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ORIGINAL RESEARCH

Online direct-to-consumer messages about non-invasive prenatal genetic testing

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Abstract Non-invasive prenatal testing (NIPT) has been integrated into clinical care at a time when patients and healthcare providers increasingly utilize the internet to access health information. This study evaluated online direct-to-consumer information about NIPT produced by commercial laboratories accessible to both patients and healthcare providers. A coding checklist captured areas to describe content and assess concordance with clinical guidelines. We found that the information presented about NIPT is highly variable, both within a single website and broadly across all websites. Variability was noted in how NIPT is characterized, including test characteristics and indications. All laboratories offer NIPT to test for common sex chromosome aneuploidies, although there is a lack of consistency regarding the conditions offered and information provided about each. Although indicated for a subset of women at increased risk of aneuploidy, some laboratories describe the use of NIPT for all pregnant women. A subset of laboratories offers screening for microdeletions, although clinical practice guidelines do not yet recommend for general use for this indication. None of the online materials addressed the ethical issues associated with NIPT. This study highlights the need for clear, consistent, and evidence-based materials to educate patients and healthcare providers about the current and emerging applications of NIPT.

KEYWORDS: commercial laboratories, direct-to-consumer, internet, non-invasive prenatal testing, prenatal care

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Introduction

Non-invasive prenatal testing (NIPT) uses cell-free fetal DNA (cff DNA) to assess the risk of fetal trisomy 21, trisomy 18 and trisomy 13, with a greater sensitivity and specificity than conventional serum analyte screening tests (Bianchi et al., 2014; Norton et al., 2012). In addition, NIPT can be used to identify sex chromosome aneuploidies (SCA) that formerly could be detected only by using invasive diagnostic procedures. Currently, as outlined by clinical practice guidelines, NIPT is indicated for these conditions and for pregnant women who, on the basis of maternal age, reproductive history or a positive finding on other screening tests, are at increased risk for fetal aneuploidies (ACOG, 2015; Benn et al., 2013; Devers et al., 2013; Dondorp et al., 2015; Gregg et al., 2013). However, the use of NIPT in the general obstetric population is forthcoming (Greene et al., 2013; Wapner et al., 2015).

NIPT can be differentiated from conventional screens in two main ways. First, it can screen for a larger number of chromosomal aneuploidies than serum analyte screens can. Furthermore, because of the rapid pace of cff DNA technology, the capability of NIPT has quickly expanded to include the ability to identify subchromosomal variants - specifically, a set of microdeletions associated with clinical phenotypes (Wapner et al., 2015). It is anticipated that detailed genetic information will become accessible when NIPT is used to conduct genome-wide fetal aneuploidy detection (Bianchi et al., 2012). Research and development has progressed despite active debate about whether and how to utilize NIPT for these purposes (Allyse and Chandrasekharan, 2015; Norton et al., 2013).

Second, unlike the case for other prenatal genetic tests, industry has had an important role in the development and introduction of NIPT (Allyse and Chandrasekharan, 2015; Baudhuin et al., 2012). The stage for the introduction of NIPT was set by the small number of commercial laboratories that initially developed the technology. Each laboratory brought its own proprietary platform to market, offering a screening package to identify a unique set of genetic conditions with different sensitivities, specificities and cut-off values (Allyse et al., 2013; Mozersky and Mennuti, 2012). There is concern that the unprecedented dynamic of industry and commercial factors in the initial and continued development of prenatal genetic technologies will lead to practical and ethical issues which, in turn, will influence patients' access to NIPT in addition to the type and volume of information that can be obtained about the fetus (Agarwal et al., 2013).

The pace and context in which NIPT has emerged raises important questions about how patients and healthcare providers access information about this new screening option. Studies show that the internet is now an important source of medical information (Fox and Duggan, 2013). Currently, there is a large number of online resources available from which readers can learn about NIPT. These resources include open access peer-reviewed medical journal articles, clinical practice guidelines, public websites with evidence-based medical information, and social media sites, all of which are subject to various degrees of review (ranging from thorough to moderate, minimal, or often no quality review). This information also includes marketing materials offered by commercial laboratories that developed NIPT, which are among the lead results on an internet search on the subject (Mercer et al., 2014).

