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RESEARCHBRIEF

An update on HDI's research in the field of developmental disabilities

Adherence of cell-free DNA noninvasive prenatal screens to ACMG recommendations in providing patient education resources

Original article by Brian G. Skotko, MD, MPP, Megan A. Allyse, PhD, Komal Bajaj, MD, MS-HPEd, Robert G. Best, PhD, Susan Klugman, MD, Mark Leach, JD, MA, Stephanie Meredith, MA, Marsha Michie, PhD, Katie Stoll, MS & Anthony R. Gregg, MD, MBA published in Genetic in Medicine (GIM)
Research Brief by Stephanie Meredith & Mark Leach

Background

Cell-free DNA prenatal screens (also known as NIPS or NIPT) were released in the US by commercial labs eight years ago as screening tests for conditions such as Down syndrome, Trisomy 18, and Trisomy 13. When these screens were originally released in 2011, they were largely covered in the media as non-invasive prenatal diagnostic tests that could detect conditions with a simple blood draw. However, even though cell-free DNA noninvasive prenatal screens are more sensitive than traditional screening tests, there are still chances for false positives and, less often, false negatives. Therefore, they are considered screening tests and are not actually diagnostic (Mozersky, 2012). The introduction of this new technology and some of the confusion surrounding it prompted national medical and genetics societies to issue guidelines about the administration of these screens.

ACMG released guidelines on the administration of NIPS in 2016 and included recommendations for patient education, including (Gregg, 2016):

- Down Syndrome Pregnancy (http://downsyndromepregnancy.org/books)
- Genetics Home Reference (https://ghr.nlm.nih.gov)
- Genetic Support Foundation (https://www.geneticsupportfoundation.org)
- Lettercase/ The National Center for Prenatal and Postnatal Resources (http://www.lettercase.org)
- NSGC "Fact Sheet about Down Syndrome for New and Expectant Parents" (http://nsgc.org/p/cm/ld/ d=387)

Both Down Syndrome Pregnancy and Lettercase are programs at HDI, and HDI consulted on the development of the NSGC fact sheet. Therefore, Mark Leach and Stephanie Meredith from HDI were invited to participate as part of the Skotko et al. study to focus on the adherence of labs in providing references to patient education materials either on their websites, on their lab reports, or in their printed marketing materials.

The article "Adherence of cell-free DNA noninvasive prenatal screens to ACMG recommendations" published in Genetics in Medicine in April 2019 reviews the adherence of commercial labs to all the American College of Medical Genetics and Genomics (ACMG) recommendations for cell-free DNA noninvasive prenatal screens (Skotko et al., 2019). This HDI Research Brief aims to review what the Shotko et al. study revealed about the adherence of labs in following the ACMG recommendations for the provision of patient resources.

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Method

The Skotko et al. team assessed NIPS tests that were commercially available in the United States as of January 1, 2018 and excluded NIPS from single-health systems, single-hospital systems, academic/university settings, or umbrella labs that did not sell tests directly.

The researchers in the study indicated that they gathered patient education materials and sample reports for each NIPS test from the company web pages, resources at the exhibit booths at the 2018 ACMG Annual Meeting, and/or direct requests. In addition, authors were divided into pairs, and each group assessed one NIPS laboratory for its adherence to all of the recommendations in the 2016 ACMG position statement. This study team used a categorical rating scale for the criteria in the ACMG guidelines that pertained to laboratories: green (full adherence), yellow(partial adherence), and red (little to no evidence of adherence), and the team indicated if they were unable to assess. In the second analysis, one team member was assigned to analyze one or two recommendations across all NIPS laboratories, and the same rating system was used. Discussion and full-team analysis were used when necessary to achieve reconciliation when the two teams has different results (Skotko, et al. 2019).

When assessing the provision of patient education resources, the study team created a matrix of the five recommended patient education resources in the ACMG guidelines. The researchers indicated that if a lab listed any of one of these resources on their lab reports or publicly available websites or patient education pamphlets, then the lab earned a yellow score for making a good faith effort. The team also provided a yellow score if labs made a good faith effort to list any patient education resources —even if those resources were not recommended guidelines. A red score meant the labs provided none of the recommended resources in any publicly available medium or lab reports. A company could earn a green score if they listed at least 3 out of 5 recommended patient and provider resources on any medium available for patients.

