

ORIGINAL RESEARCH

Providers' experience with NIPS at MGH

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Providers' Experience with Cell-free DNA Noninvasive Prenatal Screening at One Hospital

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Abstract:

Objective: This study explores how a small group of providers learn about NIPS, their overall knowledge level, and what resources they provide their patients.

Method: Thirty-four obstetric providers at a single medical institution completed a survey on their knowledge, test utilization, and patient care in regards to noninvasive prenatal screening. Questions inquired about their ordering practices, sources of educational information on noninvasive prenatal screening, overall knowledge level, and information sources accessed by their patients who receive a positive noninvasive prenatal screening result.

Results: Overall, the most commonly provided source for noninvasive prenatal screening information was talking to fellow colleagues who worked at the same institution. Other utilized sources included medical conference sessions, lectures at the institution from a noninvasive prenatal screening company, and going directly to a noninvasive prenatal screening company itself. Provider knowledge level of noninvasive prenatal screening varied, with genetic counselors reporting more confidence than physicians or midwives. Patients who received a positive noninvasive prenatal screening result for Down syndrome most frequently used genetic counselors as an informational resource.

Conclusion: This study provided a profile of what providers at a single institution know about NIPS and what barriers exist. Provider-to-patient information exchange remains an important avenue for future NIPS research.

Keywords: Down syndrome, genetic counseling, women's health, prenatal care

Introduction

In the United States, expectant couples increasingly utilize cell-free DNA noninvasive prenatal screening (NIPS), a screening test for chromosomal conditions, such as trisomy 13 (Patau syndrome), 18 (Edwards syndrome), and 21 (Down syndrome), as well as sex chromosome aneuploidies. NIPS has sensitivities around 99% and false-positive rates of less than 0.1% in women with high-risk pregnancies for many of these aneuploidies.¹ Currently, about 94% of genetic counselors offer NIPS to women with high-risk pregnancies.² The test can detect fetal DNA as early as four weeks gestation, but its results are more reliable after seven weeks.³

Medical organizations now offer guidelines on NIPS use in clinical settings. The National Society of Genetic Counselors (NSGC) recommends that providers only offer NIPS to women with high-risk pregnancies,⁴ while the American College of Medical Genetics and Genomics (ACMG), the International Society for Prenatal Diagnosis (ISPD), and the American College of Obstetricians and Gynecologists (ACOG) recommend that all women be offered the screening at their first prenatal visit, even though it might not be the ideal option for some patients depending on many factors, including their personal goals

and values.^{5,6,7} All organizations recommend that women should verify positive NIPS results with confirmatory diagnostic testing, such as chorionic villus sampling (CVS) or amniocentesis. In addition, ACMG states that providers should try to thoroughly understand their patients' NIPS preferences and be able to educate them on existing limitations.⁶

Research has begun to explore provider-patient communication regarding NIPS. Some researchers recommend that a pre-test discussion should highlight the following: (1) it is a screening test and *not* diagnostic, (2) its detection rate appears to be better than that of maternal serum screening for common aneuploidies, (3) it screens for specific conditions, and (4) a positive result should be confirmed with an invasive diagnostic test². Genetic counselors can be a key resource. NSGC encourages providers to explain what information would be gained from NIPS so that an expectant patient could make an informed decision. All pregnancy options should be thoroughly discussed, and the counselor should prepare the expectant couples for every type of result that could be returned.⁸ For patients who are considered high risk or have a screen-positive result, the ACMG recommends that post-test counseling include four key discussion points: (1) the possibility of false-positive screening results, (2) confirmatory testing (CVS or amniocentesis) and its risks, (3) obtaining a cord blood sample if invasive testing is declined for postnatal confirmation, (4) and the use of accurate, up-to-date, and balanced information about Down syndrome or other tested conditions.⁹

