HHS Public Access

Author manuscript

Ethics Med Public Health. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

Ethics Med Public Health. 2016 ; 2(3): 334–342. doi:10.1016/j.jemep.2016.07.006.

"I think we've got too many tests!": Prenatal providers' reflections on ethical and clinical challenges in the practice integration of cell-free DNA screening

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Abstract

Background—The recent introduction of cell-free DNA-based non-invasive prenatal screening (cfDNA screening) into clinical practice was expected to revolutionize prenatal testing. cfDNA screening for fetal aneuploidy has demonstrated higher test sensitivity and specificity for some conditions than conventional serum screening and can be conducted early in the pregnancy. However, it is not clear whether and how clinical practices are assimilating this new type of testing into their informed consent and counselling processes. Since the introduction of cfDNA screening into practice in 2011, the uptake and scope have increased dramatically. Prenatal care providers are under pressure to stay up to date with rapidly changing cfDNA screening panels, manage increasing patient demands, and keep up with changing test costs, all while attempting to use the technology responsibly and ethically. While clinical literature on cfDNA screening has shown benefits for specific patient populations, it has also identified significant misunderstandings among providers and patients alike about the power of the technology. The unique features of cfDNA screening, in comparison to established prenatal testing technologies, have implications for informed decision-making and genetic counselling that must be addressed to ensure ethical practice.

Objectives—This study explored the experiences of prenatal care providers at the forefront of non-invasive genetic screening in the United States to understand how this testing changes the practice of prenatal medicine. We aimed to learn how the experience of providing and offering this testing differs from established prenatal testing methodologies. These differences may necessitate changes to patient education and consent procedures to maintain ethical practice.

Methods—We used the online American Congress of Obstetricians and Gynecologists Physician Directory to identify a systematic sample of five prenatal care providers in each U.S. state and the District of Columbia. Beginning with the lowest zip code in each state, we took every fifth name from the directory, excluding providers who were retired, did not currently practice in the state in

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Disclosure of interest

The authors declare that they have no competing interest.

which they were listed, or were not involved in a prenatal specialty. After repeating this step twice and sending a total of 461 invitations, 37 providers expressed interest in participating, and we completed telephone interviews with 21 providers (4.6%). We developed a semi-structured interview guide including questions about providers' use of and attitudes toward cfDNA screening. A single interviewer conducted and audio-recorded all interviews by telephone, and the interviews lasted approximately 30 minutes each. We collaboratively developed a codebook through an iterative process of transcript review and code application, and a primary coder coded all transcripts.

Results—Prenatal care providers have varying perspectives on the advantages of cfDNA screening and express a range of concerns regarding the implementation of cfDNA screening in practice. While providers agreed on several advantages of cfDNA, including increased accuracy, earlier return of results, and decreased risk of complications, many expressed concern that there is not enough time to adequately counsel and educate patients on their prenatal screening and testing options. Providers also agreed that demand for cfDNA screening has increased and expressed a desire for more information from professional societies, labs, and publications. Providers disagreed about the healthcare implications and future of cfDNA screening. Some providers anticipated that cfDNA screening would decrease healthcare costs when implemented widely and expressed optimism for expanded cfDNA screening panels. Others were concerned that cfDNA screening would increase costs over time and questioned whether the expansion to include microdeletions could be done ethically.

Conclusions—The perspectives and experiences of the providers in this study allow insight into the clinical benefit, burden on prenatal practice, and potential future of cfDNA screening in clinical practice. Given the likelihood that the scope and uptake of cfDNA screening will continue to increase, it is essential to consider how these changes will affect frontline prenatal care providers and, in turn, patients. Providers' requests for additional guidance and data as well as their concerns with the lack of time available to explain screening and testing options indicate significant potential issues with patient care. It is important to ensure that the clinical integration of cfDNA screening is managed responsibly and ethically before it expands further, exacerbating pre-existing issues. As prenatal screening evolves, so should informed consent and the resources available to women making decisions. The field must take steps to maximize the advantages of cfDNA screening and responsibly manage its ethical issues.