Results

The Skotko et al. study showed that four labs came close to meeting the requirements for the provision of patient education resources in some form, including Roche, PathGroup, and Counsyl/Myriad, which earned yellow scores, and Quest, which earned a green score, for patient education resources. Quest received a green score for providing four out of five recommended patient education resources. Roche offered two out of five patient education resources, as well as other valuable resources. Furthermore, Myriad did offer the Lettercase patient education resources in multiple mediums, as well as references to additional valuable educational resources beyond the recommendations; however, they were missing some of the other recommended materials. Myriad also later indicated in a response letter to the editor that they have additional resources in their patient/provider portal that the researchers were unable to access (Taber et al., 2019). Unfortunately, however, some labs did not offer any patient education resources even though they provide genetic information that leaves many patients with questions about the conditions included in the test.

Image 1: Lab scores for the provision of patient education resources (Skotko, 2019)

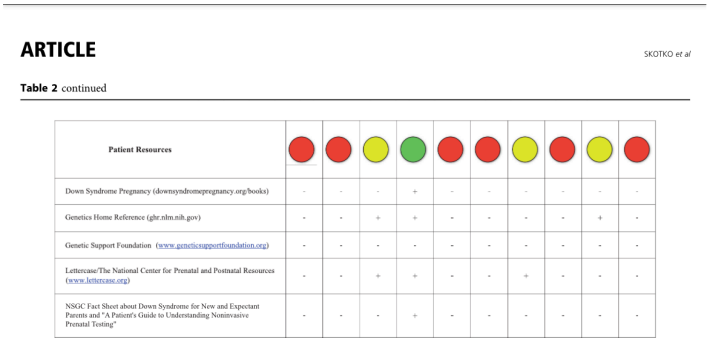

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Table 2 continued

Patient Resources										
Down Syndrome Pregnancy (downsyndromepregnancy.org/books)	-	-	-	+	-	-	-	-	-	-
Genetics Home Reference (ghr.nlm.nih.gov)	-	-	+	+	-	-	-	-	+	-
Genetic Support Foundation (www.geneticsupportfoundation.org)	-	-	-	-	-	-	-	-	-	-
Lettercase/The National Center for Prenatal and Postnatal Resources (www.lettercase.org)	-	-	+	+	-	-	+	-	-	-
NSGC Fact Sheet about Down Syndrome for New and Expectant Parents and "A Patient's Guide to Understanding Noninvasive Prenatal Testing"	-	-	-	+	-	-	-	-	-	-

Table 1: Lab scores for the provision of patient education resources

Commercial Lab	Test Name	Results
Integrated Genetics	InformaSeq	Red
Sequenom	MaterniT-21 PLUS	Red
Roche	Harmony	Yellow
Quest	QNatal	Green
Natera	Panorama	Red
Lab Genomics	Determine 10	Red
Counsyl/Myriad	Prelude	Yellow
NxGen	Informed Prenatal Test	Red
PathGroup	PathGroup NIPS	Yellow
BioReference	ClariTest	Red

Importance of Patient Education Resources

Fundamentally, the point of assessing the performance of labs in the provision of patient and provider education resources is because the most recent research still suggests that patients and providers are not receiving the support and information they need following test results suggesting a positive diagnosis.

Expectant parents indicate that they want more than a list of the medical issues associated with a condition when receiving a prenatal diagnosis; they want information about early intervention, recreational opportunities, life outcome information, and other available supports and services. (Sheets et al., 2011) In addition, research by Levis et al. shows that women who are pregnant or who plan to become

pregnant want culturally diverse educational materials that contain clinical information about Down syndrome as well as information about living with a child with Down syndrome (2012). Specifically, research participants in the Levis study also said they wanted photographs that show the realities of living with Down syndrome, and the researchers specifically identified the Lettercase booklet produced by the Human Development Institute as meeting the needs of pregnant women.

Image 2: Lettercase National Center for Prenatal and Postnatal Resources" Down syndrome booklet available at lettercase.org

This information is important because the Nelson-Goff study found that parents repeatedly report that despite the recommendations in the guidelines, patients often do not receive the full spectrum of information about the condition from their medical providers and describe negative experiences about how their child's diagnosis was communicated to them. In fact, 35% of patients indicated a negative experience when their clinician conveyed a prenatal diagnosis of Down syndrome compared to only 11% reporting a positive experience (Levis et al., 2013). So for every one patient who had a positive diagnosis experience, 3 patients had a negative experience.

