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Informed Consent in the Genomics Era

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Informed consent, the process of gathering autonomous authorization for a medical intervention or medical research participation, is a fundamental component of medical practice. Medical informed consent assumes decision-making capacity, voluntariness, comprehension, and adequate information. The increasing use of genetic testing, particularly genomic sequencing, in clinical and research settings has presented many new challenges for clinicians and researchers when obtaining informed consent. Many of these challenges revolve around the need for patient comprehension of sufficient information. Genomic sequencing is complex—all of the possible results are too numerous to explain, and many of the risks and benefits remain unknown. Thus, historical standards of consent are difficult to apply. Alternative models of consent have been proposed to increase patient understanding, and several have empirically demonstrated effectiveness. However, there is still a striking lack of consensus in the genetics community about what constitutes informed consent in the context of genomic sequencing. Multiple approaches are needed to address this challenge, including consensus building around standards, targeted use of genetic counselors in nongenetics clinics in which genomic testing is ordered, and the development and testing of alternative models for obtaining informed consent.

As use of genomic testing continues to increase, genetic counselors play a valuable role in genetics clinics and in other clinical and research settings. A genetic counselor's skill set includes the ability to facilitate the consent process for genomic testing, and this can be particularly useful in settings in which other team members may be less familiar with genetics and the complexities of informed consent for genomic sequencing. The increasing use of genomic sequencing by specialists outside of genetics also presents an opportunity for genetic counselors to help ensure that patients providing informed consent understand the information relevant to making an informed decision about testing and have the opportunity to get answers to their questions. Here we describe the history and evolution of informed consent in general medicine, in genetic counseling, and most recently in the genomics era; proposed

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approaches for adapting the informed consent process in a genomics context; and future directions, including the important role for genetic counselors in obtaining informed consent for genomic testing.

HISTORY OF INFORMED CONSENT

Informed consent is the process by which clinicians and biomedical researchers gather *autonomous* authorization for a medical intervention or research participation (Appelbaum 2007; Beauchamp 2011). The concept of informed consent evolved from the idea that patients and research participants have the right to make autonomous decisions about their bodies. Medical informed consent, whether clinical or research focused, assumes decision-making capacity of the person consenting, voluntariness, and comprehension of adequate information (Bunnik et al. 2013a).

Obtaining informed consent is a process. In a genetic counseling setting, this process generally entails a conversation in which the clinician or researcher conveys information about the medical intervention or research study, including the associated risks and benefits, and the patient conveys information about their health-related goals, expectations, priorities, preferences, and concerns. The clinician may assess patient understanding of the information conveyed by asking questions or utilizing a teach-back method. Based on this feedback, the clinician may try different teaching approaches to tailor the information and discussion to the patient's needs. The patient has the opportunity to ask questions, and the person obtaining consent facilitates a discussion with the goal of determining if the proposed intervention or study aligns with the patient's goals and values. Ideally the dialogue takes place over time—a patient may feel differently about the intervention or study at different times, and ongoing communication between the clinician and the patient is key to ensuring responsiveness to the patient's viewpoint as his or her circumstances change (Bernat and Peterson 2006). The process of informed consent is typically documented through both parties signing a form.

Although the concept of informed consent seems as though it must be nearly as old as medicine, in reality it is remarkably new. In fact, for most of the history of medicine, medical ethicists were more concerned with how best to conceal potentially stress-inducing information from patients to reduce harm and anxiety. Even the Hippocratic oath encouraged physicians to keep their patients in the dark as a means of protecting them from undue stress (Beauchamp 2011). It was not until 1947 that the Nuremberg code, created in response to medical experiments conducted in Nazi concentration camps, established the need for voluntary consent and an informed assessment of risks and benefits. It does not, however, specify what information should be conveyed to potential research subjects (Moreno et al. 2017).

Informed consent is not just an ethical and moral concept but also a legal concept developed in the courts, starting with a series of cases beginning in the 1950s. In 1957 the term "informed consent" first appeared in the case of *Salgo v. Leland Stanford Jr University Board of Trustees* (Salgo 1957), in which a patient underwent a novel medical procedure without his physician warning him of the potential risks, including the paralysis that ultimately afflicted him. The ruling by the court focused on the duty of clinicians to disclose risks associated with any recommended procedure but also emphasized the need for patient understanding, reinforcing the idea of patients as autonomous individuals who should be empowered with information to make decisions in their own best interest.

