onset disorders for which medically beneficial interventions are available.¹⁰ There exists an ethical gray zone, however, when it comes to

predictive testing of minors for late-onset diseases or carrier status, particularly when there are no clear medical treatment or prevention options.

The arguments against predictive testing of minors were first proposed when clinical genetic testing was conducted on a small scale, primarily for adult-onset conditions with little or no available treatment. Such positions highlight the potential for psychological harm to the minor being tested, negative effects on the family as a whole, risk of social discrimination and restriction, as well as violation of future autonomy.¹⁰ This reasoning supports the American Medical Association (AMA), ACMG, and American Academy of Pediatrics' current recommendations to proceed with tests when the child is at risk for actionable conditions, to defer to parental discretion when the child is at risk for a pediatric-onset condition without effective intervention, and to delay testing until the age of majority when the child is at risk for a late-onset condition lacking effective prevention or treatment.^{11,12}

Arguments in favor of predictive testing of minors have gained traction in recent years. Supporters point to research emphasizing the psychological benefits of decreased uncertainty, positive effects on the family, an adolescent and family's right to plan for the future, the prevention of harm that could result from not testing, and the principle of autonomy—both the right of parents to decide what is in their child's best interest and the capacity of adolescents to make informed decisions about their health care. The authors of a recent review article on predictive testing of minors have noted that many of these arguments are testable, empiric claims, thus making further research to establish better guidelines and develop best practices essential.¹⁰

RETURN OF RESULTS

As the costs of molecular diagnostic techniques fall and test efficiencies and capabilities rise, increased use of panel-based genetic testing and nontargeted whole-genome and exome sequencing will dramatically increase the frequency of incidental and secondary findings—that is, information not directly related to the original testing indication. The nomenclature in this field has evolved in recent years, with the term “incidental findings”

covering both anticipatable and unanticipatable results not intentionally pursued at the outset of testing and “secondary findings” connoting those results that are not the primary target of testing but are nevertheless reasonably sought. As testing sensitivities increase and bundled testing becomes more cost-effective, the lines between these 2 categories are likely to blur further.

Clinical Considerations: The Case of Secondary Findings

The frequency of returnable secondary findings in study cohorts has been well documented. In a recent study of 1000 individuals' exomes, researchers identified 239 unique, potentially pathogenic single nucleotide variants from among 114 genes associated with medically actionable conditions linked to 23 of the participants. Extrapolating these findings, the study concluded that 3.4% of patients of European descent and 1.2% of patients of African descent can reasonably expect to have highly penetrant pathogenic or likely pathogenic variants uncovered incidentally on exome sequencing.¹³ The discrepancy along ancestral lines speaks to the relative dearth of research at present on populations not of European descent, a consideration for practitioners ordering genetic tests for particular patient groups. It should be noted that frequency estimates of incidental findings vary between studies.^{14,15} Some of the variation relates to the inclusion or exclusion of individuals with a recognized family history of a Mendelian disorder, as well as the threshold used to assign pathogenicity to variants.

When physicians receive incidental or secondary findings in the course of testing, a question arises concerning what should be related to the patient. There is robust bioethical debate on the disclosure of such findings in clinical practice. There is consensus in the medical community that secondary findings with actionable clinical significance should be returned.

However, there is a spectrum of opinion about which conditions and variants meet these criteria, and the extent to which patient preference should be taken into account. Although studies have found widespread support among lay people for the return of

clinically actionable secondary findings,¹⁶⁻¹⁸ some patients can be expected to invoke their right not to know.¹⁹ Such a situation pits autonomy and beneficence in direct opposition to each other. Supporters of disclosure advocate overriding a patient's refusal of information when the incidental findings have confirmed clinical utility.²⁰ Yet the territory of "clinical utility" can be uncertain, particularly where material information is concerned. Providers may disagree whether findings such as carrier status, nonpaternity, consanguinity, or certain sex chromosome anomalies—which have the potential to impact both the patient and his or her family—meet the threshold of clinical utility.

Others advocate for a "right not to know" specific genetic information. Arguments against disclosure have ranged from respect for patient autonomy to the net harms of psychological impact, stigmatization, and overtreatment—particularly with regard to variants of unknown significance or results with low clinical utility. Countering this position is the argument that a lack of disclosure could impact later treatment decisions and thus reduce future autonomy.

