


Patient-Centered Obstetric Care in the Age of Cell-Free Fetal DNA Prenatal Screening

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Abstract

Purpose: The clinical introduction of innovative prenatal genetic technologies challenges patients and providers to find new ways of fostering informed decision-making in a setting characterized by complexity and uncertainty. As prenatal genetic technology advances, important questions remain about how to structure patient-centered conversations that effectively prepare pregnant patients to make informed choices about the different genetic conditions for which this new form screening may be used. **Methods:** Focus groups were conducted with 23 pregnant women to identify informational needs and decision-making preferences regarding emerging and anticipated applications of cell-free fetal DNA screening, the newest form of prenatal genetic screening. **Results:** Participants were in favor of obtaining more genetic information about the fetus than provided by conventional screens but acknowledged the challenges inherent in navigating the unique complexities of the decision-making process. The provider–patient relationship was seen as an important resource to navigate the associated uncertainties at each stage of the screening process. Participants emphasized the need for initiatives to support a personalized, accurate, and unbiased discussion about prenatal genetic risk and assessment. **Conclusion:** Continued advances in prenatal genetic screening call for new approaches to structure patient-centered communication to facilitate increasingly complex decisions about fetal genetic risk and assessment.

Keywords

patient experience, obstetric care, cell-free fetal DNA screening, informed decision-making, patient–provider communication

Introduction

Advances in the science of cell-free fetal DNA (cffDNA) and next-generation sequencing technologies have a significant impact on the delivery of prenatal care. Initially, cffDNA screening was indicated for trisomies of chromosomes 21, 13, and 18, providing greater accuracy for these conditions and in an earlier time in the pregnancy compared to conventional screens (eg, the Quadruple screen) (1,2). Soon thereafter, it became possible to screen for conditions that were not part of routine prenatal testing, specifically conditions associated with common sex chromosome aneuploidies (3,4). Now, cffDNA is marketed to screen for a series of subchromosomal conditions, including microdeletions, and other rare chromosomal abnormalities (5,6). At the same time, efforts are well underway to leverage next-generation technologies to conduct more detailed fetal genetic analysis, opening the door for expectant parents to

learn about the risk of a host of other fetal genetic variants in the earliest weeks of pregnancy (7,8).

The complexity of the technology and the pace at which it is emerging raise important questions about how obstetric patients can individualize decisions about new options such

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as cffDNA screening. Studies of patient preferences show that effective decision-making regarding the use of prenatal genetic tests requires knowledge of the conditions that can be detected, the different options to identify the risk or presence of those conditions, and the implications of those procedures and results for the woman, her pregnancy, and family (9). A core component of the decision-making process is melding medical data and fact with one's values and beliefs about parenthood, disability, quality of life, and pregnancy termination (10,11). Despite the continued rapid translation of new genetic technology, it is unclear how to best support pregnant patients with this process. Although patients will increasingly be tasked to acquire and manage a large volume of information upon which to base their assessment of the clinical utility of cffDNA screening, the manner in which women will value, prioritize, and triage information to enable decision-making about expanded screening is unknown. Models to structure the informed consent process to maximize women's decision-making preferences have been considered, including the ability to opt in or out of testing for specific conditions included in a screening panel and batching disorders into broad categories (12). However, there is a paucity of empirical data to guide how patients and providers can work together to navigate the complexities of this technology as the scope of cffDNA screening expands.

Advances in cffDNA technology shed light on the widening gap between the availability of new prenatal genetic tests and structures to effectively support patients in the decision-making process (13,14). In response, we conducted a study to identify patient perspectives on the clinical infrastructures needed to support patient-centered educational and decision-making needs to address the rapidly evolving landscape of prenatal genetics and genomics.

Materials and Methods

Patient Recruitment

Focus groups were conducted from October 2015 to January 2016 to gain insight into pregnant women's perceptions of expanded applications of cffDNA screening and their educational needs and decision-making preferences regarding its clinical utility. Women, 18 years of age or older, who were currently pregnant, receiving prenatal care at the Cleveland Clinic Health System, English speaking, and could provide consent for research participation were eligible for participation. Patients who were postpartum or had experienced an obstetric complication in the current pregnancy (eg, miscarriage or fetal demise) were excluded from participation.