Providers in the U.S. have expressed concern that NIPS may trigger patient anxiety, the potential for false positives, and the risks of invasive follow-up testing.¹⁰ Clinical geneticists in Japan were concerned about the lack of overall knowledge of NIPS among pregnant women and, therefore, were unsure whether NIPS should be implemented.¹¹ In New Zealand, a small study found that 56% of providers raised the high cost of NIPS as an ethical issue. These clinicians also felt that the misunderstanding of NIPS as a diagnostic test and the test's false positives would lead to patient disadvantage or distress.¹²

Many researchers have focused on patient uptake of NIPS at different healthcare sites.^{13,14,15,16,17} However, scant research has focused on providers' knowledge of NIPS and their experience in ordering such tests. Musci et al. (2013)¹⁰ asked providers about the advantages and limitations of NIPS as well as the population of women they predicted offering the test to, the latter of which was also explored by

Buchanan et al. (2014).² Neither study, however, assessed providers' comfort level, overall knowledge, and specific resource utilization for NIPS. For this study, we ask these questions of clinicians at Massachusetts General Hospital (MGH) to look at provider readiness and the use of NIPS to prenatally diagnose Down syndrome.

Material and methods

Participants

Eighty-three obstetric providers (obstetricians/maternal-fetal-medicine specialists, prenatal genetic counselors, and midwives) at MGH were initially recruited for the study, which was approved by MGH's Institutional Review Board. Healthcare professionals provide care for MGH's diverse patient population, which included an outpatient population that was 16% Hispanic, 7% African American, and 6% Asian in 2015.¹⁸ MGH's obstetrics and gynecology inpatient services consisted of 7% African Americans, 21% Hispanics, and 10% Asians. NIPS tests are available to all pregnant patients, regardless of pregnancy risk. Patients who choose either NIPS or another type of prenatal screening typically attend pre- and post-test counseling from genetic counselors to learn about the options that are available to them and to discuss the results and next steps. Due to Massachusetts' low uninsured rate (4%) for health insurance, many patients receive financial assistance for NIPS and other pregnancy-related care.¹⁹

Responding clinicians were screened for study eligibility at the start of the survey--to be included in the research, physicians had to self-report ordering NIPS in the last 12 months. Participants received an e-mail, inviting them to participate in a voluntary, electronic questionnaire that was administered using REDCap.²⁰ The questionnaire assessed participants' knowledge, test utilization, and patient care in regards to NIPS. Non-respondents were re-invited by e-mail one additional time two weeks after the original invitations were sent. Survey responses were collected in September and October 2013. Respondents were not offered an incentive for survey completion.

Ordering Practice

Participants were asked which of the following statements best described their ordering practice for NIPS: "I order the test only for pregnant women who are considered high-risk"; "I order the test for all pregnant women, both low- and high-risk"; "I order the test on a case-by-case basis based on my clinical judgment"; "I generally do not offer this test to any patient but will order it if a pregnant woman specifically requests it"; and "Other."

Sources of Educational Information on NIPS for Providers

Participants were asked if they "frequently," "often," "sometimes," or "never" used each of the following sources of information to learn about NIPS: reading journal articles about NIPS, attending sessions on NIPS at national medical conferences, a lecture at MGH from a NIPS company, a lecture at MGH about NIPS from someone not affiliated with a NIPS company, participation in a webinar on NIPS, talking to colleagues at MGH, talking to colleagues outside of MGH, calling a NIPS company for more information, visiting the webpage of an NIPS company, or other.

Provider Knowledge Level of NIPS

Participants were asked, using a 5-level Likert scale that ranged from "strongly agree" to "strongly disagree," to indicate how strongly they agreed or disagreed with the following statements about NIPS: "I am knowledgeable about the science behind NIPS"; "I provide sufficient pre-test counseling for NIPS"; "I provide sufficient post-test counseling for positive NIPS results"; and "I am knowledgeable about resources available to my patients who have received a positive NIPS results."