Patients are one population turning to the internet for medical information, including women who are currently pregnant or are considering a pregnancy. Studies of internet usage by select populations of pregnant women have shown that some use the internet to obtain information about the pregnancy prior to their prenatal visit and to supplement information provided by their healthcare provider after their visit (Huberty et al., 2013, Song et al., 2012); they also use it to find information about prenatal genetic testing options (Farrell et al., 2014, Farrell et al., 2015a). In addition, internet-based materials produced by commercial laboratories have become an important resource for pregnant women to gain information about NIPT (Farrell et al., 2014).

Healthcare providers are another population who utilize web-based materials to acquire knowledge and develop clinical practice patterns around the use of new tests, procedures and therapeutics (Bennett et al., 2004; Casebeer et al., 2002). Some physicians use internet-based educational materials more frequently than traditional, printed materials (Google/Hall and Partners, 2009). Web-based information developed by commercial laboratories has also become an educational resource for obstetric healthcare providers to develop and update their knowledge base about NIPT (Farrell et al., 2016). While online educational tools are an ideal mode through which to provide continuing education for physicians, there is concern about the biases that can be introduced when industry has a role in medical education (ACOG Committee on Ethics, 2012).

Despite the growth of NIPT and the role of the internet as a source of information about new tests, little is known about the content of online information produced by commercial laboratories about this new screening option. Given the availability of direct-to-consumer information on the internet about NIPT (Mercer et al., 2014) and trends in how pregnant patients and healthcare providers utilize electronic educational resources, we examined the online information presented by leading commercial laboratories regarding this new screening test. The objectives of this study were to evaluate the content of these websites and determine whether the information they presented was accurate, comprehensive and consistent, both in terms of characterizing NIPT and current clinical guidelines about its use.

Materials and methods

An internet search using the term 'non-invasive prenatal testing' in Google, Yahoo! and Bing was conducted during April 2015 to identify commercial laboratories that currently offer NIPT. At the time of the search, five US commercial laboratories were identified (Table 1).

Websites provided information targeted at two distinct consumer groups: patients and healthcare providers. Screen shots of each commercial laboratory's website were saved as PDF files and labelled with the date of capture. These images contained information visible to all readers, including patient-specific and healthcare provider-specific resources. The files were separated by content targeted at specific reader groups for combined and categorical analyses.

We utilized content analysis methodology (Morgan 1993) to evaluate the websites in our study sample. This methodology involves using a coding checklist to categorize

Table 1 NIPT commercial laboratories in study sample.

Name	NIPT product	URL
Ariosa Diagnostics	Harmony™ Prenatal Test	http://www.ariosadx.com/expecting-parents/ http://www.ariosadx.com/healthcare-professionals/
Illumina, Inc.	verifi®Prenatal Test	http://www.illumina.com/clinical/reproductive-genetic-health/patients/non-invasive-prenatal-screening.html http://www.illumina.com/clinical/reproductive-genetic-health/healthcare-professionals/non-invasive-prenatal-testing.html
Integrated Genetics	informaSeq℠ Prenatal Test	https://www.labcorp.com/wps/portal/integratedgenetics
Natera, Inc.	Panorama™ Prenatal Screen	http://www.panoramatest.com/en/expecting-parents/about-panorama http://www.panoramatest.com/en/healthcare-provider/overview
Sequenom	MaterniT21®PLUS Prenatal Test	https://laboratories.sequenom.com/patients/maternit21-plus/ https://laboratories.sequenom.com/providers/maternit21-plus/

NIPT = non-invasive prenatal testing.

the content of text into discrete codes that can be quantified. The coding checklist was developed by building upon the checklist used in our previous website analysis (Mercer et al., 2014) to meet the specific objectives of this study. Specifically, the coding checklist was structured to capture key content areas drawn from clinical guidelines regarding indications of NIPT published by the American College of Obstetricians and Gynecologists, the American College of Medical Genetics and Genomics, the National Society of Genetic Counselors and the International Society for Prenatal Diagnosis (ACOG, 2015; Benn et al., 2013; Devers et al., 2013; Gregg et al., 2013). It was also constructed to capture content related to counselling, decision-making, informed consent, values and ethics, as outlined in the policy statement of the American Society of Human Genetics and the European Society of Human Genetics (Dondorp et al., 2015). The manner in which each laboratory categorized (screening, diagnostic, not specified) and described (non-invasive, assessment of specific conditions, sensitivity, specificity, false-positive and false-negative rates, and analytic method) NIPT - as well as cost, insurance coverage, and the return of results to the clinician - was analysed. Links to downloadable brochures or checklists were also captured for analysis. Content areas of the coding checklist are summarized in Table 2.