International Classification of Diseases, Tenth Revision codes were used to extract information from electronic medical records to construct a database of eligible participants. The list was randomized, and a recruitment letter was sent with instructions to contact the research coordinator by

telephone or e-mail if interested in participating. Recruitment fliers placed in the prenatal outpatient clinics supplemented recruitment. All study procedures were approved by the institutional review board of Cleveland Clinic (#15-813) prior to study initiation.

Data Collection

After providing informed consent, participants completed a short survey to collect demographic and reproductive history information and then participated in a focus group discussion. The focus group was structured using a moderator guide developed in conjunction with experts in obstetrics, maternal-fetal medicine, prenatal genetics, ethics, and medical decision-making. Questions were based on a version developed and tested as part of our prior work (15) and modified to address study aims. Modified items were piloted and revised prior to data collection. The guide contained a series of open-ended questions to probe the participants' perspectives regarding expanded applications of cffDNA screening. This included questions pertaining to (1) existing and recent applications of cffDNA to screen for microdeletions and rare chromosomal trisomies, and (2) emerging applications of cffDNA screening as based on the current state of the science. The second set of questions addressed the use of cffDNA to screen for variants associated with medical or cognitive conditions of varying severity and age of onset based on current cffDNA research and literature about genetic and genomic testing in the context of newborn and adult-medicine (16,17).

The focus group was proceeded with a brief description of current application of cffDNA screening as used at our institution to assess trisomies 21, 13, and 18, as well as sex chromosome aneuploidies. The introduction included a discussion of emerging and anticipated advancements of cffDNA screening. A research team member, who also is a former genetic counselor, was present to provide clarification of presented concepts. Focus groups were 60 to 90 minutes in duration. Discussions were audio recorded with the participants' permission. The digital recordings were transcribed verbatim and verified for accuracy.

Data Analysis

Data analysis was an iterative and progressive process of data immersion, open coding, constant comparison, documentation, and theme identification, which is an inductive approach consistent with grounded theory (18,19). Through immersion, two analysts identified content domains in the transcripts to create a coding tree that was used to systematically organize the data. The data analysts coded each transcript using Nvivo (20) and simultaneously composed memos to record emergent themes as well as insights and interpretations of the data (21). The research team held regular data analysis meetings to review coded data, identify themes, and determine the point at which data saturation had been met.

Table 1. Demographic and Reproductive Characteristics of Participants (n = 23).

Characteristic	n (%)
Advanced maternal age (≥ 35 years at delivery)	10 (43.5%)
Age (years)	Mean: 32.2 Range: 22-40
Cell-free fetal DNA screen	
Yes	10 (43.5)
Pregnancy history	
Primigravida	7 (30.4)
Trimester of pregnancy	
1st	1 (4.3)
2nd	14 (60.9)
3rd	8 (34.8)
Race and Hispanic origin	
Asian alone	1 (4.3)
Black alone	4 (17.4)
White-non-Hispanic	15 (69.6)
White-Hispanic	1 (4.3)
Other/multiracial	1 (4.3)
Education	
Community college/technical school	7 (30.4)
College graduate	6 (26.1)
Graduate/professional degree	10 (43.5)

Results

Participant Characteristics

A total of 23 women participated in 6 focus groups with a mean attendance of 4 women per group. The participants ranged in age from 22 to 40 years; 10 were of advanced maternal age (AMA), that is, ≥ 35 years of age at delivery. Ten participants reported that they had cffDNA screening that included assessment of trisomies 21, 13, and 18, as well as the sex chromosomes, during their current pregnancy; 8 of these participants were AMA. None of the participants reported undergoing invasive diagnostic testing in the current pregnancy. The demographic and reproductive characteristics of the study sample are presented in Table 1.

Major Themes From Focus Group Narratives

Three major themes emerged: the clinical utility of expanded applications of cffDNA screening, uncertainty and meaningful decisions about the information gained from cffDNA screening, and navigating testing options within the patient-provider encounter. Additional data for each theme are listed in Table 2.