Information Sources for Patients with a Positive NIPS Result for Down Syndrome

Participants were asked about their firsthand experiences with patients who had received a positive NIPS result for Down syndrome. They were asked if their patients “frequently,” “often,” “sometimes,” or “never” utilized certain information sources that could educate them on the decisions they face during their pregnancies. These sources were provider-disseminated information, the Internet, a genetic counselor, talking or meeting other families who have children with Down syndrome, talking or meeting other families who terminated a fetus with Down syndrome, talking or meeting other families who offered their baby with Down syndrome up for adoption, connecting with a support group, like the non-profit Massachusetts Down Syndrome Congress, connecting or talking with the MGH Down Syndrome Program, or other.

Data Analyses

All statistics were generated using SAS 9.4 (SAS Institute, Cary, NC). Frequencies were calculated by provider type. Responses of “Don’t know” were treated as missing data. Exact Kruskal-Wallis tests were used to test for associations between provider type and the utilization of educational information resources for providers, provider knowledge level of NIPS, and utilization of patient information sources. Each response measure was treated as an ordinal variable. Two-tailed p-values less than 0.05 were considered significant without correction for multiple comparisons, reflecting the exploratory nature of the study.

Results

Of the 83 health care professionals invited, 40 providers responded, of which six physicians were excluded because they had not ordered any NIPS tests within the past 12 months. We did not exclude genetic counselors or midwives, who do not traditionally order tests, based on this criterion; all data

collected from genetic counselors and midwives who completed the survey were used in analysis. The remaining 34 providers included 23 obstetricians/maternal-fetal medicine specialists, seven prenatal genetic counselors, and four midwives.

Sources of Educational Information on NIPS for Providers

Eighty-two percent (19/23) of physicians, 100% (7/7) of genetic counselors, and 100% (4/4) of midwives reported talking often or frequently to colleagues at their institution (Table 1). The least commonly used source was a lecture from a NIPS company. Physicians more often consulted journal articles than genetic counselors, while midwives consulted journal articles least often. Genetic counselors more often attended a NIPS company lecture, browsed NIPS company websites, and called NIPS company representatives than physicians or midwives. Only genetic counselors reported use of webinars as a source of information.

Provider Knowledge Level of NIPS

Most providers endorsed agreement or strong agreement with statements of knowledge of NIPS and their ability to provide appropriate NIPS counseling (Table 2). Genetic counselors asserted greater confidence in their ability to provide pre-test counseling for NIPS. Fifty percent (2/4) of midwives reported that they did not feel knowledgeable about the science behind NIPS or their ability to provide sufficient pre-test counseling.

Information Sources for Patients with a Positive NIPS Result for Down Syndrome

One hundred percent (22/22) of providers, 86% (6/7) of genetic counselors, and 100% (4/4) of midwives reported referring their patients with a positive NIPS result for Down syndrome to genetic counselors (Table 3). No group of providers reported referring patients to other families who had terminated their pregnancy or offered their baby with Down syndrome up for adoption. Genetic counselors were more likely to refer patients to support groups or to the MGH Down Syndrome Program. Physicians sometimes referred expectant couples to nonprofit community-based support groups, such as the Massachusetts Down Syndrome Congress (mdsc.org).

Discussion

This study provides a profile of what providers at one tertiary care institution know about NIPS and how they obtain their information about NIPS. The majority of providers in the study self-reported that they were knowledgeable about the science of NIPS and could explain it to their patients in a way that was understood. However, such feelings were not universal, as 14% of prenatal genetic counselors, 9% of physicians, and 50% midwives still reported a need for better education on the science behind NIPS.

Most providers reported that they often or frequently learned about NIPS by talking to other colleagues who work at the same institution. While there is no current standardized method to introduce new advances in medicine like NIPS and ensure that that knowledge is maintained, options exist for each kind of preferred learning, whether visual, motor, auditory, or symbolic.²¹ Among our study sample, other utilized sources included medical conference sessions, a lecture at the institution from a NIPS company, and going directly to a NIPS company itself. Webinars were never used among physicians and midwives, while three out of seven genetic counselors used them. While webinars are a convenient and informative resource, they can be long and unengaging, which could make them an unattractive option. In addition, various technological roadblocks can prevent professionals from accessing webinars, either due to lack of tech savvy or because necessary plug-ins may be difficult to install on work computers depending on providers' administrative privileges. In acknowledging the convenience of webinars, MGH has created an accessible webinar on NIPS and the delivery of a prenatal diagnosis at mghacademy.org/downsyndrome.²²

