Ethics of genomic technologies in medicine

Amanda Courtright-Lim
Mary Drago

Abstract

This article explores the rapid shift of genomic technologies from biomedical research to medical applications. This has led to the development of precision medicine, which can use genetic testing, gene therapy and gene editing for targeted care based on genetic information. The evolution of this targeted approach has advanced from using genetic information to inform care to developing care tailored to individual genomic information. Physicians are compelled to integrate genomic technologies for optimal patient care. Through multiple case studies, the authors highlight ethical considerations that physicians face when incorporating these technologies, emphasizing informed consent for transparent integration. Subsequently, addressing broader societal concerns, the article underscores the importance of equitable access. This exploration aims to provide physicians with a foundation to ethically facilitate access to these technologies that meet the needs of all patients.

Keywords Autonomy; equitable healthcare; gene editing; gene therapy; genetic testing; genomic technologies; informed consent; social determinates of health

Key points

- Genomic technologies — genetic testing, gene therapy and gene editing — are being integrated into medicine
- Physicians will be looked to as gatekeepers to help patients access these novel medical approaches
- Ethical concerns arise when patients are not adequately informed of the risks, benefits and alternatives of novel treatment options
- The integration of these genomic technologies can widen the disparity gap in healthcare if they are not adopted in an equitable manner
- Physicians are best positioned to assist in an ethical adoption of novel genomic technologies into medicine

Introduction

The field of genomic research has been moving at an exponential rate, which has often outpaced the ethical discourse of the resulting genomic technologies. These genomic technologies have been moving into medical practice, but often before all ethical considerations associated with the technology have been addressed. This is the result of a combination of slow regulatory processes, the fast-paced biotech industry and patients' desires for the resulting applications. With this shift, physicians, especially in specialty areas, have found themselves needing to engage in these genomic technologies to provide optimal care for their patients.

This article explores the use of these technologies to evaluate the ethical considerations that arise when they are implemented in medical care. To do this, we must first evaluate the growing field of precision medicine and the genomic technologies being used — genetic testing, gene therapy, and gene editing — to provide targeted care based on genetic information. Then, we explore the ethical considerations associated with informed consent and equitable access that arise from integrating these technologies into practice. The goal is to provide physicians with insight into the newest technologies and their treatment options while spotlighting that there are ethical considerations that they should be aware of with these treatment options.

Genomic technologies

Precision medicine, previously referred to as personalized medicine, is medical care for a particular group of patients that can be informed by environment, lifestyle and the person's genomic/molecular profile. The idea of personalized medical care was introduced to the public in the late 1990s, with growing interest in its integration into the healthcare system.

Over the last two decades, the field of biotechnology has produced technological advancements that have been integrated into healthcare. One group of advancements are focused on the latter area of precision medicine —individuals' genomic/molecular profiles. The integration into healthcare has opened up new possibilities in identifying and treating a disease based on an individual's genetic information. Medical physicians, both generalists and specialists, should understand the nature of these technologies and their limitations for appropriate use in treating patients. A necessary aspect of this is understanding the scope of these various technologies and how they can be used to care for patients.

Genetic testing (Table 1) is one of the earliest technologies in this space that looks to evaluate genetic changes to predict or diagnose a condition. A practitioner in a medical setting or an individual in a direct-to-consumer setting may order genetic testing. Regardless of the origin of the order for the test, it is important that patients understand whether the genetic tests are screening tools or diagnostic tests; even more importantly, it is necessary to understand how the result might guide care.