Over the next 15 years, courts refined the concept of informed consent by establishing standards and defining exceptions for when informed consent is not required (Nelson-Marten and Rich 1999; Beauchamp 2011). A series of court cases in the 1970s, in particular *Canterbury v. Spence*, laid the foundations for a patient-oriented standard for disclosure (Spence 2008; Beauchamp 2011). In this 1972 case, a patient undergoing surgery because of a herniated disc was paralyzed. He sued his physician, claiming that he had not been warned of the risks involved in the surgery. The physician argued the risk was small and disclosing it could have provoked

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unnecessary anxiety. The Court of Appeals of the District of Columbia ruled against the physician, stating that he had had an obligation to disclose the risk of paralysis to the patient and described the following types of information as necessary to achieve informed consent: the condition being treated, the nature of the intervention, the likely results, alternative forms of treatment, and serious risks or complications that could result from the intervention (Murray 2012). This ruling dramatically shifted the standard practice of disclosure from the previous physician-centric approach, in which the appropriate amount of information required for informed consent was determined by what other physicians would have done in similar circumstances, to a patient-centric approach, in which the appropriate amount of information is defined as the amount of information a "reasonable patient" would need to make an informed choice about whether to proceed with a given intervention (Beauchamp 2011). Court cases that followed *Canterbury v. Spence* added further disclosure requirements to this standard, but the precise details of the legal requirements for achieving informed consent vary by state (Spector-Bagdady et al. 2018).

As the standards for informed consent have continued to evolve in the courts and in practice, genetic testing technology has evolved alongside it. In the 20-plus years since genetic testing became commonplace in clinic and research settings, physicians, researchers, and ethicists have attempted to apply the standards of informed consent used in medicine more generally and found some of them to be particularly challenging in a genetic context. For example, informed consent requires decision-making capacity, but decision-making capacity may be uncertain in families with suspected genetic conditions that include intellectual disability, autism, or neurodegeneration. The bar for appropriate decision-making capacity may vary depending on the level of risk involved in the intervention or genetic test—riskier interventions generally require a higher level of decision-making capacity and comprehension. Voluntariness may be compromised by family members for whom the testing can also have implications (resulting in subtle, or not-so-subtle, coercion within the family), or clinicians who convey strongly that testing is in the patient's best interest. Comprehension is difficult to achieve and assess when the topic is complicated, as with genetic tests. Finally, the question of what counts as sufficient information has been the topic of numerous court cases and publications and still remains very subjective and dependent upon the patient's needs. Although some of these challenges also arise in consent processes in other areas of medicine, they arise much more frequently in genetics, in part because genetics, by definition, involves the whole family, and because patients in this setting are more likely to have developmental disabilities that may compromise understanding.

INFORMED CONSENT IN GENETICS AND GENOMICS

Informed Consent in the Pregenomics Era

Prior to next-generation sequencing, genetic testing was an iterative process in which a clinician created a differential diagnosis, began by testing the one or two genes most likely to yield a diagnosis, and then tested other genes if the prior test was negative. The traditional genetic counseling approach to informed consent in this context had an educational focus, providing information about the testing process; potential benefits, risks, and limitations of testing; and education about the natural history and potential treatment(s) of the condition(s) for which testing was being performed (Ormond 2013). Although this approach is similar to that used for other medical tests or interventions, the details of the consent conversation differed, particularly with regard to the risks. The most significant risks associated with clinical genetic testing are psychological and social—for example, the risk of anxiety or stress related to presymptomatic knowledge that one may develop a genetic condition for which there may not be any treatments or preventive measures, and the potential risk of stigma or discrimination due to such a genetic test result. The familial nature of genetic information also presents

unique risks. Individuals within a family may have experience living with a genetic condition and may approach an informed consent process with strong feelings about what they do and do not want from testing and what they may do in response. There can be differences in opinion among family members about testing, creating stress or conflict. In research genetic testing, additional risks occur at a group or community level and can include the potential for stigmatization. For example, in 2003 members of the Havasupai tribe discovered that DNA samples collected for type II diabetes research had been used to study schizophrenia, migration, and inbreeding without their knowledge or consent (Garrison and Cho 2013). Community engagement and consent are critical to mitigate these types of problems.