The clinical utility of information gained from expanded applications of cffDNA screening. Participants recognized the potential impact that expanded applications of cffDNA screening could have on prenatal decision-making and experience of pregnancy. Overall, most participants were in support of and interested in using cffDNA screening to identify serious, childhood-onset conditions that could result in life-threatening or major life-altering diseases. For some,

learning about severe, childhood-onset conditions other than the common autosomal aneuploidies would help inform the decision to end the pregnancy if confirmed with diagnostic testing: “I think it is beneficial also to understand if there would be any abnormalities because . . . some moms might choose to not have that child because of all of the associated problems . . . you would have a big decision on your hands” (FG5). Others viewed cffDNA screening as a way to optimize outcomes if a condition was identified. This included the opportunity to organize medical, psychosocial, and financial resources not only for the child but also for the family to prepare to care for the child. One participant added: “I would like to know a lot of different conditions that are serious, that would make the life of the child, at least for my point of view, a very different experience, that would make my life a very different experience” (FG2).

Participants expressed more variability regarding the use of cffDNA screening to screen for conditions that may be less severe or not manifest until later in childhood or adulthood. For some, such information could help develop a plan of care after birth, including surveillance and early intervention to prevent or mitigate illness if and when possible. As 1 participant said, “There is a level of preparedness that you would want to have . . . If you could be armed with that information from the beginning and try to have a treatment plan in place, I think it is a great thing” (FG3). This information could offer the opportunity to avoid delayed diagnosis if a complex condition were suspected. As 1 participant noted, “You know to start watching for the signs so that you catch it very early on versus watching someone go through two or three years of misdiagnosis” (FG3).

Other participants voiced concern about obtaining this type of information during pregnancy and how such information would impact the life of a child. A foremost concern was the possible negative impact of possessing information about a child’s future health before the time of birth. “I think to me you are labeling someone before they are born . . . You start putting labels on the baby before it is even born and then, the next thing you know, the parents and everyone around the baby is kind of changing their environment according to a test” (FG4). There was also concern about the impact of this information on parenting: “Would I be this nervous mother always being terrified and then as my child grew into adulthood and they weren’t taking care of themselves thinking—or would I be able to let it go thinking everything is a chance in life?” (FG3).

Uncertainty about making an informed decision based on information provided by expanded applications of cffDNA screening. Participants provided insight about the amount and type of information they would need to make an informed decision about cffDNA testing. There was agreement that patients should be informed of the different conditions that cffDNA screening may detect in addition to the screen’s accuracy for each condition and options to act on this information either before or after birth: “I would like to know which ones

Table 2. Focus Group Themes and Illustrative Quotes.

Theme	Quotes
Utility of information gained from expanded applications of cffDNA screening	<p>Preparedness: “I think the technology is amazing and also really beneficial to know what to expect and how to prepare if there are going to be special needs particularly in the early stages of infancy and childhood.” (FG5) “I would want to address it right away and right after birth or be prepared that the baby is going to probably be in the NICU and need extra attention so that I would know for the baby and even so I could plan for my son at home.” (FG6)</p> <p>Decisions about pregnancy: “I think it is beneficial also to understand if there would be any abnormalities because . . . some moms might choose to not have that child because of all of the associated problems . . . I mean that would be a very tough decision for me. I mean you would have a big decision on your hands.” (FG5) “I would like to know a lot of different conditions that are serious, that would make the life of the child, at least for my point of view, a very different experience, that would make my life a very different experience. I think having a child and raising a child is a big responsibility as it is . . .” (FG2)</p> <p>Doubt: “So for me I don’t think it would make a huge difference if there were things that we couldn’t do anything about, those kinds of disorders or those kinds of issues.” (FG3) There is just too much out here that would really just boggle my mind and I see myself as a very positive person. So, whatever is going to happen, is going to happen. Whatever is going to be, is going to be. Yes, there are steps that you can probably take to prepare for that. But, at the end of the day, you are still in the same situation. (FG1)</p> <p>Outlook: “You are labeling someone before they are born . . . You start putting labels on the baby before it is even born and then, the next thing you know, the parents and everyone around the baby is kind of changing their environment according to a test.” (FG4) “Would I be this nervous mother always being terrified and then as my child grew into adulthood and they weren’t taking care of themselves thinking? Or, would I be able to let it go thinking everything is a chance in life?” (FG3)</p>
Uncertainty about making an informed decision based on information provided by cffDNA screening	<p>Volume of information: “It is more so the volume of information. I am like, ‘Wow. My child is going to have what?’ <i>It is just overwhelming. Very overwhelming.</i>” (FG 1)</p> <p>What to do with information: “I would like to know which ones [conditions] can I prepare for adequately and which ones do I have no control over and I will just have to deal with it when it happens.” (FG2) “Doing the test only tells you about condition but it doesn’t really help you to find a cure or try to make the condition better. So, I felt like, you can know millions of information from your genes but, if you don’t know how to treat or how to deal with it, there is no point in testing. Knowing is one thing. But, how to deal with it, is another completely different level. Current medicine doesn’t always have the solution to all of the conditions that they find.” (FG2)</p>
Navigating testing options within the patient–provider encounter	<p>Obstetric clinician as medical expert: “I go to you [clinician] for the science aspect of it and I want you to tell me how everything is working . . . Just give me the information and I will decide what I want to do with it. That is basically where I want that relationship.” (FG3) “It was very black or white, yes or no and I appreciated that actually because we didn’t have to give up anything. Believe it or not, you didn’t have the fear of judgment whatever your decision was. It was a very internal decision. It was just clinically offered as something that you could do.” (FG5)</p> <p>Pros and cons of clinician’s exploration of patient values and beliefs “So I think they should have that discussion with you to see what your value system is, to see what your thought process is, because not everyone has that support system.” (FG4) “Even if you went in knowing about it [cffDNA screening] and you knew, because of your age or some other things going on, it was probably the right thing for you, I think that should be something where you are sitting down and a little bit less intimidating situation . . . Unfortunately for us, medicine has become the doctor who gets 15 minutes with you. They cram so much in there that the sensitivity how they present information has gone out the window.” (FG4)</p>