For example, in prenatal medical settings, women can opt into genetic screening to identify whether they are carriers of a specific condition. If testing identifies a significant marker, follow-up

Amanda Courtright-Lim *MA is a Senior Program Coordinator in Biomedical Ethics at the Mayo Clinic, Phoenix, Arizona, USA. Competing interests: none declared.*

Mary Drago *PhD is a former President of the Arizona Bioethics Network, Phoenix, Arizona, USA. Competing interests: none declared.*

Genetic technology definitions

Genetic testing — an application that uses information from the person's genetic make-up to gather insights into potential health risks, identify specific conditions or tailor treatment strategies based on genetic information.
Examples: Non-invasive prenatal testing, pharmacogenetic testing.
Gene therapy — a form of treatment that uses viral genomes to modify a person's genome of specific cells with the goal of preventing or treating a condition caused by an individual's genetic make-up.
*Examples: Zolgensma — survival motor neuron 1 (*SMN1*) gene therapy, Luxturna — retinoid isomerohydrolase (*RPE65*) gene therapy.*
Gene editing — a group of therapies that use an editing system found in bacteria in combination with a person's own DNA repair machinery to add, delete or alter a location in an individual's genome.
Example: Casgevy — CRISPR/Cas9 genome-edited cell therapy for sickle cell disease, CAR-T cell therapy.

Table 1

screening should be performed on the biological father, followed by diagnostic genetic testing of the fetus to determine if the mutation was inherited. If the result comes back positive, the practitioner can assist the family in making a decision on whether they continue the pregnancy. If they choose to continue, specialists must be involved in the follow-up care for the child's genetic condition. In this situation, genetic screening and diagnostic testing are used, but the decision to continue the pregnancy happens as a result of the diagnostic testing. The next example will demonstrate that decisions can also be made based on genetic screening results.

Genetic screening is not a diagnostic measure but a tool to identify the risk of a certain condition. Screening testing can be used to initiate follow-up testing, continue monitoring to determine the presence of the suspected condition, or engage in preventive interventions to reduce the chance of disease onset. In the case of breast and ovarian cancer, mutations in the *BRCA* gene increase the risk of developing the disease by as much as 60%. Although this marker is not a diagnosis, 27.8% of individuals had a prophylactic bilateral mastectomy to remove breast tissue, and 64.7% had bilateral salpingo-oophorectomy, to remove the ovaries and fallopian tubes, to reduce their risk of developing breast and ovarian cancer by 90%.[1]

In this case, treatment decisions in care are based on the risk of developing breast cancer and not the presence of the disease. What is paralleled across both the prenatal genetic diagnosis example and the breast cancer genetic risk screening example is that they involve evaluating genetic information to make decisions on an individual's care. That genetic information is at the root of the other two more recent genomic technologies to consider.

Gene therapy (Table 1), also known as gene replacement therapy, emerged in 1990 and had approved therapies coming off clinical trials in the 2010s. As mentioned earlier, precision medicine is focused on providing treatment for targeted populations. Gene therapy uses genetic information as part of the therapy. Specifically, it is a treatment designed to address a specific genetic condition.

These therapies involve using a viral vector to introduce the functional gene into a cell population. That functional gene can have either a short-term or a long-term activation period. For the gene therapies discussed in this section, the functional gene is not inserted into the genome of the targeted cells. Instead, it functions in the viral vector under its own promoter mechanism as part of the safe measures. These therapies are not meant to reverse a condition but to slow the progression of the disease.

The first therapy approved under this known mechanism was in 2017 for Luxturna from Spark Therapeutics. In this initial drug, functional cells must still be present in the affected eye being treated. If no retinal cells are present, the treatment cannot be administered as it cannot reverse the cell loss. This builds on the wider model of medications as agents that reduce the progression of the disease. This is an approach that looks to harness the affected cells to stop the progression or reverse the disease, in effect looking to eliminate the condition.

Gene editing (Table 1) is a subform of gene therapy that focuses on altering the genome in relation to a disease. In contrast to the initial gene therapies, the focus is to alter the DNA of the target cells to establish a functional pathway. Also referred to as gene-editing therapies and clustered regularly interspaced short palindromic repeats (CRISPR) therapies, this approach can be used to alter cells outside the body before they are reintroduced (*ex vivo*), or inside the body (*in vivo*).