Two members of the research team independently used content analysis methodology (Morgan, 1993) to evaluate and code the content of the websites. Members of the research team met to compare coding and develop a consensus between the coders.

In addition, the readability of the content of each commercial laboratory website targeted at patients was assessed using the Flesch Reading Ease (FRE) and Flesch-Kincaid Grade Level formulas (Aliu and Chung, 2010; Kars et al., 2008). The content of each website was downloaded into Microsoft Word, which has a built-in tool to compute FRE and Flesch-Kincaid Grade level scores. Reading ease was evaluated on a scale of 0-100 by using the FRE score: the lower the score, the more difficult the content. Adapting the FRE scores as per D'Allesandro (D'Allesandro et al., 2001), the following designations were used: (i) easy reading, >80 (less than a sixth-grade reading level); (ii) adequate or standard reading, 60-80 (sixth- to eighth-grade level); and (iii) difficult reading, <60 (ninth-grade level or greater). The Flesch-Kincaid Grade Level formula, which translates reading scores into a reading grade level (Aliu and Chung, 2010), was calculated for the patient-directed content of each commercial laboratory website.

The final data were entered into an Excel database and exported to the Statistical Package for Social Sciences (SPSS) Version 19 (IBM Corp., USA) for statistical analyses. Frequencies of informational content of all websites were calculated across and within laboratory websites for targeted reader groups.

Results

The commercial laboratory websites were among the first three pages of listings based on the search term 'non-invasive prenatal testing' on all three search engines.

Description of NIPT

All five commercial laboratories described their product as a non-invasive prenatal test that could analyse cff DNA in maternal blood starting from 9-10 weeks' gestation. Laboratories varied in the manner in which they described NIPT. Four laboratories described NIPT as a screening test; two of these laboratories included this description in both patient and healthcare provider materials and one included it in the patient materials only. The fourth laboratory referred to NIPT as a screening test in the healthcare provider materials, but described it as a diagnostic test in an educational video link on the patient-directed website, although in another location in the patient-directed materials it mentioned that additional confirmatory testing was recommended (although the term 'screening' was not used). The remaining laboratory did not specifically categorize the test as a screening or diagnostic test in either the patient or healthcare provider content.

Information regarding the specificity and sensitivity of the screening test varied among the laboratories' websites. Four of the five laboratories discussed the chance of a false-positive result in both patient and healthcare provider

Table 2 Content areas of coding checklist.

Content
Description of NIPT
Categorization
Non-invasive blood test
Analytic method
Sensitivity
Specificity
False positive
False negative
Cost and insurance
Conditions assessed
Autosomal aneuploidies
Sex chromosome aneuploidies
Microdeletion syndromes
Fetal sex
Indications
Advanced maternal age
Reproductive history
Second tier test
General obstetric population
Report of results
Risk level
Positive/negative
Detected/not detected
Not reportable
Recommends confirmatory diagnostic testing
Patient education and counselling
Role of healthcare provider in testing process
Informed consent
Values
Ethical considerations
Educational resources/links

NIPT = non-invasive prenatal testing.

materials. Two laboratories addressed the possibility of a false-negative result. One included this information in both patient and healthcare provider content and the other did so in patient material only. The content of the five laboratories' websites is summarized in Table 3.

Conditions assessed using NIPT

Autosomal and sex chromosome aneuploidies

The laboratories consistently presented information about the use of NIPT to test for common autosomal aneuploidies. Across the board, all laboratories included information about the use of NIPT for trisomy 21, trisomy 18 and trisomy 13, in both patient and provider materials. While all laboratories provided information about the utilization of NIPT to identify SCA, some variability was noted in content specific to these conditions. Each of the laboratories included information about Klinefelter syndrome and Turner syndrome in materials for both healthcare providers and patients. Four laboratories addressed the use of NIPT for Triple X in both the patient and provider materials. The remaining laboratory included this information in the provider materials only. Four of the five laboratories reported that their NIPT platform could assess fetal sex in both patient and healthcare provider content (Table 3).