[conditions] can I prepare for adequately and which ones do I have no control over and I will just have to deal with it when it happens” (FG2). At the same time, there was consensus among the group that it would be exceedingly difficult to obtain and

comprehend detailed information about each of the possible conditions. Furthermore, it would be equally difficult to utilize this newly acquired information to make an informed decision about if and how to use such information. As described

by 1 participant, “It is more so the volume of information. I am like, ‘Wow. My child is going to have what?’ . . . It is just overwhelming, very overwhelming” (FG1).

Participants’ uncertainty was also a function of the medical community’s incomplete understanding of rapidly expanding genetics technology and, in turn, the real significance of a genetic variant on the future health and the well-being of a child. As 1 participant said, “Doing the test only tells you about condition but it doesn’t really help you to find a cure or try to make the condition better. So, I felt like, you can know millions of information from your genes but, if you don’t know how to treat or how to deal with it, there is no point in testing. Knowing is one thing but how to deal with it is another completely different level. Current medicine doesn’t always have the solution to all of the conditions that they find” (FG2).

Navigating testing options within the patient–provider encounter.

There was an awareness among the group that the continued evolution of cffDNA technology and the nuanced complexity of the decision-making process would require a modified and expanded approach to the typical conversations that providers have with patients about testing options. As 1 participant said, “[cffDNA screening] is so new . . . I think technology with this has changed . . . we haven’t caught up with how we handle the conversation” (FG4).

Participants considered the provider–patient relationship an important resource for helping them to decide whether or not to undergo screening or diagnostic testing, what testing option to utilize to obtain genetic information about the fetus, and how to subsequently formulate prenatal care decisions based on the kind of information that could be obtained with expanded panels. Overall, participants valued the clinician’s expertise in guiding their prenatal genetic screening and diagnostic testing options.

One set of participants viewed their obstetric care provider as a medical expert whose role was to convey the characteristics and indications of the screen, and weigh a woman’s personalized risk (eg, age and reproductive history) when recommending cffDNA screening. Participants who shared this opinion stated that their providers should structure discussions focused on the scientific and medical aspects of cffDNA. As 1 participant noted, “At the end of the day I want her medical opinion and her experience to weigh her decision and . . . say, ‘As your doctor, looking at your history, this is what I think you should do medically speaking’” (FG6).

Others perceived providers as a resource to guide couples to explore their options and consider the personal and ethical implications of expanded cffDNA screening. As described by 1 participant, “I know that not all patients have deep insight about what they are going to do or a deep understanding of the consequences of testing. So I think that sometimes clinicians have to encourage patients to think about certain things; otherwise patients just avoid thinking about it” (FG2). By guiding pregnant women to consider their values and preferences in the context of cffDNA screening, providers could encourage patients to discuss aspects of the

screening process that they may not have yet fully explored, either individually or as a couple.