Résumé

L'introduction récente du dépistage prénatal non invasif (dépistage cfDNA) exempt de cellules à base d'ADN dans la pratique clinique devait révolutionner le dépistage prénatal. Le dépistage cfDNA de l'aneuploïdie fœtale a démontré une meilleure sensibilité et spécificité que le dépistage sérique classique et peut être effectué au début de la grossesse. Cependant, on ne sait pas si et comment les pratiques cliniques assimilent ce nouveau type de test dans leurs processus de consentement et de conseil éclairés. Depuis l'introduction du dépistage cfDNA dans la pratique en 2011, l'absorption et la portée ont augmenté de façon spectaculaire. Les professionnels sont sous pression pour rester à jour avec l'évolution rapide des échantillons cfDNA, gérer la demande croissante des patients, et suivre l'évolution des coûts de test, tout en essayant d'utiliser la technologie de manière responsable et éthique. Bien que la littérature clinique sur le dépistage cfDNA a montré des avantages pour les populations de patients spécifiques, elle a également identifié des malentendus importants entre les professionnels et les patients sur le pouvoir de la

technologie. Les caractéristiques uniques du dépistage cfDNA, par rapport aux technologies de dépistage prénatal établies, ont des implications pour la prise de décisions éclairées et le conseil génétique qui rentrent en compte pour assurer une pratique éthique.

Cette étude a exploré les expériences des professionnels à la pointe du dépistage génétique non invasif aux États-Unis pour comprendre comment ce test modifie la pratique de la médecine prénatale. Nous avons cherché à savoir comment l'expérience de fournir et d'offrir ce test diffère des méthodes plus anciennes de dépistage prénatal. Ces différences peuvent nécessiter des changements dans l'éducation du patient et les procédures de consentement pour maintenir une pratique éthique.

Nous avons utilisé l'annuaire en ligne du Congrès américain des médecins obstétriciens et gynécologues pour identifier un échantillon systématique de cinq fournisseurs de soins prénatals dans chaque État américain et le District de Columbia. En commençant par le code postal le plus bas dans chaque état, nous avons pris tous les cinquièmes noms de l'annuaire, à l'exclusion des prestataires qui étaient à la retraite, ne pratiquait pas actuellement dans l'état dans lequel ils ont été énumérés, ou ne sont pas impliqués dans une spécialité prénatale. Après avoir répété cette étape deux fois et l'envoi d'un total de 461 invitations, 37 professionnels ont exprimé leur intérêt à participer, et nous avons réalisé des entrevues téléphoniques avec 21 fournisseurs (4,6 %). Nous avons développé un entretien semi-dirigé comprenant des questions sur l'utilisation de fournisseurs de dépistage et les attitudes envers le cfDNA. Un seul intervieweur a mené et enregistré toutes les interviews par téléphone, les entretiens ont duré environ 30 minutes chacun. Nous avons développé en collaboration un dictionnaire par un processus itératif d'examen de la transcription et de l'application du code, et un codeur primaire a codé toutes les transcriptions.

Les professionnels de soins prénataux ont des points de vue variés sur les avantages du dépistage cfDNA et expriment une gamme de préoccupations concernant la mise en œuvre du dépistage cfDNA dans la pratique. S'ils ont convenu de plusieurs avantages de cfDNA, y compris une précision accrue, un retour plus rapide des résultats et une diminution de risque de complications, une préoccupation exprimée est qu'il n'y a pas suffisamment pour conseiller et éduquer les patients sur les options de dépistage et de dépistage prénatal. Les professionnels ont également convenu que la demande pour le dépistage cfDNA a augmenté et ont souhaité plus d'informations émanant des sociétés professionnelles, des laboratoires et des publications. Les fournisseurs étaient en désaccord au sujet des implications sur la santé et sur l'avenir du dépistage cfDNA. Certains fournisseurs prévoyaient que le dépistage cfDNA diminuerait les coûts des soins de santé lorsqu'ils seront appliqués largement et a exprimé son optimisme pour l'élargissement des échantillons de dépistage cfDNA. D'autres craignaient que le dépistage cfDNA augmenterait les coûts au fil du temps et se sont demandé si la possibilité d'y inclure les microdélétions pourrait être fait sur le plan éthique.