The psychoeducational approach to consent for genetic testing emerged at a time when there were limited data about the potential psychological and social harms of genetic testing and even more limited interventions available for most genetic conditions than exist today. Extensive information was shared in hopes of providing patients with as comprehensive an understanding of the risks as possible. This was possible because it was typically only one condition being tested for (such as Huntington's disease), and the penetrance of the first conditions for which clinical testing was available was typically quite high (as these were the conditions for which it was easiest to establish gene–disease relationships), which removes much of the need to assess the patient's tolerance for uncertainty as part of the consent discussion. Studies suggest that this traditional model was not particularly effective at equipping patients with an understanding of information the authors considered necessary for providing informed consent (Joffe et al. 2001; Lee et al. 2011). Over time, a more traditional psychoeducational model of informed consent for genetic testing evolved to be an interactional and patient-centered approach, mirroring the evolution toward shared decision-making models in other parts of medicine (Kunneman and Montori 2017).

Despite the differences in the nature of the risks of genetic testing as compared to many other types of medical procedures, approaches to genetic testing consent remained primarily information-laden, and this was readily modified to accommodate the single-gene (or small-panel) genetic testing that was available until 2011. However, it has become increasingly clear that this consent approach cannot be scaled to genomic sequencing, and clinicians and researchers face a number of challenges in their efforts to achieve informed consent in the context of genomic sequencing (Ormond et al. 2010; Berg et al. 2011; Bester et al. 2016).

Genomic Sequencing Has Changed Models of Consent

Next-generation sequencing made it possible to obtain a great deal of genetic information quickly and cost-effectively, leading to widespread adoption of panel-based genetic testing and increasing use of exome and genome sequencing in both clinical and research settings. The availability of genomic data created new challenges around informed consent as we have traditionally understood it (Patch and Middleton 2018), including how and whether it is even possible to satisfy the previously accepted standards for informed consent for tests with such expansive implications (Williams et al. 2014; Samuel et al. 2017). Many of the specific challenges of achieving informed consent in the context of genomic sequencing relate to defining the requirement for adequate information and comprehension (see Table 1; Bunnik et al. 2013a). The question of how much information is "adequate" is deeply subjective and poorly defined, and the appropriate amount of information required for a patient to make an informed decision as per the predominant patient-centered standard presents challenges for clinicians. Some patients and families desire significantly more information than others to feel prepared to decide about genomic testing. For example, patients with more lived experience with a condition may have different information needs than a patient with no such familiarity. Clinicians often struggle to determine how much detail to provide about genomic sequencing and how to appropriately simplify the information to

Table 1. Major and unique concepts in informed consent for genomic sequencing

Concepts that differ between genetic and genomic consent	
Concept	***Difference between genetic versus genomic consent***
Scope of test	Scope of test is much larger in genomic testing (e.g., includes all genes rather than just one or a few genes)
Limitations of test	Sequencing-based tests like genomic cannot identify all mutation types Higher chance of uncertain results with genomic sequencing
Potential risks	Genomic data is identifiable in ways genetic data is not, increasing the privacy risks Insurance risks due to secondary or incidental findings Genomic testing can cause stress or anxiety due to: • Learning about unexpected family relationships (e.g., nonpaternity or consanguinity) • Learning about unexpected health risk (e.g., due to secondary or incidental findings)
Concepts that are similar between genetic and genomic consent	
Description of test process/procedures	
Expected benefits	
Costs or payments	
Voluntary nature of the test	
Alternatives to the test	
Confidentiality/privacy	
How/when/to whom results will be returned	
Future use of data/samples	

make it understandable (Ormond et al. 2010; Klima et al. 2014). Too much detail or complexity can negatively impact comprehension, lead to a loss of attention, and/or create unnecessary anxiety. Too little can lead to decisions that are inconsistent with the patient's values or goals. Achieving balance represents the primary challenge when obtaining informed consent for genomic testing and is another reason for the importance of approaching consent as a dialogue between clinician and patient, as the clinician must elicit information about the patient's values, objectives, preferences, and concerns in order to determine what information that patient might need in order to make an informed decision. The patient must also be given an opportunity to ask questions about the information conveyed and to cover any additional information he or she may need to incorporate into the decision-making process.