Microdeletion syndromes

Three of the laboratories offered screening for microdeletion syndromes and presented information about this capability. Two laboratories addressed the use of NIPT to detect 1p36 deletion syndrome, Cri-du-chat syndrome, Prader Willi syndrome, and 22q11 deletion syndrome. This information was included in content targeted at both patients and healthcare providers. The third laboratory addressed the use of NIPT for these syndromes in the healthcare provider materials only. Information regarding the use of NIPT to detect Angelman syndrome was presented by two laboratories; in both cases, this information was included in both patient and provider materials. Reporting on testing for other microdeletions, including 11q, 8q, and 4p-, varied across laboratories.

Indications for NIPT

Laboratories varied in their presentation of information regarding indications for NIPT. Three laboratories stated that NIPT is indicated for women who are of advanced maternal age. The remaining two laboratories indicated that NIPT is available for women of all ages, regardless of age-related aneuploidy risk. Reproductive history was noted as an indication by four of the laboratories, although only one laboratory included this information in the patient material. Four laboratories presented NIPT as a follow-up test that could be used after a positive serum-screening test or after a sonographic finding of a fetal anomaly. Two of those laboratories included information about this indication in both patient and healthcare provider materials. Of the two remaining laboratories, one addressed this only in the patient information, and the other only in the healthcare provider information (Table 3).

Report of test results

All five laboratories presented information on the manner in which NIPT results are reported in content targeted at both patients and providers. Three laboratories described that results are reported as a risk level (e.g. high risk or low risk) and included this information in both patient and provider materials. One laboratory described the report of a 'positive' or 'negative' for trisomy 21, trisomy 18 and trisomy 13, and an 'additional finding' for other chromosomal abnormalities. The remaining laboratory reported results as 'aneuploidy detected,' 'no aneuploidy detected' and 'aneuploidy suspected (borderline value).' Only one addressed the possibility of a non-reportable result, and this information was only provided in the patient material. All laboratories recommended diagnostic testing to confirm a result that indicates the presence of a chromosomal abnormality: two laboratories provided this information in both patient and healthcare provider materials, two provided it in the patient materials but not in the healthcare provider materials, and one provided it in the healthcare provider materials but not those for patients.

Table 3 Review of commercial laboratories' website content.[a]

Content	Laboratory 1		Laboratory 2		Laboratory 3		Laboratory 4		Laboratory 5	
	Patient	HCP	Patient	HCP	Patient	HCP	Patient	HCP	Patient	HCP
Description of NIPT										
Screen	-	X	X	X	X	X	-	-	X	-
Diagnostic	X	-	-	-	-	-	-	-	-	-
Unspecified	-	-	-	-	-	-	X	X	-	-
False positive	-	-	X	X	X	X	X	X	X	X
False negative	-	-	-	-	X	X	X	-	-	-
Conditions assessed										
Trisomy 21	X	X	X	X	X	X	X	X	X	X
Trisomy 21 description	X	-	X	-	-	-	-	-	X	-
Trisomy 18	X	X	X	X	X	X	X	X	X	X
Trisomy 18 description	X	-	X	-	-	-	X	-	X	-
Trisomy 13	X	X	X	X	X	X	X	X	X	X
Trisomy 13 description	X	-	X	-	-	-	X	-	x	-
Klinefelter syndrome	X	X	X	X	X	X	X	X	X	X
Klinefelter description	X	-	X	-	-	-	X	-	-	-
Turner syndrome	X	X	X	X	X	X	X	X	X	X
Turner description	X	-	X	-	-	-	X	-	-	-
Triple X	X	X	X	X	X	X	X	X	-	X
1p36 deletion	-	X	-	-	X	X	X	X	-	-
Cri du chat syndrome	-	X	-	-	X	X	X	X	-	-
Prader–Willi syndrome	-	X	-	-	X	X	X	X	-	-
22q11	-	X	-	-	X	X	X	X	-	-
Angelman syndrome	-	-	-	-	X	X	X	X	-	-
Fetal sex	X	X	X	X	X	X	X	X	-	-
Indications										
All populations	-	-	-	-	X	X	-	-	X	X
AMA	X	X	-	X	-	-	X	X	-	-
Reproductive Hx	X	X	X	X	X	-	X	X	-	-
F/u positive screen	X	X	-	X	X	-	X	X	-	-
F/u positive U/S	X	X	-	X	-	-	X	X	-	-
Report of results										
Risk level	-	-	X	X	X	X	-	-	X	X
Positive/negative	-	-	-	-	-	-	X	X	-	-
Aneuploidy detected/not	X	X	-	-	-	-	-	-	-	-
Reports no result	-	-	-	-	X	-	-	-	-	-
Confirmatory testing	X	X	X	-	X	X	-	X	X	-
Education/counselling										
Role of HCP	X	X	X	X	X	X	X	X	X	X
Questions for HCP	-	-	X	-	-	-	X	-	X	-
Electronic form	-	-	-	-	X	-	-	-	-	-
Additional resources/links	-	X	X	-	X	X	X	-	X	-
Decision aid	-	-	-	-	-	-	-	-	-	X
Informed consent	X	X	X	-	-	X	-	-	-	-
Insurance/financial assistance	X	X	X	X	X	-	X	X	X	X