Les perspectives et les expériences des fournisseurs dans cette étude permettent d'avoir un aperçu de l'avantage clinique, de la charge sur la pratique prénatale, et du futur potentiel du dépistage cfDNA dans la pratique clinique. Compte tenu de la probabilité que la portée et l'acceptation du dépistage cfDNA vont continuer à augmenter, il est essentiel d'examiner comment ces changements auront une incidence sur les fournisseurs de soins prénataux de première ligne et sur les patients. Les demandes de professionnels pour obtenir des conseils et des données supplémentaires ainsi que leurs préoccupations sur le manque de temps disponible pour expliquer

aux patients les options de dépistage et de tests indiquent des problèmes potentiellement lourds. Il est important de veiller à ce que l'intégration clinique du dépistage cfDNA soit gérée de façon responsable et éthique avant qu'il ne se développe davantage, aggravant les problèmes préexistants. Comme le dépistage prénatal évolue, de même devrait évoluer le consentement éclairé et les ressources disponibles pour que les femmes puissent prendre leur décision. La discipline doit prendre des mesures pour maximiser les avantages du dépistage cfDNA et gérer de façon responsable les questions éthiques qui s'y rapportent.

Keywords

Cell-free DNA; Non-invasive prenatal screening; Reproductive ethics; Implementation

Introduction

> << Je pense que nous avons trop de tests ! >> : réflexions des professionnels en prénatal sur les défis éthiques et cliniques liés à l'intégration de la pratique du dépistage de l'ADN libre fœtal

Prior to its clinical integration, many providers and test developers hailed cell-free DNA-based non-invasive prenatal testing screening (cfDNA screening) as a revolution in prenatal screening and testing [1,2]. The nature of the blood draw procedure itself, namely its ease and lack of procedural risk, made cfDNA screening an appealing complement to existing invasive technologies [3,4]. In addition, research showed that, for the most common trisomies, cfDNA screening outperformed other maternal serum screening technologies due to its increased sensitivity and specificity. Specifically, cfDNA screening was validated for trisomy 21 in 2011 [5–8], with additional data published in 2012 supporting the expansion of screening panels to include trisomy 13 and 18 [5,9,10].

These advantages have contributed to the dramatic increase in the uptake of cfDNA screening since its clinical introduction [11]. However, the scope of cfDNA screening has also changed significantly. cfDNA screening panels now often include screening for sex chromosome aneuploidies, and several testing companies have recently begun offering screening for subchromosomal conditions in their cfDNA screening panels [12–15]. Professional societies continue to change and update their guidelines to reflect ongoing laboratory developments [16,17].

It is not clear whether and how clinical practices are assimilating this new type of screening into their prenatal care infrastructure, particularly in regards to informed consent and counselling processes. Existing literature indicates substantial variation in the clinical integration of cfDNA screening not only internationally but also within certain countries [18–21]. In the United States, one recent survey found that general obstetricians, rather than specialists, initially discuss cfDNA screening with patients four times out of five, and three quarters have these conversations during the initial patient visit; only about half said they regularly send their patients to a specialist for in-depth conversations [22]. Furthermore, while the clinical integration of cfDNA screening has shown benefits for specific patient

populations [23,24], significant misunderstandings about the technology have been identified among providers and patients alike [25,26].

Ethical concerns about issues, such as sufficient pre-test counselling, informed consent, costs, and equitable access have accompanied cfDNA screening from the start of its clinical use [27–29]. These and other ethical tensions are exacerbated by the growing scope and uptake of cfDNA screening [30–34], and few, if any, of the ethical challenges have been resolved over the last several years. Prenatal care providers bear a significant burden in attempting to navigate these challenges [35]. specifically, prenatal care providers are under increasing pressure to stay up to date with rapidly changing cfDNA screening panels, manage growing patient demands, and keep up with changing test costs, all while attempting to use the technology responsibly and ethically.

This study explores the experiences of prenatal care providers at the forefront of non-invasive genetic testing to understand how cfDNA screening has changed prenatal practice and to identify how the experience of providing and offering this testing differs from previous prenatal testing modalities. Prenatal care providers significantly influence the decisions of their patients; therefore, it is essential to assess prenatal providers' attitudes toward and experiences with cfDNA screening in order to determine how this screening can be implemented most responsibly in patient care.