Challenges of Obtaining Informed Consent for Genomic Sequencing

Genomic sequencing is complex, and it can be difficult for a clinician or researcher to know how deep to dive into that complexity when having a consent conversation with a patient. Currently, genomic testing is most often used when the patient's differential diagnosis is too broad to make single-gene or panel testing practical. The potential range of results is limited only by the number of conditions associated with specific genes (now more than 4000 and rising) (OMIM). This means the possible results are too numerous and diverse to discuss using the traditional consent approach. Rather, clinicians should describe the types of results to patients in broader strokes—for example, describing the possibility that the patient could learn he or she has a genetic difference that provides information about prognosis, including whether treatments or preventative measures are currently available. It can be challenging for patients to understand that, unlike many medical tests they may have had in the past in which the result is binary and immediately actionable, their doctor cannot tell them in pretest what will happen next if the genomic sequencing result is positive, because it depends on what that result is. Patients may also struggle to understand the possibility that the result may change over time (e.g., if a variant of uncertain significance is reclassified as pathogenic several years

later) or the possibility that the test will yield unexpected findings that are unrelated to the primary reason for testing (often called secondary or incidental findings). The issue of future re-analysis of genomic data also raises questions about the extent of clinicians' and researchers' duties to conduct such analyses and their obligations to discuss the possibility as part of the initial informed consent, which have recently been addressed in policy statements by the American College of Medical Genetics and the American Society of Human Genetics (Bombard et al. 2019; David et al. 2019).

Describing the potential benefits and risks of genomic sequencing presents similar challenges. For patients, one of the most significant benefits is the possibility of receiving a diagnosis (Dillon et al. 2018; Dragojlovic et al. 2018) or, in some cases, identifying multiple diagnoses that are at play (Posey et al. 2017). This shortens their "diagnostic odyssey" and can potentially lead to new management recommendations or treatments, provide information about recurrence risk, shed light on prognosis, and provide a support network of other families dealing with the same diagnosis (Lambertson et al. 2015). It is faster than a more iterative approach to genetic testing (Petrikin et al. 2015) and increasingly cost-effective (Farnaes et al. 2018; Stark et al. 2019). As for traditional genetic testing, the main risks associated with genomic sequencing are psychological, social, and familial, including learning about unexpected biological relationships (consanguinity, misattributed parentage) when multiple family members contribute samples for interpretation.

As genomic testing has gained traction in the media and popular science, patients tend to overestimate its capabilities (Roberts et al. 2018; Wynn et al. 2018), necessitating a discussion about the patient's expectations for the testing and the likelihood of receiving diagnostic results in order to provide a realistic projection of the clinical utility of genomic sequencing (Bernhardt et al. 2015). Additional logistical concerns that participants may want to consider at the time of consent include time limitations, provider expertise, and the rapidly changing potential scope of the test (McGuire and Beskow 2010; Hallowell et al. 2015; Burke and Clarke 2016).

Incidental and Secondary Findings Present Specific Challenges and Opportunities

One of the most consequential differences between single-gene or panel testing compared to genomic sequencing is the potential to receive results that are not related to the primary indication for testing. Incidental findings refer to results with potential health significance that are identified in the process of searching for a variant that explains the patient's phenotype but are not sought out purposefully. Secondary findings are also unrelated to the reasons for testing, but these are actively sought out by the testing lab, usually because the identification of such results would allow for prevention or early identification of a serious but preventable or treatable medical condition (Green et al. 2013). Practices have varied widely among laboratories regarding the options and specifics around the return of incidental or secondary findings (O'Daniel et al. 2017), and in an effort to provide guidance to laboratories, the American College of Medical Genetics and Genomics (ACMG) first issued recommendations for the return of secondary findings for patients undergoing genomic sequencing in 2013 (Green et al. 2013). These guidelines proposed a list of 56 genes in which secondary findings be returned to patients undergoing genomic sequencing. Subsequent revisions have included minor changes to the list of genes, as well as a major revision to allow patients to opt out of receiving secondary findings (ACMG Board of Directors 2015). Independent work groups have also assessed the medical actionability of the genes included on the secondary findings list (Hunter et al. 2016). The most recent update by the ACMG includes a list of 59 genes, most of which have been implicated in autosomal-dominant hereditary cancer or cardiovascular conditions for which there are well-established guidelines for early detection of disease or prevention (Kalia et al. 2017).