AMA = advanced maternal age; F/u = follow-up; Hx = history; HCP = healthcare provider; NIPT = non-invasive prenatal testing; U/S = ultrasound.
[a] Laboratories are not listed in any particular order.

Patient education and counselling

All laboratories provided information on the role of the healthcare provider in pre- and post-test patient counselling in both patient and provider materials. In addition, all laboratories provided links or down-loads of additional educational resources. Three laboratories provided a list of questions that patients could bring to their prenatal visit to facilitate discussions about NIPT with their healthcare provider. One laboratory provided an electronic form for patients to enter their contact information and that of their provider so that the laboratory could share this information with the designated provider to help initiate discussions about NIPT. All five laboratories provided resources and/or

links for readers to access additional information about genetic conditions. Most were focused on trisomy 21, trisomy 18 and trisomy 13. Some websites included information regarding SCA and microdeletions. Sources of information included documents developed by the commercial laboratories, professional organizations and advocacy groups. Three laboratories had links to clinical practice guidelines; two of these laboratories offered microdeletion screening, although such indications were not addressed in the referenced document. One of the five laboratories provided downloadable tools intended for use by healthcare providers to assist in patient education and counselling.

Three laboratories included information about informed consent: one provided the information to healthcare providers only; the second provided the information in both patient and provider materials, and the third provided the information in patient-directed materials only. None of the website content provided by the commercial laboratories addressed personal values and ethical considerations as they relate to the decision-making process for NIPT.

All five laboratories included information regarding insurance coverage or financial assistance for NIPT. Four laboratories addressed these topics in both patient and provider materials. The remaining laboratory included financial information in the patient materials only. The specific cost of the test was not reported by any of the websites.

Readability of patient-targeted websites

Readability scores were determined for the patient-directed material produced by the individual laboratories. All of the patient-directed materials were written at a difficult reading level, based on a mean FRE score of 41.8 (range 39.1-50.2). The mean Flesch-Kincaid Grade Level was 11.34, and ranged from approximately the tenth-grade level (10.3) to the college level (13.1).

Discussion

NIPT has been integrated rapidly into the delivery of prenatal care, both in the USA and internationally. The first stages of this process began at a time when medical information on the internet increased exponentially, changing fundamental paradigms of how individuals access information about new tests and procedures (McMullan, 2006). Furthermore, NIPT emerged during a time when direct-to-consumer marketing initiatives by industry filled a void when other educational resources about this new screening option were not readily available. As a result, the educational materials of commercial laboratories who developed NIPT have become a source of information for both pregnant women and obstetric providers (Farrell et al., 2015a; Farrell et al., 2016). This is significant because of how individuals seek and respond to direct-to-consumer materials developed from healthcare companies. Specifically, studies show that some individuals perceive direct-to-consumer materials as a reliable source of information (DeLorme et al., 2010; Huberty et al., 2013; Menon et al., 2002; Närhi, 2007; Peterson et al., 2003). This finding was initially observed among those who were exposed to such information on the television or in print advertisements (Menon et al., 2002; Närhi, 2007). Studies show that this perception may also carry over into consumers' use of internet-based marketing materials (DeLorme et al., 2010; Huberty et al., 2013; Peterson et al., 2003). At the same time, studies demonstrate how industry-developed educational materials may influence patients' and healthcare providers' behaviours (ACOG Committee on Ethics, 2012; Fogel and Teichman, 2014). Additional data are needed to further understand the factors that influence readers' opinions about direct-to-consumer materials and behaviours in response to them. Yet, the studies that are currently available shed light on how patients and physicians may utilize industry-produced materials accessed online to learn about new medical options. Given these factors, we conducted a study to examine the content of information contained about NIPT within the websites of commercial laboratories.

