4.3.4 Non-Invasive Prenatal Testing

Meredith Vanstone, PhD

Co-Authors: Mita Giacomini, PhD; and Jeff Nisker, MD, PhD, FRCSC, FCAHS

Educational Objectives:

1. Understand the ethical implications of private prenatal genetic tests that require support and services from the public system.
2. Prepare a response to encountering patient requests for private-pay services that balances the best interests of your patient and the public health care system.
3. Learn about the essential elements of supporting informed choices about NIPT and other prenatal tests.

Case

Sally Smith is a 33 year old married mother of three. You have been her physician for many years, caring for her through all three pregnancies. By all observations she is a devoted mother who is delighted with her growing family. Her past medical history is unremarkable and she has no health concerns.

Ms. Smith presents at your office to confirm her fourth pregnancy. As you work through the questions and information you need to present at this first prenatal visit, she asks if she can have the new Down Syndrome test she has heard about, that will tell her whether or not her baby has Down Syndrome at 9 weeks gestation. You talk to her about some of the NIPT options, informing her that these tests are available from several companies for those who can pay privately, but they are not accurate enough to be considered diagnostic, and any results should be confirmed with an invasive diagnostic test such as amniocentesis or CVS. You also discuss how NIPT compares to publicly-funded non-invasive prenatal screening tests, including differences in detection rate, timing, and cost. Ms. Smith has lots of questions about her options and her visit quickly runs over the allotted time as you discuss the various differences between NIPT and conventional screening tests. Ms. Smith decides to go home and think about the information further, as she wants to discuss the tests with her husband and look more closely at their family budget. You agree that if she wants to proceed with one of the tests, she will re-book to complete the necessary paperwork.

Questions

1. You are now late for your next patient and will end up playing catch-up all day, due to the time you spent discussing NIPT with Ms. Smith. You are committed to spending as much time with each patient as needed, but does this apply when that time is spent discussing a private test?
2. NIPT is not publicly funded in most jurisdictions, but it can be obtained privately. If a patient pays privately for NIPT, they may gain earlier access to some public services, such as counselling services and pregnancy termination. Do you consider this preferential treatment? Does it seem a fair and equitable use of public resources?
3. When you do counsel about NIPT, how can you discuss this testing option to best facilitate informed decision-making by your patients?

Discussion

NIPT is an example of a test which is only available to women who can pay privately in most Canadian jurisdictions. In some jurisdictions, such as Ontario, it is available publicly if a woman is identifiably at high risk. In this case, your patient has an average risk for fetal aneuploidy.

Introduction to NIPT

This case addresses a new strategy for prenatal testing: Non-Invasive Prenatal Testing via fetal DNA in maternal blood (NIPT). NIPT is a new prenatal testing strategy that may detect a limited number of genetic conditions as early as nine weeks gestation, by analyzing small amounts of fetal DNA present in maternal blood.(1, 2) Professional society guidelines, including one from the Society of Obstetricians and Gynecologists of Canada, are clear that NIPT should be considered a screening test, as it is not sufficiently accurate to be considered diagnostic.(3-5)

Currently, we have two types of prenatal screening and testing in Canada. Canadian clinical practice guidelines recommend that non-invasive screening (e.g. Integrated Prenatal Screening or IPS) be offered to all pregnant women.(6) IPS uses a series of non-genetic blood tests and ultrasound measurements to screen for chromosomal aneuploidy (e.g. Down syndrome) and physical anomalies such as neural tube defects.(6) IPS does not provide a definitive result; if a woman has a worrying finding from IPS, she is offered diagnostic invasive prenatal testing (either amniocentesis or chorionic villus sampling). Confirmatory invasive testing can provide a more definitive diagnosis, but it carries a risk of miscarriage.(7) NIPT has been shown to be more accurate at detecting Trisomy 21 than screening tests such as IPS,(8-10) is available much earlier in the pregnancy, and does not have a risk of miscarriage, although confirmatory invasive testing is still recommended.(3)

In Canada, the test is offered by a number of private companies for prices ranging from $800-$2700. In most Canadian jurisdictions, patients are responsible for paying for this test themselves, although policy may change and some provinces may choose to fund certain applications of the test, as seen in Ontario in early 2014.(11) Test manufacturers heavily

promote NIPT, including placing promotional literature and test kits in some public health care facilities such as hospital prenatal clinics and private doctors' offices. Professional society guidelines, including that of The Society of Obstetricians and Gynecologists of Canada (SOGC), recommended NIPT for women at above average risk for trisomy 13, 18, and 21, with positive results confirmed by invasive diagnostic testing.(3, 4, 12)

Access to Tests and Publicly Funded Health System Resources

NIPT is currently available privately, with some very limited public funding. For example, since early 2014, the Ontario Health Insurance Program has funded NIPT for women who are identified to be at high risk for fetal aneuploidy. (11) However for most Canadian women, including Ms. Smith in our case study, NIPT is not publicly funded. However, despite the fact that NIPT is not publicly funded, it makes use of public health care resources, including physician time for counselling, dating ultrasounds, confirmatory amniocentesis, and pregnancy termination and related services. There are two potential issues related to access here: 1) inequity of access to NIPT itself and 2) preferential access to related services, typically earlier access.