Most laboratories performing clinical genomic sequencing now offer patients the option to receive secondary/incidental findings, at a min-

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imum pathogenic variants in the 59 genes endorsed by ACMG for return. Many labs offer additional options beyond the 59 genes, and there remains a great deal of variability among laboratory policies for reporting secondary findings and how those options are presented (Ackerman and Koenig 2018).

Secondary and incidental findings present both opportunities and challenges that are largely unique to genomic sequencing. Patients who consent to receive secondary findings could potentially learn that they have a significant risk of developing a life-threatening condition for which medical interventions are available. For example, if a female patient receives a pathogenic *BRCA1* variant secondary finding, she can mitigate the high risk of developing cancer by undergoing earlier and more frequent screening. Additionally, her family can be offered cascade testing, which is especially important as emerging data suggests that perhaps 50% of these families do not have a family history that would meet guidelines for clinical testing (Manickam et al. 2018).

Similar to the risks associated with primary genomic findings, those associated with secondary findings are largely psychological and social, including the short-term distress patients may face when learning about significant unexpected risks for serious genetic conditions (Sapp et al. 2018; Hart et al. 2019), discordance among family members about whether to test for secondary findings, insurance implications, and false-negative or false-positive results (Appelbaum et al. 2014; Ormond et al. 2019a).

Obtaining Informed Consent for Secondary Findings

Recent studies suggest patients undergoing genomic sequencing struggle with comprehension (Hellwig et al. 2018; Roberts et al. 2019). Information overload may contribute to patients' challenges with comprehension, and that problem can be exacerbated when the consent discussion includes secondary findings in addition to the primary purpose of testing (Turbitt et al. 2018). In such cases patients sometimes struggle to understand the difference between the two, confounding the risks and benefits and in some cases misunderstanding the main purpose of the test. Discussing secondary findings may add time to the informed consent process. This creates logistical challenges and can also lead to information overload, which can make it difficult to achieve the level of comprehension necessary to consent to testing. Family discordance about who wishes to learn secondary findings can further complicate decision-making. For example, a secondary finding in a child is most often assumed to be present in one of the parents; if one parent elects to receive secondary findings and the other does not, one parent's status may reveal the other's by default. Practically, the parents must therefore be in agreement about the decision. Even outside the immediate family, it is possible that secondary findings could cause disruption to the family—for example, some family members may resent being presented with the knowledge of a genetic condition in the family (Hallowell et al. 2013). The risk for insurance discrimination is a particularly complicated part of any consent conversation regarding secondary findings, because the individual is being identified with a risk that was previously unknown, as compared to primary findings, in which the patient by definition has a preexisting medical condition that led to testing. Laws such as the Genetic Information Nondiscrimination Act [GINA (2008)] protect such patients from being denied health insurance because of a genetic difference, but GINA does not apply to life insurance, long-term care insurance, or disability insurance. These risks are complicated and largely hypothetical, making them difficult to explain, which in turn may inflate their significance in the minds of patients.

EXPLORING ALTERNATIVE MODELS OF CONSENT

Recognizing that people have struggled with using traditional models of consent to accommodate the new challenges presented by genomic sequencing, many have proposed alternatives. One such model is called staged (also known as tiered or layered) consent (Bunnik et al. 2013b; Appelbaum et al. 2014). This is a varia-

tion on the concept of generic consent first coined by Elias and Annas (1994), which proposes that patients should receive general pretest information that covers the possible test outcomes and their significance broadly and have the opportunity to ask relevant individual questions and personalize the content that they need. Staged consent and disclosure would occur as new findings arise, in part to alleviate the challenge of time pressure, to avoid overwhelming the patient with information, and to separate two decisions at the time of consent: whether or not to have the test for the diagnostic reasons and whether or not to receive secondary findings. Staged consent and disclosure processes also have the potential benefit that family members can independently decide whether to learn information related to the primary test indication and whether to learn about secondary findings. Yu et al. (2013) have demonstrated that patients and families are interested and engaged in a staged consent and disclosure process when offered it through an online portal. In fact, online platforms for genomic sequencing consent and return of results have continued to evolve as a cost-effective way of promoting participant understanding and engagement (Tabor et al. 2017), and increasing patients' comprehension and recall of what they learned in the consent process (Angiolillo 2004; Appelbaum et al. 2014). However, a staged process may be more logistically complicated and time-consuming for clinicians, who would be required to schedule multiple clinic visits or telemedicine sessions. This would add cost and create risk that patients who are lost to follow-up would not receive important information about their health. Although the staged approach could go a long way toward mitigating the challenges of achieving informed consent in the context of genomic sequencing, it may not be practical in many clinics or for underserved patient populations with limited access to the internet or with language or literacy barriers.