Methods

The data from this study were collected via semi-structured interview with a national sample of prenatal care providers, and analysis was conducted following iterative transcript coding.

Recruitment

We used the online American Congress of Obstetricians and Gynecologists (ACOG) Physician Directory to identify a systematic sample of five prenatal care providers in each U.S. state and the District of Columbia. Beginning with the lowest zip code in each state, every fifth name was taken from the directory, excluding providers who were retired, did not currently practice in the state under which they were listed, or were not involved in a prenatal specialty. Using publicly available contact information, a first round of study invitations was sent via U.S. mail in July 2014 ($n = 255$). In October 2014, this process was repeated for providers in states in which the study team had not yet conducted an interview, contacting five additional providers in those states, except in one state (Vermont) where the end of the directory listing was reached and we were able to contact only one additional provider ($n = 206$).

Study invitations included an invitation letter, an IRB-approved information sheet, a self-addressed stamped return card, and study staff contact information. Individuals were contacted only once by mail. Individuals who expressed interest in participating were contacted up to two times by email or phone, depending on their preferred contact method. Across both mailings, 37 providers expressed interest in participating, and we completed telephone interviews with 21 providers (4.6%).

Data collection

The study team developed a semi-structured interview guide that included questions about providers' use of and attitudes toward cfDNA screening, based on topics identified through a review of the literature and previous conversations and interviews with practicing prenatal care providers. A single interviewer conducted and audio-recorded all interviews by telephone. Interviews lasted approximately 30 minutes each.

Analysis

Audio-recordings were professionally transcribed verbatim and all transcripts, with personally identifying information redacted, were uploaded to the online qualitative analysis software Dedoose (www.dedoose.com). The study team collaboratively developed a codebook through an iterative process of transcript review and code application. A primary coder then coded all transcripts, of which four transcripts were selected at random and coded to consensus with a secondary coder.

Results

The study participants ($n = 21$) were located in 19 U.S. states, in every major region of the U.S. The providers practiced in community-based general practice ($n = 15$), academic medical centers ($n = 4$), or fertility clinics ($n = 2$). The majority were general obstetricians, while the remaining providers were maternal-fetal medicine specialists, fertility specialists, or genetic counsellors. Eighteen providers offered cfDNA screening in house at the time of the study, with ten providers limiting cfDNA screening to high-risk pregnancies only.

These prenatal care providers expressed varying perspectives on the advantages of cfDNA screening and expressed different concerns regarding the implementation of cfDNA screening in practice. Based on the coding and analysis of the interview transcripts, four areas of consensus and four areas of disagreement were identified among the perspectives of the care providers. In order to maximize readability, some quotations have been marginally edited.

Areas of consensus

cfDNA screening advantages—The majority of providers stated at least one advantage to cfDNA screening in comparison to existing prenatal testing technologies. Some providers explained that the main advantage was increased accuracy over conventional maternal serum screening: "Compared to how many false positives I get with the quad screen and the first trimester screen, you know, [cfDNA screening] is much better". Others noted that the earlier return of results was a key advantage, saying, "Earlier is better" and "You can get results sooner". Providers mentioned that earlier results can aid with decision-making as needed and also suggested their patients often wanted to know the sex of the baby as early as possible. A third advantage identified by the providers was the decreased risk of complications compared to diagnostic testing. They explained that cfDNA screening, unlike invasive diagnostic testing, is not associated with miscarriage, and some expressed optimism that cfDNA screening decreased the number of women seeking invasive testing. One

provider stated, “The benefit is that it’s a non-invasive test. I think that it’s almost as good as an amniocentesis, but you don’t have to worry about miscarriage. I think it’s a superior test”.

Time—While providers were optimistic about the accuracy, earlier return of results, and decreased risk of cfDNA screening, many expressed concern that there is not enough time to adequately counsel and educate patients on their prenatal testing options. It was clear to the providers that cfDNA screening is substantially different than previously available screening tests, but they identified challenges in explaining those differences to patients. One provider explained, “I don’t think there’s enough time in the day to sit down and ask every single person about every test”. Another considered the issue of time in conjunction with limited reimbursement: “I think the problem is that time for counselling is limited, so for us to spend 15—20 minutes potentially going through this and not make any additional money for it, no one’s going to want to do it”. In addition to expressing concerns about the time entailed in pre-test counselling, some providers proposed solutions, including educational videos or referral centers.