The internet provides a novel interface for patients to obtain information about new genetic technologies prior to and following the potentially complex discussions that take place during the clinical encounter. Such information is particularly relevant in the context of obstetrics, where healthcare providers face limited time and resources to convey an increasing volume of information to pregnant women about prenatal care and their genetic testing options (Allyse et al., 2013; Farrell et al., 2015b). Web-based information cannot replace the important discussions that take place between a patient and her healthcare provider. Yet, such information does play a vital role in how patients frame not only their expectations and decisions about their healthcare options but also requests of their healthcare provider regarding the use of new tests and procedures (Farrell et al., 2014).

This study of commercially developed websites highlights the need for clear and consistent materials to educate patients and healthcare providers about the current and emerging applications of NIPT. For instance, overall, we observed a high degree of variability in the presentation of information about NIPT, both within and across the commercial laboratory websites. This finding was most prevalent among the materials developed for patients and was independent of the different approaches and capabilities of the NIPT platforms of each company. Some of the commercially developed web materials accurately described NIPT as a screening test; however, others did not. This finding may not be an issue for healthcare providers who have an existing knowledge base about prenatal screening and diagnostic tests. Yet it raises concerns for patients who use commercial laboratory materials to initially learn about NIPT or to supplement their knowledge about this testing option. This result is significant, as studies show that patients often search internet sites targeted at healthcare providers to obtain comprehensive or detailed information for themselves (Wood et al., 2000). Thus, the variability of information presented by the commercial laboratories about NIPT may make it difficult for patients to gain an accurate picture of the utility of this test.

Variability in the manner with which laboratory websites described the indications of NIPT was also noted. The use of NIPT to screen for common autosomal aneuploidies,

including trisomy 21, trisomy 18 and trisomy 13, has been accepted by professional organizations (ACOG, 2015; Benn et al., 2013; Devers et al., 2013; Dondorp et al., 2015; Gregg et al., 2013). All of the commercial web-based materials presented information regarding screening for these conditions. However, while the advantages of using NIPT to screen for these conditions were emphasized across all marketing materials, information about the limitations of NIPT was limited. In general, website content highlighted screen sensitivity and specificity for the detection of trisomy 21. Yet there was limited discussion about sensitivity, specificity or positive predictive value for trisomy 13, trisomy 18 or other identifiable conditions, each having its own detection and false-positive rates. Studies demonstrate that these concepts remain important factors in a patient's decision-making about the utilization of the NIPT, despite its superior performance compared with conventional analyte screens (Farrell et al., 2015a; Tischler et al., 2011).

Overall, there was also less consistency regarding the presentation of information about SCA. All laboratories presented information about the use of NIPT to detect Klinefelter syndrome and Turner syndrome. Yet there was variation in the information presented about other SCA that can be detected and are associated with known clinical syndromes. This finding may be a reflection of the proprietary decisions of the commercial laboratories and the specific conditions they choose to assess, as well as of their respective platform's test performance for the conditions. However, even among the laboratories that offer testing for these other SCA, materials about these conditions were not equally and consistently addressed in both the patient and healthcare provider materials. The lack of information about SCA is concerning, as patients are not as familiar with these conditions as they are with others (Agatisa et al., 2015; Lau et al., 2012). Furthermore, healthcare providers have less experience in providing counselling regarding physical and cognitive issues associated with SCA than they do for other conditions (Cleary-Goldman et al., 2006). In conjunction with providing information about SCAs, many of the websites highlighted the ability of their screening platform to assess fetal sex. The capability to detect fetal sex may be presented as an advantage of NIPT by some (Farrell et al., 2014) but has important medical and ethical implications that should also be considered (Chandrasekharen et al., 2014; Chapman and Benn, 2014).

Another finding was the variation in and across the websites' content regarding the use of NIPT for the detection of microdeletions in addition to departures from current clinical practice guidelines. Presently, clinical practice guidelines do not recommend the general use of NIPT for the detection of microdeletions. Yet, three of the laboratories presented information on their websites about their specific platform's ability to detect certain microdeletions. The differences among the laboratories' microdeletion offerings and educational resources may be a reflection of market incentives for commercial NIPT laboratories to provide large and unique testing platforms before competing laboratories do (Agarwal et al., 2013; Hayden, 2012). However, both the lack of consistency in the direct-to-consumer materials among the commercial laboratory websites, and marketing NIPT to screen for microdeletions, raises important concerns regarding the pathways and oversight with which new genetic technologies are introduced into obstetrics.