Increasingly, researchers and clinicians are turning to new conceptual approaches and technology in search of ways to streamline information exchange for both clinicians and patients. For example, the Consent and Disclosure Recommendations Workgroup of the National Institutes of Health (NIH)-funded Clinical Genome Resource has developed a conceptual framework and tools that genetics experts can apply to suggest a "communication starting place" for ordering clinicians. The recommended communication approach can then be tailored based on patient characteristics and using clinical judgment (Ormond et al. 2019b). A common application of technology to genetic testing has been in the creation of decision aids to facilitate increased patient participation in health-care decision-making by defining the decisions that must be made, providing information about the interventions or tests being offered, and clarifying the patient's personal values (https://decisionaid.ohri.ca/). Even before genomic sequencing was widely available in clinical and research settings, decision aids created in the context of more traditional genetic testing were shown to improve patient understanding (Kuppermann et al. 2014; Ekstract et al. 2017). More recently, researchers and clinicians have created online decision tools to help facilitate the consent and disclosure process for genomic sequencing, and results show promise that patients find these tools helpful (Birch et al. 2016; Bombard et al. 2018; Shickh et al. 2018). A major advantage to using technology as part of the consent and disclosure process is that it can reduce the need for clinician time, which decreases costs. Further, potential participants can review information or seek further information using available links to enhance their understanding of the goals of the research and the potential harms and benefits. It can also alleviate some of the challenges associated with the current shortage of genetics clinicians and provide valuable assistance to nongenetics health-care providers who will increasingly encounter genomic testing in their clinics. Previous studies of primary care physicians and nongenetics specialists have demonstrated these providers are enthusiastic about the potential benefits of genomic sequencing but many lack confidence in their knowledge and abilities surrounding genomics (Nippert et al. 2011; Carroll et al. 2016). There remains much to learn about the efficacy of decision aids for consenting to undergo genomic sequencing with regard to their impact

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on patient knowledge, satisfaction, and posttest outcomes such as psychological well-being. Decision aids can also present practical challenges in clinic, particularly if they were created in a language or cultural context that is foreign to the patient. Additionally, overreliance on decision aids without access to providers to answer questions may allow individual patient misunderstandings about testing to go unchecked.

As a large part of the burden of the consent process for genomic sequencing relates to secondary findings, some models have been proposed to address these challenges specifically. In a research setting, one such proposal is a governance model. This model addresses the challenges associated with consent for secondary findings by suggesting the creation of a governing group in which stakeholders (including research participants) can provide input about key questions, including whether research participants should receive unexpected findings, what types of unexpected results, and how these should be returned. This approach takes some of the burden off of the consent process because participants agree to be governed by the decisions of others (Koenig 2014). This approach is being used in large genomics studies such as the Clinical Sequencing Evidence-generating Research (CSER) consortium (Amendola et al. 2018). Another approach to secondary findings in research settings involves outsourcing such results to a third party. In this approach, a research participant undergoing sequencing would not receive any incidental or secondary findings but would be provided with their data in order to pursue secondary findings with another genetic specialist or company. Therefore, consent for secondary findings and the determination of which types of results to receive would no longer be part of the consent process for the primary genomic research (Appelbaum et al. 2014). Many clinical labs offer patients the opportunity to request their raw data, as do some genomic research studies, and although most clinical labs also offer, at a minimum, the secondary findings options recommended by the ACMG, access to raw data allows patients to go much further in their search for potentially medically relevant data (Kalia et al. 2017; Ackerman and Koenig 2018; Fowler et al. 2018). Although this is helpful in that it reduces the burden on the initial consent process and preserves patient autonomy, patient access to raw genomic data also has significant risks in that its analytic and clinical validity can be variable and there is no guarantee outside genomics services will be accurate in their interpretations or have the expertise to convey the significance of findings appropriately—limitations that patients should comprehend before obtaining their raw data for further interpretation (Appelbaum et al. 2014). Finally, a model that has been proposed to address challenges with consent for secondary findings is that of "binning" secondary findings into categories to simplify the options presented to the patient/participant (Berg et al. 2011). With the binning model, patients have the option of saying yes or no to receiving categories of secondary findings stratified, for example, by level of risk and/or actionability. This model is already widely used in both clinical and research settings—for example, when patients are given the option to receive actionable secondary findings from the ACMG's list of 59 genes described above (Shahmirzadi et al. 2014; Ackerman and Koenig 2018).