Demand—Providers reported that cfDNA screening was an appealing option to their patients and that, as a result, demand for cfDNA screening has increased over time. “We get a lot of people that want to do the cfDNA test early,” said one provider. Another provider described a perpetuating cycle in which more patients demand the test as it is offered in more clinics: “Because it was offered, patients were going to want it, and everyone in the area was offering it. I thought it was a great addition”. Providers also expressed concerns about the impact of direct-to-consumer marketing on future patient demand: “I think some of the mistakes especially drug companies have made is they’ll do direct patient marketing; and if that starts to happen with something like this and patients walk in our office and we’re not fully educated about the certain test, that’s not a good thing”.

Need for guidance—Many providers noted a need for additional education and clarifications about cfDNA screening. In particular, they focused on improved education and guidance more for providers than for patients, although several also described a need for patient education materials. With regard to provider education, one participant explained, “I think we just need to be educated as these new tests roll out, as they test for different disorders”. Collectively, the providers indicated that there has been too little education available for providers to stay informed about the rapid changes in cfDNA screening. One provider admitted, “We’ve had a lot of people approach us, you know, a variety of ‘do my cell-free DNA test, it’s better, it does this, it does that’. It’s very hard as a practitioner to know which one’s better or worse, up, down, you know, it’s hard. They come and present data, but, you know, it’s tough”. Some providers also suggested that improved provider education goes hand in hand with better patient education: “It’s made me feel better about what I am able to offer my patients”.

Providers listed a variety of sources from which they would like additional information and guidance. Specifically, they mentioned wanting more information from testing labs, prenatal academic literature, and professional societies. They also expressed a desire for more published data on populations to whom cfDNA screening should be offered: “I would like there to be more published data about it in the low risk population so that it could be offered

to everyone". Another explained, "If it's shown to still be good in the larger patient population and that's published in a reputable journal and I read the paper and it looks pretty good to me, then I will offer it to everyone".

Providers suggested that they often look to professional societies for guidance but that the current state of professional education and guidance is lacking. One explained, "I do think there needs to be more education about what is available now, what these test for, the false negatives, the false positives etc. It would be a really good thing if it came from the ACOG". Another admitted, "I usually wait for some higher body to tell me, you know, if they say this is the policy I do what I'm told".

Areas of disagreement

Test expansion—Providers expressed variable opinions regarding the expansion of cfDNA screening panels to include microdeletions; some expressed concerns regarding the utility and the reality of explaining microdeletions to patients while others expressed optimism about gaining more information about the fetus. Providers who were apprehensive about testing expansion discussed the struggle to stay up to date with ever-changing test panels, questioned the utility of expanded panels, and noted the challenge of explaining expanded panels at an appropriate level for patients to make informed decisions. "I'm not convinced upon the utility and the screening for all those things," said one provider.

Providers who were optimistic about expanded panels primarily cited the power of additional information. One provider explained, "I think some people might be scared that so much information is easily accessible, but I think it's good". Another exclaimed, "Oh I think it's going to get better and better and better". One provider called the expanded panels a "double-edged sword," given that "things can be identified that we don't know what they mean. Sometimes that's a problem, but it can also identify the cause of abnormalities that don't require us to do anything further…I think it's great".

Costs—With respect to health care costs, providers expressed conflicting opinions about the impact of cfDNA screening. Some believed that cfDNA screening would decrease costs of prenatal testing by decreasing the frequency of invasive diagnostic testing. Others argued that any cost change associated with a decrease in diagnostic testing would be overcome by the increasing cost of cfDNA screening based on its scope and uptake.

The providers who anticipated that cfDNA screening would increase health care costs cited expanded panels and populations as the probable root causes. "If everyone decides to get that done, if just all the pregnant ladies get it done, you know, pretty soon everybody's going to want to get it done … That's incredible, we can't afford that," exclaimed one provider. Another provider situated cfDNA screening within the context of other prenatal technologies and broad health care spending: "New tests? I think we've got too many tests! I mean we only have limited health care dollars".