This sub-therapy is focused on addressing single-gene disorders. The first therapy, which received approval in the UK and USA in late 2023, is exagamglogene autotemcel (exa-cel), under the brand name Casgevy. This therapy uses the CRISPR editing mechanism to alter the haemoglobin genome underlying transfusion-dependent b-thalassaemia and severe sickle cell disease. It does not directly target the genetic change associated with these conditions. Instead, it harnesses the pathway to express a form of haemoglobin that does not lead to the crescent-shaped blood cells associated with these conditions. The current discourse is that this is not a true cure, as the individual still has sickle cell disease in their genome, but the physical effects of the disease are reduced and in many cases eliminated for those in the clinical trial. This sets the precedence that it is possible to address genetically driven diseases through a gene editing approach.

The emergence of gene editing and gene therapy as innovative treatments opens up new avenues for using the genome in medical contexts. Just like genetic testing before them, however, these novel approaches raise important ethical considerations. Healthcare practitioners should be mindful of these concerns as they incorporate these cutting-edge genomic medical technologies into patient treatment.

Consideration of genomic technologies in medicine

Physicians should be aware of three points when looking at integrating these latest genomics technologies into their practices. First, preceding the success of these approved genetic tests and therapeutic approaches are the early versions of these genetic tests and therapies that failed. Second, those failed approaches had negative impacts on real-life patients and altered the public's trust in novel genomic therapies. This leads to the final point: physicians should be vigilant about understanding genetic tests and genetic therapies before offering them to their patients. That vigilance relates to not only the science of these technologies and how they work, but also the social impact that these genomic approaches have in healthcare more broadly.

This vigilance is important not only because physicians are the gatekeepers to these treatment options, but also because of the significant trust placed on them by patients. Patients and family members often ask their doctors' opinions about a treatment option before making a decision about the course of care.[2] As gatekeepers, physicians will be looked to for guidance on these treatment options as these approaches are integrated into practice. That integration process is fraught with ethical considerations. Focusing on these considerations, physicians must ensure that patients are informed when making decisions about therapies. They must also use their position to facilitate the equitable application of these technologies to allow for justice-based medicine so that these novel genetic technologies in medicine are integrated in a manner that aligns with ethical, legal and social considerations.

Consideration – informed consent

Participating in genetic testing, gene therapy or gene editing mandates the provision of comprehensive informed consent. This practice is not only ethically sound, but also a legal imperative. For physicians using innovative genomics technologies, it is crucial to ensure that patients are well informed. This contributes to the ethical foundation of applications as well as serving as a legal safeguard against potential litigation. While each case is unique, tailored to the patient's medical condition, the common thread lies in educating the patient about the advantages, risks and alternatives associated with the testing, procedure or intervention. The essence of informed consent lies in the knowledge imparted to the patient, regardless of the specific context requiring it.

The novelty of each genomic technology introduces a landscape where both risks and benefits are still in the process of identification. Patients should be aware of the limited insight that we have about the longer term benefits and risks, as well as know that new information will become available as the application of these technologies grows. To be able to impart that knowledge, physicians themselves must understand these precision technologies. Current data show that physicians are receiving inadequate training in genomic medicine and should seek additional education to supplement those gaps. To be ethically sound, physicians should be transparent with their patients about their understanding of technologies, and know when to involve professionals who are able to engage in adequate informed consent.

In Table 2, Case 1, the physician faced with a patient who does not want to share their genetic testing results with their extended family, even though that information could benefit those individuals. The patient's resistance to sharing is grounded in cultural norms. It is both unethical and legally inappropriate to go around the patient to inform the family. What is more appropriate is to provide counselling for this information that engages with that individual's culture.

In an ideal situation, a genetic counsellor should be engaged as they have the training or access to resources that allows them to approach the situation with cultural competence. This allows the patient to be fully educated, in a manner that aligns with their culture, to make an autonomous decision about sharing the genetic testing information. Physicians should understand that decisions may not align with their own cultural beliefs about what should be done and that their place is to inform a patient and not undermine that individual's choice.