A presidential commission and several physician body recommendations have encouraged disclosure, though they vary in their support for provider discretion. The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, meeting in the 1970s and 1980s, used the example of nonpaternity as a starting point for discussion and advised that "full disclosure, combined with careful counseling that goes well beyond information-giving, would seem most likely to fulfill the principles of autonomy and beneficence. When circumstances preclude this, however, an approach that accurately provides information on the genetic risk, even when the individuals counseled are sometimes left with an incomplete understanding of the reasons, is generally preferable."²¹ Some 40 years later, the Presidential Commission for Bioethics adopted a markedly different stance when it issued its set of practice guidelines for clinicians, researchers, and DTC providers and specified that "clinicians should engage in shared decision making with patients about the scope of

findings that will be communicated and the steps to be taken upon discovery of incidental findings.

Clinicians should respect a patient's preference not to know about incidental or secondary findings to the extent consistent with the clinician's fiduciary duty."²²

In 2016, the ACMG updated its 2013 recommendations for the return of results for pathogenic mutations, which now includes 59 specified genes with disorders with high penetrance and actionable interventions.²³ Three years earlier, the group incited controversy when it recommended return of results for 56 enumerated genes despite patient preferences to the contrary, citing the fiduciary duty of clinicians and laboratory personnel to prevent harm regardless of patient wishes. At that time, the ACMG asserted that "this principle supersedes concerns about autonomy, just as it does in the reporting of incidental findings elsewhere in medical practice."^{24,25} This position met with considerable backlash,²⁶⁻²⁹ and in 2015 the group published updated guidelines recommending that providers discuss "opt-out" provisions with patients during the consent process, thereby allowing the opportunity to refuse analysis of genes unrelated to the original indication for testing.³⁰

With regard to minors, the ACMG currently advocates reporting incidental findings regardless of the patient's age, because pediatric sequencing may be the only opportunity for such results—which have relevance to the health of one or both parents—to come to light. In contrast, an older AMA guideline advised entering the secondary finding information into the medical record but deferring a discussion of the results until the child reaches majority or is making reproductive health decisions.¹² In the era of the Health Insurance Portability and Accountability Act and patient-accessible electronic medical records, the viewpoint expressed in the AMA guideline may not be implementable.

Research Considerations

In recent years, there has been a growing call for returning clinical trial results to study participants. Although the return of results is ethically and practically nuanced in the clinical

sphere, the essential duty of a provider to secure the welfare of his or her patient provides a measure of clarity. In the research realm no such physician-patient relationship exists, and a researcher's legal and ethical obligations to return results to subjects are murky.

At the heart of the distinction between research and clinical practice is a divergence of purpose. Clinical practice seeks to optimize health outcomes for an individual, whereas research pursues generalizable knowledge through hypothesis testing to optimize health outcomes for a population. Emerging from these differences are separate sets of legal obligations, ethical duties, and governing regulations covering clinicians and researchers, as well as separate sets of rights and protections owed to patients and subjects. Although researchers must protect subjects from harm, they have no duty to provide clinical benefit. Although laboratories conducting clinical genetic tests used in patient care must adhere to federally mandatory quality oversight and receive Clinical Laboratory Improvement Amendments (CLIA) certification, sites conducting genetic tests for research purposes alone are technically exempt,³¹ though this exemption is controversial and contested when studies return individual research results. More recently, the FDA has made recommendations for next-generation sequencing testing in the research setting, particularly when there is return of results.³² Furthermore, because many clinical trials take place overseas, the requirement to adhere to regulations and standards may become less clear.

The right to information critically distinguishes patients and research participants. In clinical practice, patients have an undisputed right to access their information under the Health Insurance Portability and Accountability Act. In research, participants are granted no such unrestricted right to information; in fact, institutional review boards retain the right to determine whether specific disclosures may harm subjects. Furthermore, subsequent researchers may want to use genetic data for future investigations, making it difficult to keep participants abreast of the various uses of their genetic data.

The obligation of researchers to return genetic testing results to subjects was at the heart of a 2002 Wisconsin case, *Ande v. Rock*, in which plaintiffs sued researchers, alleging wrongful birth due to the failure of physicians to discuss the risk of conceiving a child with genetic or congenital abnormalities.³³ At issue was a state-wide, randomized controlled study involving newborn screening for cystic fibrosis (CF). The research was intended to assess whether early diagnosis of CF and subsequent nutritional intervention improved outcomes. Information on the research was included in a pamphlet that all parents received before their infant underwent mandatory newborn screening.