Regarding inequity of access to NIPT, we may ask whether improved prenatal testing is a right or a privilege, and how much of an "improvement" NIPT offers over the existing system. If NIPT provides a benefit to pregnant women, should it be made available to all pregnant women? How much of a benefit would it have to provide? How would we gather and evaluate evidence of this benefit? While NIPT is more accurate than other non-invasive screening tests for detecting trisomy conditions,(8) and does not carry the risk of miscarriage that invasive diagnostic tests like amniocentesis do, value judgments are required to evaluate whether this benefit is "enough". This is a challenging question and policy decisions about what medical services or devices will be paid for by public money involve consideration of many different factors. There are certainly other examples of technologies or tests that may provide a benefit, but which are not publicly funded because they are too expensive, or would provide a benefit to too few people, or because they replace something which is deemed adequate.

In the current Canadian context, where most women accessing NIPT would have to pay for it themselves because of a lack of public funding, we may be more concerned about what other publicly-funded benefits they may incidentally be accessing because of their ability to pay for NIPT. This section is adapted from an article we have published on this topic.(1) Women who pay privately for NIPT may access a more accurate test, earlier in their pregnancy.(8-10) This early access to a private test may facilitate earlier access to public services (e.g. counselling, termination), which is of benefit because it typically means less risk to the woman and her fetus. Women who aren't able to pay for NIPT would also be afforded access to these public services, but at a later gestational age. This is ethically relevant because of the issues of fairness, or equity. When earlier access to publicly funded services is enabled by privately purchased NIPT, economic privilege facilitates preferential access to these services, creating a two-tiered system where personal financial resources enable access to better care.

Women who can pay privately for NIPT may benefit greatly from this earlier access, both physically and psychologically. For example, pregnancy termination at an earlier gestational age may be less physically risky and emotionally traumatic.(13-15) Women who pay for NIPT may even save money for the health care system. These two factors seem like significant benefits, and they are. However, we must also consider that these benefits are only available to women of economic means. Should we be advocating for equal access to NIPT and related services for all women? Is it fair for some women to have access to longer counselling sessions or earlier pregnancy termination because they were able to pay for NIPT?

We can think of the analogy of the private MRI clinic. In many places in Canada, especially close to the American border, patients will pay privately for MRIs in order to expedite the next phase of their care. For example, a private MRI might mean an earlier surgical appointment. After the private MRI, the patients receive the same care as they would have if they had waited for a publicly funded MRI, they just access that care more quickly. This can have a significant benefit- earlier treatment may result in fewer surgical complications and more successful rehabilitation, benefitting the patient and saving money for the health care system. We may sympathize with these patients, as it seems as if they are not harming anyone by using their private resources to secure quicker care. However, a commitment to equity means that it is not fair for people who can pay to have better or faster health care than those who cannot afford to pay.

This issue places the individual clinician in a delicate situation, with potentially conflicting duties and priorities. There is the duty to the patient in front of you, who has questions and wants to discuss a test she can pay privately for, which may have significant benefit to her. There is the duty to the other patients you will see that day, who may have to wait longer for their appointments if you run over time talking about NIPT to one (or more patients). There is the duty to your patients and potential patients who may benefit from NIPT but do not have the ability to pay. There is the duty to act as a health advocate, promoting the health of your patients and community by taking efforts to change practices or policies.(16) There is the duty to act as a manager, fairly allocating scarce health care resources.(16)

These duties are often in conflict and there is no easy answer about how to prioritize them. Physicians may wish to consider the principles of informed choice, of offering information that is relevant to a patient's needs to make a decision about a particular intervention.(17) If you judge that most people in this patient's position would desire information about NIPT in order to make an informed choice about whether or not to participate in other screening or testing modalities, then you could consider providing information about NIPT to be part of your work in counselling about publicly available tests.(18) The next section will discuss how physicians can facilitate informed choices about NIPT and other prenatal tests.

Informed Choices and the Role of Physicians

Informed decision-making is recommended for women considering all types of prenatal screening or testing, including NIPT. Informed decision-making can promote autonomous decision-making, and supports a woman to make a choice that is consistent with her values.(17, 19) In the case of the existing prenatal screening and testing system, it is

recommended that the physician facilitate a conversation to help each woman make an informed choice about the available testing options, and revisit that conversation (and/or refer to a genetics counsellor) after the results of the test are received.(6, 20) There is ample literature available to assist physicians in facilitating conversations to support informed decisions about traditional prenatal screening and testing options. (19-24) Does NIPT change the nature of informed choice or the role of the physician in facilitating the informed choice conversation?