Although participants spoke of the importance of bringing their values and beliefs into conversations with their provider, they also voiced concern about the potential for a negative impact of discussions of values and beliefs regarding the quality of life, disability, and pregnancy termination on the patient–provider relationship. Specifically, there was concern about their provider’s bias in the counseling process in response to such information. “We had that kind of conversation [about personal values] and I think it actually led to a bias on what kind of information he [the obstetrician] offered and how it [the discussion] went from there . . . I feel like had we not been up front with it he may have discussed it more, maybe expanded the conversation more” (FG3). Participants were in agreement about the need for providers to individualize conversations.

Discussion

Patient experiences can affect if and how they access and utilize emerging technologies. Although the significance of patient experience is apparent in other areas of medicine, it is particularly salient in the context of prenatal care where decisions about the use of a genetic test may impact not just the current pregnancy and the patient’s family but also her future reproductive decision-making. A key component of the successful translation of new prenatal genetic technologies is a robust informed consent process that helps patients learn about the indications, risks, benefits, and limitations of prenatal screening and contextualize that information with their goals and values regarding pregnancy, quality of life, and family (10,22). How the shared decision-making discussions will take place between patients and their providers regarding the use of innovative applications of cffDNA technology and changes in the practice of medicine is uncertain.

Changes in cffDNA technology and clinical practice guidelines about its use signal the need for ongoing challenges in ensuring patients have the information and support to make patient-centered decisions about its use. For instance, emerging clinical practice guidelines recommend offering cffDNA screening to all women, not just those with an increased risk of aneuploidy based on age or reproductive history. Part of this process will be to ensure that both high-risk and average-risk patients understand the indications and limitations of the screen. This includes a discussion about screen sensitivity, specificity, and positive predictive value of cffDNA screening, values that will vary for each condition. Large-scale studies report that the positive predictive value as well as negative predictive value of cffDNA screening for high-risk women are superior compared to those of low-risk (also referred to as average-risk) women (1,23). Inevitably, continued expansion of cffDNA will result in an increased number of false-positive as well as false-negative results. Conveying these concepts to patients in a way that enables them to make an informed decision about cffDNA screening will become increasingly important and problematic.

A primary finding of our study is that the patient-provider relationship will be a key resource for confronting the medical and ethical challenges posed by the continued expansion of cffDNA screening. One challenge conveyed by participants is the real and potentially increasing presence of decisional complexity and uncertainty with the ability to identify numerous different genetic conditions using cffDNA screening. Decisional complexity and uncertainty are not novel findings in the area of obstetrics. These factors have been shown to confound the decision-making process of pregnant women who utilize prenatal microarray technology as part of diagnostic testing procedures (eg, chorionic villus sampling and amniocentesis) (24–26). This study demonstrates that decisional complexity and uncertainty will be intensified with the expansion of cffDNA screening, affecting a broader population of women and taking place at the beginning stages of the risk assessment process.

Even in the context of expanded indications for cffDNA, women believed that their decisions regarding the use of the screen should be structured in an informed fashion similar to that currently used for the common autosomal and sex chromosome aneuploidies. Pregnant women have reported obstacles in having informed, patient-centered discussions about their prenatal screening and diagnostic testing options (27–29). The prospect of expanded cffDNA screening presents additional challenges not just to obtaining patient-centered information but also managing it in a way that would result in a decision that is informed and reflects the goals and needs of the pregnant women.

Another issue pertains to the communication of a volume of complex information to patients. Studies have demonstrated patients' concerns with information overload in the context of prenatal diagnostic testing (30). Our findings show that expanded applications of cffDNA screening will likely exacerbate this concern. The volume as well as the complexity of information obtained through cffDNA as well as how to interpret risk information about a host of different conditions in the context of one's pregnancy, values, options, and beliefs will challenge the shared decision-making process. Although it was important to be familiar with each condition, participants expressed uncertainty about how to acquire that information and then interpret it in a meaningful way. This may be an opportunity to draw upon the lessons learned from diagnostic microarray, where counseling patients about groups of disorders based on patient risk assessment and values may assist in navigation-associated decisional complexity and uncertainty (12).