Under the research protocol, excess blood drawn during screening was provided to the investigators and tested for CF. The researchers notified families in the treatment arm when their child tested positive for CF and offered to place the infants on a nutritional support regimen; families in the control arm were not notified if their child tested positive for CF. When an expectant couple in the control group learned of their 2-year-old daughter's CF diagnosis during clinical care unrelated to the study and their second child was subsequently diagnosed with CF at birth, they sued the researchers for medical malpractice. The Wisconsin Supreme Court ultimately held the researchers not liable. Reasoning that the provision of medical care is tightly bounded from a legal perspective by the requirement of a physician-patient relationship—a contractual agreement involving medical treatment—the court held that the return of results in the research setting failed to meet the bar for a physician-patient relationship.

Notwithstanding the outcome of this case, there are compelling ethical arguments for disclosing genetic findings to individual subjects. A number of consensus statements, guidelines, and committees have used clinical relevance and actionability as the benchmarks for returning individual results to study participants.^{31,34-36} If results are to be returned, the possibility of disclosing such findings must be discussed during the informed consent phase, and the subject must have indicated a willingness to receive information. Furthermore, it is essential that planning for returning results be made during the development of clinical

research protocols, because this will ensure that the practical mechanisms and funding are in place for this undertaking.

Although there are decreasing numbers of advocates for withholding individual research findings that are urgent and actionable,³⁷ a number of commentators have nevertheless broached concerns about returning results in the research setting. Such points tend to focus on the poorly understood nature of exploratory findings,³⁴ the unresolved question of whether individual research results in genetic studies are in fact subject to CLIA,³¹ the resource burden of verifying results in CLIA-certified laboratories before return,^{38,39} and the risk of therapeutic misconception, which occurs when a subject incorrectly believes that participation in a study will provide a clinical benefit.^{40,41} Although these constraints are often a practical necessity, they may make it difficult for participants to grasp fully the information being provided to them, and may lead to more confusion and distress than warranted.

Further cost considerations and practical concerns weigh heavily. Much clinical research is undertaken in settings in which there is little long-term follow-up, and funding for continued monitoring is scarce. These concerns are compounded for research based in countries with less developed health care systems. In such situations, practical follow-up becomes more difficult, and even the most well-intentioned researchers may be unable to return results.

Last, an additional layer of complexity arises when physicians have both treatment and research relationships with patients. Given the broad ethical consensus, challenges to investigators moving forward will include working with institutional review boards to define returnable results and determining the means by which findings will be delivered to study participants.

PRIVACY AND CONFIDENTIALITY

Privacy and the Threat to Anonymity

The right to privacy is tightly guarded in the American legal and cultural traditions, and Americans have come to expect informational privacy in health care delivery and health sciences research.⁴² Informational privacy is the freedom from intrusive, public access to

personal information, and within the health care sphere, confidentiality—the duty of entrusted third parties to safeguard an individual's data—is a closely associated concept.⁴³ These values run up against the current direction of genetics research, which trends toward collaboration, data sharing, and large-scale research networks. Although data sharing in genomics research has enabled genome-wide association studies and research on rare conditions, such practices make the guarantee of subject anonymity harder to secure.⁴⁴

Threats to anonymity in the age of genomics have intensified with the growth of the genetic genealogy market. Genetic genealogy companies, such as 23andMe and [Ancestry.com](https://www.ancestry.com), offer to provide customers with information on distant patrilineal relatives by genotyping. In the past, these companies have focused on polymorphic short tandem repeats on the Y chromosome and have maintained massive databases linking Y-chromosome haplotypes to surnames. More recently, Y-chromosome single nucleotide polymorphism and autosomal single nucleotide polymorphism chip-based genotyping and next-generation sequencing have been used.⁴⁵ The privacy, security, and ultimate intention of these companies raise ethical quandaries about how private sensitive, genetic information will be and how accessible this data could be for both personal and commercial purposes.