The second and fourth cases in Table 2, will underscore that what seems ethically appropriate may not be socially or legally appropriate. The latest genomic technologies have always been represented as cutting-edge tools that will change the current approach to medicine. If we look at the oldest technology – genetic testing – genomic assessment is being used to determine a cancer treatment plan, or whole-genome testing can be carried out on an ailing infant on a neonatal intensive care unit to determine if they have a rare disease that needs to be considered in their care plan. These techniques are changing aspects of medicine, but we must remember they are just tools – tools that may not be appropriate for use in all situations.

If we look at Case 2, we have a parent who is being offered a novel technique, with chimeric antigen receptor (CAR) T cell therapy as the last option for treating their child's cancer. In this case, the parent seems resistant to seeking treatment in part because she is worried about her daughter's quality of life. Patients should weigh both the risks and benefits of treatments, and that can include the mental impact of a treatment plan. It is important that physicians balance offering treatment and making patients aware of alternative options, such as comfort measures in the situation of terminal cancer. In this case, if a parent selects to seek comfort measures for this child, that is their right as the legal guardian to make that autonomous decision about the course of their child's care.

It is important to note that there have been legal conflicts in the UK regarding treatment options with patients who are minors. In these situations, the child was terminally ill with an irreversible condition, but the family wanted to continue care. The hospitals argued in courts that the child's best interests need to be valued, that seeking experimental treatment and continuing life-sustaining treatment would provide no benefit, and that all treatment was prolonging the suffering of the terminally ill child.[3]

Legal precedent in the UK has allowed the court to resolve the conflict between the patient's guardian(s) and the physician(s) in determining what course of care is in the child's best interest. Even though these situations were legally resolved, there was a significant concern among the public regarding taking away the parent's right to make decisions for their child, creating a conflict in the legal precedence and the social perspective. In this case an argument could be made that the parent does not have the child's best interest in mind when selecting not to access CAR-T cell therapy, but it also raises the concern that it is socially impropriate for the physicians to override a parent's decision for their

Case studies

Case 1: genetic testing

A man in his late 20s presents to A&E with a bloated abdomen and significant stomach and back pain. During the admission, it is established that he has stage 2 pancreatic cancer. Surgery is performed, and the tissue is sent for genomic analysis. The results come back indicating the individual has a mutation in the *RABL3* gene, which is associated with an increased risk of cancer. The man's father and three uncles all died from pancreatic cancer. The treating oncologist knows his patient has no siblings but has multiple male cousins, most of whom have children. The practitioner suggests the results be shared with the man's extended family, as they may be at an increased risk for developing pancreatic cancer, which has a low survival rate when caught in stages 3 and 4. The man declines to share the information on the grounds that it is not culturally appropriate to discuss your health with your extended family.

Case 2: Gene editing: CAR-T cell therapy

An 8-year-old girl has been referred to the paediatric allogeneic stem cell service in Glasgow by a specialist from Royal Aberdeen Children's Hospital. The child has B cell acute lymphoblastic leukaemia and is no longer responding to standard-of-care treatment. The child's mother has travelled for 4 hours by train and bus to the appointment to have her daughter evaluated for CAR-T therapy, which involves reprogramming a patient's own immune system cells to target their cancer. At this appointment, the mother learns that her daughter is a candidate, but she will need to travel to a children's hospital in England for treatment. The mother is unsure if she has the financial means to do this and also worries that being away from the family will tarnish her daughter's final months if she does not respond to treatment.

Case 3: Gene editing: sickle cell anaemia

Your 41-year-old patient has had multiple sickle cell vaso-occlusive crises (VOCs) and recently learned that the UK has authorized a therapy for the treatment of sickle cell anaemia and β-thalassaemia using CRISPR technology. She wants to secure treatment not only for herself, but also for her now 15-year-old daughter. Her daughter has not experienced any VOCs, but the mother would still like the treatment anyway to keep her daughter from suffering the stigma she has endured when continually presenting to A&E in a crisis and requiring pain medication.