Participants perceived a clear clinical utility to obtain information about serious, life-threatening, or debilitating childhood-onset conditions. In effect, the participants grouped disorders by severity as they voiced ambiguity about the clinical utility of cffDNA screening to learn of genetic conditions with less severe phenotypes or phenotypes with later onset in childhood or adulthood. Some participants voiced concern about the impact of such knowledge on quality of life of a child and the potential consequences of labeling a child with a genetic condition prior to birth. Others thought that such information could help bypass a

“diagnostic odyssey” by pinpointing the source of a child's illness early and to proactively develop a plan for intervention. Studies show the far-reaching implications of information generated by presymptomatic genetic testing for an individual and his or her interactions with health-care professionals, family, and the public (31). Also there are concerns about the impact of this information on the pregnant woman, not just on her experience of pregnancy but also on the expectations placed on her to utilize such information to be a “good mother” (32). The potential negative consequences of gaining genetic information during childhood regarding later onset conditions have been discussed for several years. This includes concern about stigmatization or discrimination in addition to the impact of such information on the relationship between the parent and child, which has been an area of debate for decades (33–35). The gravity of such issues raises relevant concerns in the prenatal context as well.

Participants suggested that the patient-provider relationship was a main resource for navigating the anticipated challenges and uncertainties associated with expanded cffDNA screening. The importance of the patient-provider relationship has been observed in the decision-making process for existing prenatal genetic screening and diagnostic testing options, particularly when uncertainties abound (25,26). In the setting of expanded cffDNA screening, this relationship would become essential to help patients navigate the choices posed by advances in prenatal genetics in a way that educational materials or decision aides alone could not.

Although there was agreement about the growing importance of the obstetric provider in the decision-making process for expanded cffDNA screening, there was disagreement about what form that assistance would take. Although some felt that the provider's role should be limited to that of a conduit of information, others expressed that providers could play a broader role and help patients explore their personal beliefs and values as part of the decision-making process. These findings emphasize the need for strategies that promote individualized, patient-centered counseling regarding cffDNA screening, beginning with a shared decision-making process that identifies patient's goals, needs, and preferences in the decision-making process.

Although expressed as strategies to mitigate the challenges anticipated with expanded cffDNA screening, these approaches would require additional robust medical education efforts, as studies show the difficulties faced by providers to meet the needs and preferences of patients in the decision-making process (29). These efforts must be focused on ensuring that providers achieve and maintain competence in the medical and ethical aspects of cffDNA screening, including concepts of risk and uncertainty (30). Leading professional organizations are instituting continuing medical educational programs that will form the core of these efforts. Yet, based on the findings of this study, the development of providers' knowledge base may not fully meet the anticipated needs for patients. Such interventions must also focus on developing skills to foster a patient-centered, shared

decision-making process and cultural competency skills to discuss issues related to disability and termination in a culturally sensitive fashion. Studies show that patients in different clinical situations welcome discussions of personal values, practices, and beliefs with their provider (36,37). Yet, these are topics that providers are often not comfortable discussing (29,38). Thus, efforts going forward must address not only provider knowledge but also communication skills to meet the anticipated needs for patients. Such efforts will increase with the growing complexity and uncertainty associated with the use of cffDNA screening.

Although this study demonstrates important insight into the challenges associated with the continued expansion of cffDNA screening, there are limitations that should be acknowledged. The study included a limited population of women who sought care at one major medical center. Additionally, we acknowledge the potential impact of self-selection bias on the study findings. As our findings describe the perspectives of a specific sample of women, additional studies are needed to further understand the needs of a larger and more diverse population of women across the United States. This study asked women to characterize aspects of the decision-making process, as they relate to emerging and anticipated future applications of cffDNA screening. In some cases, these were indications that already exist but not broadly implemented or anticipated to develop with advances in molecular diagnostics or commercialization of the technology. We also acknowledge that women's perceptions of decision-making regarding cffDNA screening may be influenced by their experiential knowledge with the screen as it is currently offered and their prior reproductive history. Further research will be needed to elucidate the evolving clinical utility of cffDNA screening among the socioeconomically diverse population of women who receive prenatal care in the United States.

This study sheds light on the importance of patients' experience with the clinical implementation of new prenatal genetic technologies. With advances in next-generation sequencing technologies, expectant parents will encounter increasing decisional complexity and uncertainty when facing the choice of if and how to utilize genetics to learn about the health of the fetus. In turn, there may be increasing reliance on effective patient-provider interactions to navigate such decisions in a way that is evidence-based and patient-centered. This calls for providers to work closely with patients to ensure they have the resources and support to make decisions that reflect the needs and priorities of patients.