Several cases have been reported of male adoptees and children of anonymous sperm donors using genetic genealogy services to identify the surname of their biological father; by genotyping themselves and searching the available databases, these individuals have been able to find paternal relatives and ultimately uncover the identity of the biological father.⁴⁶ Users of DTC genetic testing services have also experienced the incidental discovery of nonpaternity or previously unknown half-siblings.^{47,48} As the Internet facilitates the aggregation of information and more research creates accessible large-scale genomic repositories, the potential for reidentification only promises to increase in the coming years. Given these recent cases, researchers have postulated that identifying individuals in sequencing projects would be possible by using similar methods. In a 2013 study, researchers were able to reidentify previously deidentified

personal genomes using open-access, online resources; the researchers in this particular study had a 12% success rate in recovering the surnames of American white males through data triangulation.⁴⁹

The explosion in health information made possible by sequencing technologies has raised fears of discrimination against presymptomatic individuals found to be susceptible to genetic conditions. During the 1990s and early 2000s, these concerns were especially strong with respect to the insurance industry. The Genetic Information Non-Discrimination Act (GINA) was passed by the United States Congress in 2008 to counter widespread concerns about discrimination. Despite the legislation's relative longevity and reach, many physicians are unaware of GINA or limited in their knowledge of its content.⁵⁰ The result of 13 years of debate in Congress, GINA prohibits health insurers and employers of 15 or more individuals from discriminating on the basis of genetic risk profile and bars these groups from requesting or requiring an individual to undergo genetic testing. Under GINA, an individual's genetic information encompasses family history up to and including fourth-degree relatives.⁵¹ Despite its expansion of protections for individuals at risk for genetic disorders, GINA has been criticized for a number of shortcomings.⁵² Specifically, it does not cover life insurance, disability insurance, and long-term care insurance, and employers may still make conditional offers of employment contingent on employee disclosure of all health records, per the Americans with Disabilities Act.⁵³ Furthermore, the law applies only to individuals at risk for developing a disease with genetic basis, not to patients with known, existing disease. In addition to GINA, legal protections related to genetic discrimination and privacy are provided by laws in many, but not all, states.

Duty to Warn: The Limits of Confidentiality

Although physician-patient privilege forms a cornerstone of American medical practice, confidentiality in the doctor-patient relationship is not inviolable. A physician's ethical and legal obligation to break confidentiality has been established by the duty to warn doctrine, which emerged from 2 rulings in the case of *Tarasoff v. Regents of the University of*

California. The suit involved a graduate student, Prosenjit Poddar, who became obsessed with a fellow student, Tatiana Tarasoff, and told his psychologist that he was planning to kill her. Although the therapist contacted the police, Poddar was deemed rational and ultimately released; no direct warning was given to Tarasoff or her family. When Poddar killed Tarasoff some months later, Tarasoff's family sued the university and several of its employees. The California Supreme Court found that therapists have a duty to protect identifiable victims of an intended violent crime by warning them directly, notifying the authorities, or taking any reasonable, necessary steps given the circumstances.

Although the *Tarasoff* rulings established that mental health professionals have a duty to protect third parties, the doctrine has expanded to cover medical providers as well. Such an expansion is evidenced in physician reporting of infectious diseases, impaired drivers, injuries from weapons, partner notification, intended violent crimes, child abuse, elder abuse, and intimate partner violence. The conditions warranting a *Tarasoff* invocation generally include a high likelihood of serious harm, a lack of less invasive means of warning those at risk, and an ability of the third party, once informed, to take measures to prevent harm.

Given the familial nature of genetic conditions, there arises an ethical and legal question when a physician learns the results of a patient's genetic testing: what are the physician's obligations to warn the patient's family members of their genetic risk? Complicating the analogy to *Tarasoff* conditions are the uncertain realities of many genetic disorders—the harm may not be imminent because of the late onset of a condition, the harm may not be absolute due to incomplete penetrance or multifactorial inheritance, and there may be no actionable intervention to mitigate the harm.