Of additional concern, we identified other areas of discordance between applications marketed by commercial laboratories and clinical practice guidelines for NIPT. NIPT is currently recommended for a subset of the pregnant population - specifically, women at increased risk for fetal aneuploidy because of maternal age, reproductive history, a positive analyte screening test, or an abnormal ultrasound finding (ACOG, 2015; Benn et al., 2013; Devers et al., 2013; Dondorp et al., 2015; Gregg et al., 2013). Yet two of the laboratories marketed their platform for use by all pregnant women. While this practice is forthcoming, it is currently not supported by clinical practice guidelines.

Finally, we found that the web-based marketing materials presented two additional challenges. First, personal values and ethical considerations form the basis of decisions to undergo any form of prenatal genetic screening or testing (Kuppermann et al., 2006; Lyerly et al., 2007). However, our analysis revealed a paucity of information about the ethical issues associated with NIPT. Second, specific to patients who seek information in this manner, the readability of all of the patient-directed materials on the commercial laboratory websites did not meet the National Institutes of Health and the American Medical Association's criterion that general public health information be written no higher than a sixth-grade reading level (Cotugna et al., 2005). The advanced reading level presents an additional challenge for patients who use these online materials.

The current landscape of NIPT is poised to change with the resolution of ongoing debates regarding intellectual property between these laboratories and the capability of new laboratories to perform the screening test (Agarwal et al., 2013; Hayden, 2012). Unlike the case for other prenatal screening options, commercial laboratories at the forefront of cff DNA technology have taken the lead in shaping the clinical debut and ongoing integration of NIPT into patient care. The laboratories' dual marketing messages, to healthcare providers as well as patients, have been heard. Patients are entering the clinical encounter aware of NIPT and interested in incorporating it into their prenatal care (Hill et al., 2012; Tischler et al., 201,). Thus, these laboratories have set the stage for educating patients as well as healthcare providers about NIPT, and integrating it into prenatal care, independent of guidance from professional organizations. This endeavour will undoubtedly continue as future applications of NIPT are offered by existing laboratories as well as by new commercial enterprises entering the testing arena. Both now and as the landscape of NIPT changes, it is critical that information presented is consistent, comprehensive, and in accordance with practice guidelines, as the stakes are high when informed decision-making regarding reproductive choices is at issue.

Although the internet is a dynamic platform for health information, by using an established methodology of data capture and analysis, we were quickly able to develop a picture of the informational landscape provided by commercial laboratories. Nonetheless, we are aware that this content may be in flux. In addition, we recognize that commercial laboratories are not the only source of

information regarding NIPT. However, they represent an integral resource for healthcare providers and patients (as well as members of the general public) who look to the internet for information about NIPT.

Conclusions

In light of parallel changes taking place regarding the role of the internet in the delivery of healthcare, advances in prenatal genetics, the industry's role in direct-to-consumer advertising, and the integration of NIPT into clinical care, we assessed online resources provided by commercial laboratories about this new screening test. Our findings indicate that the information presented by commercial laboratories is highly variable and, in some cases, does not correlate with clinical practice guidelines. Overall, we identified greater concordance between the sections of the materials developed for healthcare providers and patients specific to common autosomal aneuploidies, sex chromosome aneuploidies, and fetal sex but less consistency between provider- and patient-directed materials that address emerging applications of NIPT. These findings are problematic for patients who seek information outside of the clinical arena to inform important prenatal decisions and, additionally, for healthcare providers who utilize this information to learn about new technologies that affect patient care. As the technology of NIPT advances, and with a concurrent increase in online direct-to-consumer marketing efforts, healthcare providers will be presented with additional challenges to ensure patients acquire the necessary information to make informed, patient-centred decisions about the use of NIPT. This study underscores the need for accessible evidence-based, unbiased and comprehensive information about NIPT for patients and providers, as well as the need for established pathways and oversight, as regards to how new genetic technologies are introduced into prenatal care. Study findings also highlight that healthcare providers should remain an integral source of accurate and unbiased information for patients and utilize reliable sources of continuing medical education to maintain their competence. This is a prime opportunity for healthcare providers and professional organizations to rise to the challenge and develop educational resources that are directed at patients and clinicians, address current indications, and adapt as new applications of cff DNA technology emerge.

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