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References

1. Norton ME, Brar H, Weiss J, Karimi A, Laurent LC, Caughey AB, et al. Non-Invasive Chromosomal Evaluation (NICE) Study: results of a multicenter prospective cohort study for detection of fetal trisomy 21 and trisomy 18. *Am J Obstet Gynecol.* 2012; 207:137.e1-e8.
2. Bianchi DW, Parker RL, Wentworth J, Madankumar R, Saffer C, Das AF, et al. DNA sequencing versus standard prenatal aneuploidy screening. *N Engl J Med.* 2014;370:799-808.
3. Hooks J, Wolfberg AJ, Wang ET, Struble CA, Zahn J, Juneau K, et al. Non-invasive risk assessment of fetal sex chromosome aneuploidy through directed analysis and incorporation of fetal fraction. *Prenat Diagn.* 2014;34:496-9.
4. Nicolaides KH, Musci TJ, Struble CA, Syngelaki A, Gil MM. Assessment of fetal sex chromosome aneuploidy using directed cell-free DNA analysis. *Fetal Diagn Ther.* 2013;35:1-6.
5. Wapner RJ, Babiarz JE, Levy B, Stosic M, Zimmermann B, Sigurjonsson S, et al. Expanding the scope of noninvasive prenatal testing: detection of fetal microdeletion syndromes. *Am J Obstet Gynecol.* 2015;212:332-e1.
6. Mennuti MT, Chandrasekaran S, Khalek N, Dugof L. Cell-free DNA screening and sex chromosome aneuploidies. *Prenat Diagn* 2015;35:980-5.
7. Hahn S, Hoesli I, Lapaire O. Non-invasive prenatal diagnostics using next generation sequencing: technical, legal and social challenges. *Expert Opin Med Diagn.* 2012;6:517-28.
8. Drury S, Hill M, Chitty LS. Recent developments in non-invasive prenatal diagnosis and testing. *Fetal Matern Med Rev.* 2014;25:295-317.
9. Gregg AR, Skotko BG, Benkendorf JL, Monaghan KG, Bajaj K, Best RG, et al. Noninvasive prenatal screening for fetal aneuploidy, 2016 update: a position statement of the American College of Medical Genetics and Genomics. *Genet Med.* 2016; 18:1056-65.
10. Dondorp W, de Wert G, Bombard Y, Bianchi DW, Bergmann C, Borry P, et al; on behalf of the European Society of Human Genetics (ESHG) and the American Society of Human Genetics (ASHG). Non-invasive prenatal testing for aneuploidy and beyond: challenges of responsible innovation in prenatal screening. *Eur J Hum Genet.* 2015;23:1438-50.
11. Lysterly AD, Mitchell LM, Armstrong EM, Harris LH, Kukla R, Kuppermann M, et al. Risks, values, and decision making surrounding pregnancy. *Obstet Gynecol.* 2007;109:979-84.
12. Darilek S, Ward P, Pursley A, Plunkett K, Furman P, Magoulas P, et al. Pre- and postnatal genetic testing by array-comparative genomic hybridization: genetic counseling perspectives. *Genet Med.* 2008;10:13-8.
13. Van den Berg M, Timmermans DR, ten Kate LP, van Vugt JM, van der Wal G. Informed decision making in the context of prenatal screening. *Patient Educ Couns.* 2006;63:110-7.
14. Marteau TM, Dormandy E, Michie S. A measure of informed choice. *Health Expect.* 2001;4:99-108.
15. Farrell RM, Mercer MB, Agatista PK, Smith MB, Philipson E. It's more than a blood test: patients' perspectives on noninvasive prenatal testing. *J Clin Med.* 2014;3:614-31.