The providers who expected cfDNA screening to lower health care costs primarily argued that cfDNA screening reduces the occurrence of expensive diagnostic testing. "The cost is probably going to go down, and I would think that it will eventually lower health care costs

and that you wouldn't have so many false positives that then lead to additional testing and unneeded amnios," one provider explained.

Discussion

This study explores the experiences of prenatal providers at the forefront of offering cfDNA screening in order to better understand how this testing may change prenatal practice and how practices are managing the ethical issues associated with cfDNA screening. The perspectives and experiences of these providers allow insight into the clinical benefits, burdens, and potential future of cfDNA screening in clinical practice. While these providers are certainly not the only stakeholders bearing responsibility in this particular setting, they do hold an important obligation, given how frequently they are put in the position of first discussing cfDNA screening with the patient and later delivering the results [22]. In addition, these data reveal that the providers in this study perceived themselves to be gatekeepers, with a duty to provide their patients with responsible prenatal care. In 2009, a review of cfDNA screening asserted that "this technology offers safer, earlier, and easier antenatal testing than current standard practice but raises ethical, legal, and social concerns, including those around informed consent and equity of access" [36]. In spite of the changes that have occurred, the findings in our study echo and elaborate upon those early assertions.

Clinical benefit

Providers in this study were quick to discuss the advantages of cfDNA screening that they had witnessed in patient care, in comparison to other prenatal testing technologies. Providers noted cfDNA screening's increased accuracy over conventional screening, early return of results, and decreased risk over diagnostic testing. Their identified advantages reflect those specified in the literature about cfDNA screening prior to clinical integration [3,36,37]. Focus groups and surveys of pregnant women have identified many of the same benefits [26,38]. Thus, while these particular benefits are not surprising, it is encouraging that they are being confirmed in the clinical space.

Collectively, providers framed cfDNA screening in a positive light when discussing the concept of this technology from a broad perspective, saying that cfDNA screening was "a great asset". This is a significant change from literature that only a few years ago documented hesitations among providers about cfDNA screening. One study from 2011 found that only one-third of surveyed providers anticipated using cfDNA screening in practice [37]. In contrast, our interviews revealed an overall optimism from providers about the clinical use of this technology. This change over the last few years can likely be attributed to increasing familiarity with the method of cfDNA screening as well as a greater awareness of the successes associated with this technology. Ultimately, participants generally agreed that cfDNA screening is improving prenatal practice.

Burden on practice/education

Along with the benefits of cfDNA screening, however, the providers in this study indicated several significant problems with the present and future integration of cfDNA screening. specifically, providers' repeated requests for more guidance and data, in conjunction with

their concerns about time for adequate counseling, raise concerns about the responsible and ethical integration of cfDNA screening into current patient care. These providers describe an unfortunate reality in which the advantages of cfDNA screening are not currently being maximized because of the burdens of cfDNA screening in practice.

A major issue raised by these providers is that there is simply not enough time in clinical practice to devote the attention and resources needed to provide cfDNA screening. These findings are consistent with another recent study that found counselling and education resources about cfDNA screening are not being offered as often as the screen itself is offered, in spite of professional society guidelines to the contrary [39]. Indeed, in a recent survey, more than 80% of practicing obstetric care providers reported lack of time as a barrier to counseling patients about cfDNA screening [22].

In spite of its advantages, this technology has proved to be disruptive because of the time required and the lack of existing resources to guide decision-making. Our findings suggest that the integration of cfDNA screening into clinical practice requires significant consideration and special attention, rather than a simple readjustment of serum screening procedures. Providers in our study listed several innovative methods to help with these issues (e.g. educational videos and group counselling sessions), but no solution has been widely adopted.