While the alternative models described above have improved the consent process for genomic sequencing, none have completely addressed the challenges posed by this complicated test. There is still much more work to be done by researchers and clinicians, in partnership with our patients, to better promote informed consent and decision-making in the context of genomics.

FUTURE DIRECTIONS AND THE ROLE FOR GENETIC COUNSELORS

Rethinking Standards for Genomic Consent—a Need for a More Individualized, Flexible Approach

It is in the nature of genomic sequencing to be adapted and personalized, and appropriate standards for informed consent should recognize this feature of modern testing. Going forward, it is essential for clinicians and researchers to take a more individualized and flexible approach

to informed consent when it comes to genomic sequencing. The widely used standard for the appropriate amount of information to disclose to patients in order to obtain informed consent is based on what a "reasonable person" would want to know, but experienced genetics clinicians know that patients differ in their information preferences about genomic testing (Regier et al. 2015). A more practical standard may be one that is personalized based on the individual or family and their information preferences. Genetic counselors are specialists in tailoring consent discussions based on the individual patient in front of them. This tailoring can include determining the appropriate amount of information to provide a patient to facilitate informed, values-based decision-making without sacrificing comprehension and also by adapting the complexity of the information based on the patient's level of understanding. Decision-making capacity, another important requirement for valid consent, is subjective and difficult to define; thus, its definition may also need to be flexible depending on the level of risk and potential benefit involved in the context of genomic sequencing. For some families, the level of risk involved in genomic sequencing is higher than others. A higher bar for decision-making capacity may make sense in situations with more significant risks and/or lower potential for direct benefits. The challenges clinicians face in obtaining informed consent for genomic sequencing arise primarily from the use of outdated standards and models for consent, and so it will be important for genetic counselors to continue to be involved in the process of adapting such standards and models of consent for genomic sequencing.

Scaling Up for the Genomics Era

To meet the increasing demand for genomic sequencing, scalable approaches to informed consent are needed. The presence of genetic counselors in nongenetics specialty clinics and research settings can help, but as genomic testing becomes more commonplace, other approaches will be needed to meet the demand. The goals of a more individualized and a more scalable approach to informed consent may at first seem contradictory, but they need not be. Technological solutions, such as interactive video platforms and applications, hold great promise when it comes to meeting this challenge, as they are both scalable and can also allow for patients to customize their own experience based on their preferences and values. Educating nongenetics health-care providers about genomic sequencing and consent can also help facilitate the scaling up of genomic sequencing. These approaches may also help free up time for genetic counselors to spend in settings where specialized knowledge of genetics is more necessary—in the disclosure of genomic testing results to patients. Genetic counselors can further this goal by devoting time to educating nongenetics providers about genomic sequencing and consent, as well as by participating in the development of technology-based educational tools and decision aids to facilitate the integration of patient values into decision-making (Lewis et al. 2016; Adam et al. 2018; Reumkens et al. 2019). Genetic counselors can also use their skills and knowledge on a broader scale by participating in larger policy discussions about informed consent in the genomics era.

CONCLUSIONS

The widespread availability of genomic sequencing in clinical and research settings has stretched traditional approaches to informed consent. Many new models of consent have been proposed to meet the goals of informed consent in the context of genomic testing, including staged or tiered models of consent, technological approaches, and others. Going forward, genetic counselors will be integral in developing more individualized, flexible, and scalable approaches to obtaining informed consent for genomic testing.

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