Providers are not alone in needing educational materials to learn about NIPS and the options for positive test results. When expecting women and their partners first seek prenatal care, they are often subject to an overload of information. Depending on factors, such as their education level, culture, and potential language barriers, talking about the pregnancy may be easier or more difficult. During post-test counseling, "accurate, up-to-date, and balanced information about Down syndrome (or other tested conditions) should be provided," according to the ACMG guidelines.¹⁰ While our data analysis suggests

parents with positive NIPS testing are referred to genetic counselors, such information can be accompanied with a written resource for better overall comprehension.

Prior research identifies the importance of accessible educational materials for expecting women and their families to help ensure informed decision making during pregnancy.²³ For example, *Understanding a Down Syndrome Diagnosis* is a booklet that provides key information to patients receiving a prenatal diagnosis created with input from national Down syndrome organizations in addition to the NSGC, ACOG, and ACMG.²⁴ For couples electing to continue their pregnancies following a prenatal diagnosis, downsyndromepregnancy.org contains further information and resources.²⁵ The National Down Syndrome Adoption Network (ndsan.org) also has a national registry for families waiting to adopt a child specifically with Down syndrome.²⁶ However, our survey respondents did not endorse the Internet and support groups as frequent sources of information for their patients. Opportunities exist to connect expectant couples to support groups and other families either looking to adopt children with Down syndrome or who have experience with children with Down syndrome. An example within our state is the Massachusetts Down Syndrome Congress's Parents First Call Program, which consists of a group of trained mentors who volunteer their time to listen, share, answer questions, and provide information.²⁷

This single-institution study has significant limitations. First, these clinicians practice in a single, large academic medical center in the Northeast. The clinicians and patients may not be representative of the U.S. or other centers or regions. Second, our response rate, before exclusions for ineligibility, was 48%. Our study period was limited; achieving response rates of over 60% typically requires longer field periods, multiple contacts using postal mail or telephone in addition to online administration, and incentive payments. Despite the importance of physician surveys, they are often subject to low response rates, which can raise concerns about the validity and generalizability of the findings. Nonresponse among providers can be due to overall lack of time due to their busy schedules.²⁸ This survey, using one reminder and no incentives, was about average for physician survey response in the U.S. conducted online with this level of effort.^{27,29} We cannot determine among non-respondents if there would be different experiences with prenatal testing. Finally, during the time of this study, MGH had an exclusive arrangement with one NIPS laboratory, which might further reduce generalizability.

Our findings bring forth two important conclusions that can be considered in future research efforts on NIPS. Prenatal genetic counselors have different knowledge, self-education, and counseling approaches when compared to physicians and midwives. Ordering providers reported that expectant couples access a range of resources, including other families with Down syndrome as well as referrals to support groups, prior to making a pregnancy decision if they receive an abnormal NIPS result. These insights can help to design future research initiatives to better understand NIPS in clinical settings.

Disclosure

Brian Skotko serves in a non-paid capacity on the Medical and Science Advisory Board for the Massachusetts Down Syndrome Congress and the Board of Directors for Band of Angels Foundation, both non-profit organizations. He also serves on the Professional Advisory Committee for the National Center for Prenatal and Postnatal Down Syndrome Resources. Dr. Skotko occasionally gets remunerated from Down syndrome non-profit organizations for speaking engagements about Down syndrome. He has a sister with Down syndrome. He receives research support for clinical drug trials involving patients with Down syndrome from Hoffmann-La Roche, Inc. Eric Macklin serves on DSMBs for Acorda Therapeutics and Shire Human Genetic Therapies and receives research support from the Adolph Coors Foundation, ALS Association, Autism Speaks, Biotie Therapies, Michael J Fox Foundation, FDA, HRSA, NIH, and PCORI. The other authors declare no conflict of interest.

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