Although several cases have addressed whether there is a duty to warn in the age of genomics, there is little consensus among judicial decisions. One of the earliest cases to take up the question was *Pate v. Threlkel*, decided by the Florida Supreme Court in 1995.⁵⁴ The plaintiff, Heidi Pate, sued her mother's surgeon, Dr James Threlkel, 3 years after he

treated Pate's mother for medullary thyroid cancer, for which an autosomal-dominant familial form with high, but incomplete, penetrance exists. Pate alleged that Threlkel had a duty to warn Pate's mother about the potential for a genetic basis to the cancer. After developing medullary thyroid cancer herself, Pate claimed she would have pursued preventative treatment had she originally been made aware of her genetic risk.⁵⁵ The court held that "physicians may owe a legal duty to the children of a patient if the children are identified beneficiaries of the prevailing standard of care" but that duty could be discharged by warning the patient directly.⁵⁴ Or, in other words, that the provider's duty could be addressed by informing the patient that specific relatives were at risk and encouraging disclosure.

One year after *Pate*, the New Jersey Supreme Court reversed a lower court's decision in *Safer v. Estate of Pack*. The suit centered on a case of familial adenomatous polyposis. Donna Safer, the adult daughter of Robert Batkin, sued the estate of Dr George Pack, Batkin's physician, when she developed colon cancer. Pack had treated Batkin 40 years earlier for multiple polyposis, which at the time was known to have a heritable form. Safer alleged that Pack had a duty to warn his patient's family members about their potential risk so that they could benefit from early screening and surveillance. The lower court ruled in favor of Pack's estate on the grounds that physicians did not have a duty to warn someone with whom there was no physician-patient relationship and that genetic diseases were different from infectious diseases with respect to harm; this holding was then overturned by the superior court. In *Pate*, the Florida court had held that physicians could satisfy the duty to warn family members by counseling the affected patient, whereas in *Safer*, the court stipulated that physicians have a duty to warn family members directly.

Roughly 10 years later, the Minnesota Supreme Court in *Molloy v. Meier* took up the question of duty to warn a patient's parents of recurrence risks. The case centered on the malpractice issue of failure to diagnose and the concomitant liability of failure to warn. In the early 1990s, Kimberly Molloy noticed her young daughter's developmental delays and sought care from a pediatrician. The

physician noted fragile X syndrome on the differential diagnosis but did not evaluate for it when ordering chromosomal testing, the results of which were reported as normal to the parents. The child was subsequently seen by a pediatric neurologist, who similarly failed to recommend testing for fragile X syndrome. When Molloy remarried and gave birth to a second child who was subsequently diagnosed with fragile X syndrome, Molloy sued her eldest daughter's physicians for malpractice.⁵⁶ The Minnesota court held that a physician's duty "regarding genetic testing and diagnosis extends beyond the patient to biological parents who foreseeably may be harmed by a breach of that duty,"⁵⁷ thus expanding the duty to warn to parents of childbearing age about recurrence risks.

Although states have disagreed on specific legal parameters of a clinician's duty to warn family members of genetic testing results, professional societies have largely agreed that disclosure discretion should be left to the provider.⁵⁸ In 2009, the American Society of Human Genetics recommended that clinicians at a minimum inform patients about the familial implications of results, both before and after testing, and encourage disclosure to at-risk relatives.⁵⁹ Physicians have the discretion to inform family members when attempts at encouraging voluntary disclosure by the patient have failed, the risk of harm is likely, and the extent of harm is high, the at-risk individuals are identifiable, and there exists an actionable medical intervention.

CONCLUSION

With the advance of genetic and genomic technologies, the shortage of readily available genetic counselors, and the rise of at-home, DTC genetic testing, clinicians will increasingly be faced with the management and contextualization of their patients' genetic information. This will put increased pressure on providers to understand the practical and ethical complexities of genetic testing. As the role of clinicians in this process is in steady flux, it is more important than ever that the medical community engages with and understands the promises, perils, and limitations of genetic tests. Indeed, for physicians to remain relevant and continue serving their patients, this knowledge and understanding will be essential.

We have endeavored to provide an overview of the ethical principles and history underlying clinical genetics essential for physicians navigating this constantly evolving landscape. As evidence-based ethics research is conducted and the gap is narrowed between technological capabilities and provider-targeted policies and recommendations, engagement with the ethics of genetic testing will allow clinicians to better serve their patients.

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Abbreviations and Acronyms: **AMA** = American Medical Association; **ACMG** = American College of Medical Genetics and Genomics; **CF** = cystic fibrosis; **CLIA** = Clinical Laboratory Improvement Amendments; **DTC** = direct-to-consumer; **FDA** = Food and Drug Administration; **GINA** = Genetic Information Non-Discrimination Act

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