16. Howard HC, Knoppers BM, Cornel MC, Wright Clayton E, Sénéal K, Borry P, European Society of Human Genetics; P3G International Paediatric Platform; Human Genome Organisation; and the PHG Foundation. Whole-genome sequencing in newborn screening? A statement on the continued importance of targeted approaches in newborn screening programmes. *Eur J Hum Genet.* 2015;23:1593-600.
17. Golden-Grant K, Merritt JL II, Scott CR. Ethical considerations of population screening for late-onset genetic disease. *Clin Genet.* 2015;88:589-92.
18. Ryan G, Bernard H. Techniques to identify themes. *Field Methods.* 2003;15:85-109.
19. Birks M, Chapman Y, Francis K. Memoing in qualitative research: probing data and processes. *J Res Nurs.* 2008;13:68-75.
20. Bazeley P. (ed) *Qualitative Data Analysis with NVivo.* 2007; London: Sage.
21. Corbin J, Strauss A. *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory.* 3rd ed. Thousand Oakes, CA: Sage Publications, Inc; 2008.
22. Committee on Practice Bulletins—Obstetrics, Committee on Genetics, and the Society for Maternal-Fetal Medicine. ACOG practice bulletin number 163: screening for fetal aneuploidy. *Obstet Gynecol.* 2016;127:e123-e37.
23. Zhang H, Gao Y, Jiang F, Fu M, Yuan Y, Guo Y, et al. Non-invasive prenatal testing for trisomies 21, 18 and 13: clinical experience from 146,958 pregnancies. *Ultrasound Obstet Gynecol.* 2015; 45:530-538.
24. Bernhardt BA, Soucier D, Hanson K, Savage MS, Jackson L, Wapner RJ. Women's experiences receiving abnormal prenatal chromosomal microarray testing results. *Genet Med.* 2013;15: 139-45.
25. Walser SA, Werner-Lin A, Russell A, Wapner RJ, Bernhardt BA. "Something extra on chromosome 5": parents' understanding of positive prenatal chromosomal microarray analysis (CMA) results. *J Genet Counsel.* 2016;25:1116-26.
26. Werner-Lin A, Barg FK, Kellom KS, Stumm KJ, Pilchman L, Tomlinson AN, et al. Couple's narratives of communion and isolation following abnormal prenatal microarray testing results. *Qual Health Res.* 2016;26:1975-87.
27. Michie S, Dormandy E, Marteau TM. Informed choice: understanding knowledge in the context of screening uptake. *Pat Educ Counsel.* 2003;50:247-53.
28. Han PK. Conceptual, methodological, and ethical problems in communicating uncertainty in clinical evidence. *Med Care Res Rev.* 2011;70:14S-36S.
29. Farrell RM, Nutter B, Agatisa PK. Patient-centered prenatal counseling: aligning obstetric healthcare professionals with the needs of pregnant women. *Women Health.* 2015;55:280-96.
30. Bernhardt BA, Kellom K, Barbarese A, Faucett WA, Wapner RJ. An exploration of genetic counselors' needs and experiences with prenatal chromosomal microarray testing. *J Genet Counsel.* 2014;23(6):938-47.
31. Burke W, Pinsky LE, Press NA. Categorizing genetic tests to identify their ethical, legal, and social implications. *Am J Med Genet.* 2001;106:233-40.
32. Rapp R. *Testing Women, Testing the Fetus: The Social Impact of Amniocentesis in America.* Sussex, UK: Routledge; 1999.
33. Michie S, Bobrow M, Marteau T; on behalf of the FAP Collaborative Research Group. Predictive genetic testing in children and adults: a study of emotional impact. *J Med Gen.* 2001;38: 519-26.
34. Green M, Solnit AJ. Reaction to the threatened loss of a child: a vulnerable child syndrome. *Pediatrics.* 1964;34:58-66.
35. American Society of Human Genetics Board of Directors. Points to consider: ethical, legal, and psychosocial ramifications of genetic testing in children and adolescents. *Am J Hum Gen.* 1995;57:1233-41.
36. Farrell RM, Mercer MB, Agatisa PK, Smith MB, Philipson E. Balancing risks: The core of women's decision about noninvasive prenatal testing. *AJOB Emp Bioeth.* 2015;6:42-53.
37. Anderson RR. Religious traditions and prenatal genetic counseling. *Am J Med Genet Part C Semin Med Genet.* 2009;151C: 52-61.
38. Modell SM, Citrin T, King SB, Kardia SL. The role of religious values in decisions about genetics and the public's health. *J Relig Health.* 2014;53:702-14.

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Ariane Mitchum was a research assistant in the Cleveland Clinic Department of Bioethics. She has several years of experience providing research support on various projects, primarily in healthcare contexts.

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