Case 4: Gene therapy: SMA

A 13-month boy with significant developmental delay was seen by the paediatrician. The child was unable to sit without support and had very limited movement with no sign of progress toward crawling. He had also developed feeding issues and was losing weight and showing signs of laboured breathing. After the child was referred for genetic counselling, genetic testing confirmed that the child had SMA type I and was started on Spinraza treatment given every 4 months. The parents returned requesting that their child be given the latest gene treatment for SMA, a one-time gene therapy called Zolgensma. They are informed that their child does not qualify for that treatment with the NHS as it is only available for children <12 months old because of the risk of significant adverse drug reactions in older children. The parents indicate that they are willing to accept that risk, as the current treatment with Spinraza is more invasive and requires injection directly into the spine multiple times a year indefinitely.

Table 2

child's care. Demonstrating conflicts that arise in the face of developing genomic treatment options. In some situations, that decision is already made for the physicians.

Many of these new genomic technologies are still in the early phases of approval and application. Continued use of treatment can provide information that changes treatment eligibility. This is what is taking place in Case 4: the 13-month-old infant has been identified as having spinal muscular atrophy (SMA), and the parents are requesting the one-time gene therapy Zolgensma for their child. In this situation, this treatment is available but is limited to children <12 months of age in the UK because of adverse drug effects in older children. As a physician, you have to follow the legal regulations and provide only the treatment options that are approved. In the case of SMA, the physician can offer other treatment options. Based on the existing regulation and Zolgensma's current approval in the UK, the physician has selected the appropriate path. If a patient is still interested in a novel treatment, there are avenues to access them, such as a clinical trial setting. For many of these newest therapies, clinical trials are still taking place to determine the benefit to other age groups and the appropriate dosage.

Looking back to the late 1990s, gene therapy trials faced setbacks, leading to safety improvements in modern gene therapies, with today's gene therapies aiming to minimize immune reactions and secondary effects. The lesson learned from previous work paved the way for gene therapy trials to be successful and focus on determining optimal treatments for diverse patient groups. That does not, however, guarantee that all future applications will be devoid of negative outcomes. As a physician, you can support a patient's choice to seek a clinical trial by providing the trial information that is publicly available, but you should refrain from influencing the choice to participate. Instead, allow the clinical trial team to provide appropriate consent that allows your patient to make an autonomous decision to participate. As we will see, autonomous decision-making can be complex in certain situations.

In Case 3, physicians may find themselves sitting in a grey area where the regulation is still limited because the therapy is in conditional approval, meaning it has been approved by the Medicines and Healthcare products Regulatory Agency (MHRA) through the Conditional Marketing Authorization (CMA) scheme so the treatment can be marketed ahead of completing the clinic trials. This means that research is still being conducted to capture the safety and efficacy of this treatment option. This is a precarious balancing act that should only be engaged in by specialists. Here, we will get a sense of the ethical considerations those specialists are making regarding informed consent. In this case, the patient is seeking treatment for themself and their child, both of them having sickle cell anaemia. As this case indicates, the mother has experienced

hospitalization for complications of her sickle cell anaemia, but the daughter has not.

The gene-editing treatment Casgevy is authorized for use for individuals >12 years of age who have sickle cell disease and β-thalassemia. In this case, both the mother and daughter qualify. Informed consent is vital in a case like this, as it is important to outline potential risks, benefits and uncertainties. Casgevy is an invasive treatment that requires a bone marrow transplant with chemotherapy. Chemotherapy has been shown to impair fertility, and offering this treatment to an adolescent patient requires robust consent, not only for the treatment, but also for the fertility preservation that should also take place to allow for *in vitro* fertilization in that individual's adult years.

The guardian needs to be informed of these risks and procedures, but the child should also be engaged in the informed consent. In this case, the child is just short of the age of consent in the UK, which is 16. This may create a conflict between the mother and child, but it is ethically appropriate even if it is not legally required. There is also an existing precedent for this in genetic testing for the *BRCA* mutation associated with an increased risk of breast cancer and ovarian cancer. In most situations, a minor will not be genetically tested for a *BRCA* mutation even if the parent requests testing. This is too perverse for the child's autonomy to make a choice as an adult to learn about their risk for this adult-onset condition.[4]

The physician involved in this case will need to balance the best interests of the patient and not use the mother's lived experience with her own sickle cell anaemia to justify access to treatment. To adequately engage in this situation, the physician should employ additional expertise such as a genetic counsellor or medical geneticist, reproductive medicine specialist and other professionals who can support both the decision to treat and the long-term care. This can be problematic as the current distribution of healthcare in the UK context and the demand for these technologies, including the need for specialists, already cannot be met. This continued growth will widen disparity gaps and limit access to novel genomic testing and genomic therapies. Physicians should be aware of this and look at how they can help address these gaps.