Some have suggested that the non-invasive aspect of NIPT may change the nature of counselling and informed choices.(25) In many ways, making a decision about NIPT may be qualitatively different than making a decision about other types of non-invasive prenatal screening, like IPS, or about invasive diagnostic tests such as amniocentesis. For example, NIPT provides much more accurate results than other screening tests,(9, 10) earlier in the pregnancy, and without the risk of miscarriage of invasive diagnostic testing. Some have suggested that these factors may lessen the gravity of the decision to test.(26) The role of the physician in facilitating informed choice about NIPT will vary depending on how NIPT is used. If it is used according to professional guidelines, it will be offered only to women who have been previously identified as having a higher risk for fetal aneuploidy, potentially after earlier screening has returned a positive result. (3) In this instance, counselling about NIPT may take place at the same time as counselling about the earlier test result, in a discussion of options that may also invasive testing such as amniocentesis.(20) In locations where genetic counselling is available, these professionals may take over counselling about NIPT for high-risk women.

Counselling about NIPT becomes more challenging when a woman of average clinical risk identifies this test herself and raises the issue with her physician. In this situation, physicians may wish to consider whether most of the counselling should take place before or after the test. In practice, we know that pre-test counselling about screening tests is often very brief, with more detailed counselling in the event of a positive screening result. Post-test counselling may address the meaning of results, conditions screened for, and potential options available to the woman.(27) Is this appropriate for NIPT, given the higher level of accuracy and the shorter time frame to results when compared to other screening modalities such as IPS?(9, 10) The American National Society of Genetic Counselors strongly advises that women should understand the implications of a positive result *before* undergoing NIPT.(12) If uptake rates for NIPT reach that of prenatal screening, providing adequate pre-test counselling to all women would be logistically challenging.(28) Further, is spending a significant amount of time counselling about a private test (NIPT) a good use of publicly-funded physician time? This question will be addressed further in the "Public/Private Resources" section of this case.

What information should an informed choice discussion about NIPT contain? The SOGC has published guidelines for pre- and post-test counselling about prenatal screening.(20) This document does not specifically address NIPT, but many suggestions are applicable to this test. Before the test, physicians are advised to discuss how the test calculates a woman's individual risk of having an affected fetus, the meaning of a positive and negative result, and the options available after test results are received. After the test, physicians should counsel those who have received a negative result about false negative results, that further

invasive diagnostic testing is an option, and that a second trimester ultrasound will still be carried out. For women who receive a positive test, physicians are advised to ensure there is sufficient time for counselling and asking questions, and should cover topics such as the meaning of risk statistics, the option of invasive testing, details about what the test will diagnose, risks of invasive diagnostic testing, the option of pregnancy termination, that further investigation is not contingent upon a desire to terminate the pregnancy, that consultation and support will be available no matter what choice she makes. Post-test counselling may also include more information about the condition detected, including health implications and long-term outcomes for people with this condition.(20) Professional society guidelines about NIPT also suggest that physicians should discuss the differences between NIPT and traditional forms of screening, including both advantages (higher detection rate than other serum and ultrasound screening tests, lower false positive rate, risk assessment is less dependent on gestational age)(29) as well as limitations (only validated to detect a limited number of conditions in high risk women with singleton pregnancies, possibility of test failure and the need for a re-test, potential for false positive and false negative results).(5) Physicians should be clear that NIPT is considered a screening test, and is not accurate enough to be diagnostic. Multiple professional society guidelines state that NIPT results should be confirmed with an invasive diagnostic test such as amniocentesis.(3-5, 12, 29) The American National Society of Genetic Counselors suggests that before undergoing NIPT, women should receive information about the conditions detected.(12)

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Short Author Biographies

Meredith Vanstone is an Assistant Professor in the Department of Clinical Epidemiology and Biostatistics and a member of the Centre for Health Economics and Policy Analysis at McMaster University. Her research interests include social and ethical aspects of health technology policy, reproductive and genetic technologies, and the use of technology in health professional education and practice. Meredith approaches research from a socio-cultural perspective, using qualitative methods to analyze both primary and secondary data.

Mita Giacomini is a Professor in Clinical Epidemiology and Biostatistics at McMaster University, and a member of the Centre for Health Economics and Policy Analysis. She led the development of McMaster's Health Policy PhD program and previously served as its Director. She holds graduate degrees in health services and policy analysis, history of medicine and public health. Her publications have addressed topics including health policy ethics, political reasoning in health technology assessment, health resource allocation,

values in evaluation and policy-making, interdisciplinarity, and uses of qualitative evidence in health care. Current research projects focus on the roles of evidence and theory in health policy arguments, values and ethics in Canadian health policy, and the social and ethical dimensions of health technology assessment. Giacomini has provided consultation and service to local, provincial, national and international health agencies in related areas. She currently serves on the Ontario Health Technology Advisory Committee. Giacomini teaches in the areas of health policy, philosophy of science, and research methodology.

Jeff Nisker is a Professor of Obstetrics-Gynaecology at the Schulich School Medicine & Dentistry, Western University, and Scientist, Children's Health Research Institute. He holds, and has held, CIHR and Genome Canada grants to explore ethical and social issues in reproductive medicine, genetics, and exposure of pregnant women to environmental toxins. He has held a CIHR/Health Canada grant exploring public engagement for citizen deliberation regarding pre-implantation genetic diagnosis. Jeff has written or co-written over 150 scientific articles and book chapters, as well as seven plays. His plays have been performed throughout Canada, as well as in the United States, the United Kingdom, Australia and South Africa.

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