Moreover, 19 states have passed Down syndrome/Genetic Condition Information Acts because patients who had negative experiences brought their concerns to legislators to pass laws that would require or provide for the provision of accurate, up-to-date, and balanced information about genetic conditions. Nearly all of these laws include recommendations or requirements to provide the resources also identified in the ACMG guidelines. (Leach, 2016)

Therefore, the provision of educational resources as part of the adherence to the ACMG guidelines is vital toward sharing resources that can lead to better diagnosis experiences for both patients and providers.

Opportunities for Improved Adherence

The researchers in the Skotko et al. study indicated that their intent was not to censure labs but rather to give them opportunities for assessment to improve practices and ultimately improve patient and provider experiences with NIPS. Therefore, the study team plans to keep these evaluations up to date in table format at the Prenatal Information Research Consortium: https://prenatalinformation.org/table/, and they will revisit the evaluations regularly and respond to requests for updates by labs. Further, the study team indicates that they look forward to updating the scores as labs strive to fulfill the criteria, and they have already done so for two labs, Progenity and Lab Genomics, as of September 13, 2019.

Image 2: PERC lab scores for the provision of patient education resources (PERC, 2019)

	Cell-free DNA Noninvasive Prenatal Screens (Companies)										
ACMG Recommendations	InformaSeq (Integrated Genetics)	MateriT-21-PLUS (Sequenom)	Harmony (Roche)	QNatal (Quest)	Panorama (Natera)	Determine 10 (Lab Genomics)	Prequel (Myriad) previously Prelude (Counsyl)	Informed Prenatal Test (NxGen)	PathGroup NIPS (PathGroup)	ClariTest (Bio Reference)	Innatal (Progenity)
Patient Resources	🔴	🔴	🟡	🟢	🔴	🟡	🟡	🔴	🟡	🔴	🟢
Down Syndrome Pregnancy (downsyndromepregnancy.org/books)	-	-	-	+	-	-	-	-	-	-	+
Genetics Home Reference (ghr.nlm.nih.gov)	-	-	+	+	-	+	-	-	+	-	+
Genetic Support Foundation (www.geneticsupportfoundation.org)	-	-	-	-	-	-	-	-	-	-	+
Lettercase/The National Center for Prenatal and Postnatal Resources (www.lettercase.org)	-	-	+	+	-	-	+	-	-	-	+
NSGC Fact Sheet about Down Syndrome for New and Expectant Parents and "A Patient's Guide to Understanding Noninvasive Prenatal Testing"	-	-	-	+	-	-	-	-	-	-	-

Conclusion

The Skotko et al. study of the provision of patient education resources by labs is critical because research has shown that NIPS has a substantial impact on patient advocacy groups. These non-profit organizations often struggle to meet the increasing prenatal education needs of their members, and they also have limited breadth in being able to reach and support people who may undergo screening (Meredith et al., 2016). The patient advocacy organizations also often have limited funding to address these additional challenges.

In addition, new genetic conditions are constantly being added to the prenatal screening panel, and about 45% clinicians reported that they receive little to no additional training regarding prenatal diagnosis. (Cleary-Goldman, 2006) Therefore, they also need more support and access to condition-specific patient educational materials.

Consequently, labs are an important stakeholder with the funding, reach, and capacity to improve that experience. Collectively, labs have access to every patient undergoing testing and the greatest source of funding to support those patients. While we appreciate the good faith efforts by some of the labs and hope they will continue, we need all hands on deck to work together to ensure that vulnerable families are not left isolated and confused about powerful genetic information.

Human Development Institute

University of Kentucky
114 Mineral Industries Building
Lexington KY 40506-0051
859.257.1714 · TTY: 859.257.2903
www.hdi.uky.edu

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About HDI Research Briefs

HDI Research Briefs were initiated to highlight the research activities at HDI. Projects at HDI focus on individuals with disabilities and include projects with emphases in early childhood, school age persons, adults, and issues across the lifespan. Many of these projects have significant research components and involve HDI staff, students in graduate programs, and other faculty at UK. With each issue of **HDI Research Briefs**, we will try to provide a cross-section of HDI's research activities. The brief reports are typically "mini" versions of more involved studies. The brief reports are intended to give an overview of the research project and emphasize the implications of the studies.

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