The future of clinical practice

Providers in our study weighed the benefits and burdens of cfDNA screening variably, expressing differing opinions about the future of cfDNA screening. Study participants were divided on whether cfDNA screening panels should be expanded to include subchromosomal microdeletions. Providers who were sceptical of the integration of microdeletions in cfDNA screening panels cited ethical issues about informed consent and utility. Their hesitation reflects not only their desire for additional information but also the lack of clear professional guidance on expanding cfDNA screening into the realm of subchromosomal aneuploidies [17]. Other research has indicated that this collective uncertainty among providers and professional societies may contribute to patients receiving unexpected results for microdeletion syndromes without adequate pre-test counselling and post-test support [40].

In addition, providers in our study were divided regarding the impact of the health care costs of cfDNA screening. The economic impact of cfDNA screening was a point of divergence among study participants. This finding is perhaps not surprising, given the variability among recent cost analyses of cfDNA. For example, a 2015 comparative cost analysis determined that cfDNA screening is cost-effective as a firsttier screen, but only for women aged 40 or over [41]. Other recent studies have found that cfDNA screening does reduce the number of invasive procedures and can be cost-effective at certain price points or with certain restrictions, such as offering only for trisomy 21 and/or only as a contingent screen [42–44]. As more data become available, it is important that prenatal practices adjust accordingly to minimize the burden associated with cost and uncertainty.

Ethical implications

Providers in this study identified significant current challenges in implementing cfDNA screening, even without the expanded panels for microdeletion syndromes. In addition to time limitations on adequate patient counselling and education, providers in our study also noted a need for professional guidance and better information from a variety of sources, including professional societies, laboratories, and researchers. These needs hinder the ethical implementation of cfDNA screening, especially as it relates to patient education, counselling, and informed decision-making.

Many of these issues are not new to the prenatal genetic testing space [45–50]. However, cfDNA screening is a significantly different test than those that have come before it, and our findings suggest that established processes for counselling and informed consent may have not yet been adjusted accordingly. The ethical tensions identified in this study are consistent with those identified in previous studies, in which patients have expressed doubts about the utility of expanded cfDNA screening panels and desires for a formal consent process [26,51]. Thus, the ethical concerns of providers in our study appear to mirror those of their patients.

In spite of the ethical challenges, the scope of cfDNA screening technology is expanding briskly with respect both to conditions screened and populations targeted. Unfortunately, the ethical issues at stake are not being resolved in step with these changes. Rather, the ethical tensions seem to remain stagnant, as indicated by this study's data. What is at risk if the ethical aspects of cfDNA screening, such as informed consent, substantial counselling, and respect for patient choice, are not prioritised? Existing literature points to the potential for stigmatisation of disability, increased prevalence of abortions [25], improper offering of the technology, lack of respect for patient choice [52], and increased patient anxiety following test results, [40], to list a few. The advantages of cfDNA screening can only be maximized if these ethical risks are minimized.

Limitations

This qualitative study utilizes a small sample size originating from a low response rate, which may be due to the low response rate of providers generally or potentially to the method by which providers were contacted to participate [53]. This small sample size is ultimately composed of providers who were willing to participant and discuss their experiences, which may have resulted in responder bias. While we cannot claim generalisability for the themes identified in this small qualitative study, they are consistent with the findings of other studies on the views of providers and patients [21,22,35,38,51] and suggest themes for further exploration. Care was also taken to ensure that study participants reflected a variety of prenatal experiences with respect to clinical setting.

Conclusions

The clinical integration of cfDNA screening is meant to provide patients with "meaningful options for reproductive choice" [30]. Our study suggests that cfDNA screening holds the potential to fulfil this goal by providing a combination of earlier, easier, and more accurate

results compared to existing technologies. The clinical trends and ethical concerns identified in this study, however, indicate that there is room for significant improvement regarding counselling and informed decision-making. While providers agreed that cfDNA screening benefits patients, significant issues have emerged at the frontline of its integration into clinical practice.

Given the likelihood that the scope and uptake of cfDNA screening will continue to increase, it is crucial to consider how these changes will affect prenatal care providers and, in turn, patients. Providers' desire for additional guidance and data and their concerns regarding the lack of time available to explain screening and testing options suggest serious implications for patient care. As the test evolves, so must the informed consent process and the resources available to patients making decisions. Responsibly managing these ethical issues can help clinicians maximize the advantages of cfDNA screening for patients as this technology continues to advance.

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