Consideration – equitable access

Disparities in healthcare exist whether we look to privatized healthcare in the USA or public healthcare in the UK. The global coronavirus disease (COVID-19) pandemic brought these disparities to everyone's attention, but they existed before and have been evident in developing genomic technologies. Exploring all of these disparities is beyond the scope of this article; instead, exploring the case studies will give physicians insight into recognizing some disparities and allow them to consider both the social and medical needs of their patients.

For a new drug to come to market, the cost can be $2 billion (£1.5 billion) for research and development (R&D) and the completion of clinical trials. For gene therapy, the early estimate is around $5 billion (£3.9 billion) for R&D and clinical trials. Although at first glance, the prices may seem fairly similar, that changes when the costs of treatment are expanded.

Looking at Case 4, the parent is requesting the gene therapy Zolgensma for treatment, and this costs $2.30 million (£1.79 million) per dose in the UK. The other drug being prescribed is Spinraza, which costs $572,976 (£450,000) in the first year and $286,488 (£225,000) for subsequent years. That disparity in cost is because of the nature of treatment. Zolgensma, a gene therapy, requires only one dose to halt the progression of SMA. In contrast, Spinraza is a medication that is taken indefinitely to induce cells to produce functional copies of the *SMN2* gene. If Spinraza were discontinued, it would lead to progression of the disease. Zolgensma's high cost is caused by the limited patient population and the pricing strategy employed by the drug company to recover the development expenses.

The upfront cost of gene therapies like Zolgensma can mean that only a limited group of individuals, i.e. those who can afford treatment, can access it if the UK NHS does not offer it. In this case, the NHS has negotiated access, and infants with SMA1, the most severe form that causes death in early childhood, are being given treatment if identified at ≤12 months. This is around 70–80 children per year in the UK, but further clinical trials for Zolgensma may find that it benefits all forms of SMA, which would increase the pool of individuals needing treatment. This raises concerns about how the NHS would help facilitate access for all patients to this high-cost treatment. When we overlay this access concern with Case 3, we can see this issue play out further.

Case 3, for the mother and daughter with sickle cell anaemia, this drug has just come to market under conditional approval. This means the drug can be marketed for use, but the NHS has not negotiated reimbursement with the drug company to make the treatment available to eligible individuals through the NHS. This means that patients who cannot afford an estimated $2 million dollar treatment will not be able to access treatment.

One of the underlying ethical issues is that these drug companies are seeking conditional approval and not utilizing the Early Access to Medicines Scheme (EAMS). EAMS is a pathway that the drug companies can use for drugs to be offered to patients before the company receives marketing authorization. If these novel therapies are approved through EAMS, it could create pathways for patients to access these novel gene therapies as the physician now has authorization to order the treatment, and the drug company will provide it at no cost to the patient. Gene therapies or gene-editing therapies have not at the time of writing been approved under EAMS; instead, companies have obtained conditional approval for marketing the therapy. Under conditional approval, drug companies are not required to offer the therapies for free. Individuals who are prone to sickle cell anaemia are ethnic groups that originate from areas with high rates of malaria, such as India and Africa. These groups are minority populations in the UK that often experience the greatest disparities in income and would not have the means to access therapy outside of the NHS. This creates significant concerns with equitable access in the UK, as amplified in Case 2. In Case 2, a parent has learned that their child can access life-saving treatment but would need to travel a significant distance to access that care. This is a growing problem with genomic technologies as these therapies can require a significant infrastructure and specialized teams to offer treatment safely, which leads to only certain hospitals and medical centres having the means to offer that therapy. Patients and their families are often expected to travel for this care, and although there are charities and social support available, accessing them can be challenging.

Research from the USA has shown that the expectation to travel to care for those who experience lower socioeconomic status or limited transportation keeps a patient from seeking CAR T therapy clinical trials.[5] Although solutions have been offered to address these barriers, they require significant funding and infrastructure to start to create equitable access as they are rolled out in the NIH. As we saw in the last case, access should be tailored to the needs of certain groups, as social disparities are not the same in all populations.

If we look at Case 1, we have a male patient refusing to disclose an increased risk for the cancer he has, which might explain the previous deaths of his father and uncles. The rationale for not disclosing this has been ascribed to the individual's culture. There is another potential factor to consider — genetic literacy. Individuals with higher genetic literacy are more likely to undergo genetic testing and share those results. Minority groups tend to have lower genetic literacy as a result of various socioeconomic factors.

However, data suggest that, when offered genetic testing, some minority groups express greater interest and a higher likelihood of sharing their results with family compared with white participants.[6] In such instances, a genetic counsellor can collaborate with the patient to understand their resistance and determine if there is a suitable approach to sharing the results that hold health implications for their family. Until that specialist works with that patient, it is not possible to know if the patient lacks genetic literacy or if this is truly a cultural norm.

Physicians should recognize that disparities are often oversimplified and biased and can overlap with other factors associated with that patient. That is in part because many of the factors that affect equitable access are interconnected. Addressing them is not a simple fix, meaning that understanding them when working with a patient can be challenging, and this is where a physician needs to be diligent about supporting patients in accessing these novel technologies.

As physicians, it is best to adopt a nuanced perspective that allows for personalized approaches tailored to each patient's needs, culturally, socially and medically. Physicians need not only to be the gatekeepers of these technologies, but also to advocate for those who cannot reach that gate. This approach is crucial for the ethical and equitable application of precision-based therapies, particularly for underserved individuals facing genetically linked conditions with limited treatment options. ◆

KEY REFERENCES

1 Metcalfe K, Eisen A, Senter L, et al. International trends in the uptake of cancer risk reduction strategies in women with a *BRCA1* or *BRCA2* mutation. *Br J Cancer* 2019; **121:** 15–21.

2 Tucker Edmonds B, Torke AM, Helft P, et al. Doctor, what would you do? An answer for patients requesting advice about value-laden decisions. *Pediatrics* 2015; **136:** 740–50.

3 Ross LF. Reflections on Charlie Gard and the best interests standard from both sides of the Atlantic Ocean. *Pediatrics* 2020; **146:** S60–5.

4 Hercher L, Uhlmann WR, Hoffman EP, et al. Public Policy Committee of NSGC. Prenatal testing for adult-onset conditions: the position of the national society of genetic counselors. *J Genet Counsel* 2016; **25:** 1139–45.

5 Kamal-Bahl S, Puckett JT, Bagchi I, et al. Barriers and solutions to improve access for chimeric antigen receptor therapies. *Immunotherapy* 2022; **14:** 741–53.

6 Chavez-Yenter D, Vagher J, Clayton MF, et al. "Being proactive, not reactive": exploring perceptions of genetic testing among White, Latinx, and Pacific Islander Populations. *J Community Genet* 2021; **12:** 617–30.

FURTHER READING

Arabi F, Mansouri V, Ahmadbeigi N. Gene therapy clinical trials, where do we go? An overview. *Biomed Pharmacother* 2022; **153:** 1–17.

Courtright AL, Drago M. Ethics of genetic testing. *Medicine* 2020; **48:** 675–9.

Ormondroyd E, Border P, Hayward J, et al. Genomic health data generation in the UK: a 360 view. *Eur J Hum Genet* 2022; **30:** 782–9.

Schaibley VM, Ramos IN, Woosley RL, et al. Limited genomics training among physicians remains a barrier to genomics-based implementation of precision medicine. *Front Med* 2022; **18:** 1–6.