INFORMATION FOR PATIENTS

Non-Invasive Prenatal Testing (NIPT) for Down Syndrome

What is NIPT?

NIPT (also called NIPS) is a **screening test** for common genetic conditions in the fetus. In particular, it can be used to screen for Trisomy 21 (Down syndrome). NIPT analyses fetal DNA (genetic material) found in the mother's blood sample to predict if the fetus might be affected. NIPT can be done as early as 10 weeks of pregnancy. NIPT testing is done only by specialized laboratories, and is not part of routine screening in Nova Scotia. It is offered to patients who have pregnancies that are at higher risk for Down Syndrome.

What is the difference between a screening test and a diagnostic test?

A ***screening test*** gives an assessment of risk (high risk or low risk) for a specific condition(s). Screening tests can give results that are falsely positive (a high-risk result when the fetus is not affected) or falsely negative (a low risk result when the fetus is actually affected).
A ***diagnostic test*** performs at a level of certainty that is so good that it is felt to give a definite answer (yes or no).
Diagnostic tests for a fetus require a sample from the pregnancy using an invasive procedure, such as chorionic villus sampling (CVS; biopsy sample of the placenta) or amniocentesis (sample of amniotic fluid). These procedures have a risk of pregnancy loss of about 1/200-1/400.
Screening tests for a fetus are done using blood samples from the mother and ultrasound of the fetus. There is no risk of pregnancy loss by having screening tests for Down syndrome.
NIPT is considered a **screening test** and does not perform at a diagnostic level. NIPT is a blood test from the mother, and therefore has no risk of pregnancy loss.

How is NIPT different from standard screening tests for Down Syndrome?

NIPT has a performance that is much better than any other screening tests, such as maternal serum testing (MST) and ultrasound tests.
NIPT will detect more than 99% of cases of Down Syndrome; standard screening will detect 75-85% of cases.
NIPT has a false positive rate of 0.3% (only one in 350 women will mistakenly have a high risk result); standard screening has a false positive rate of 3-5% (one in 20-35 women will mistakenly have a high risk result).

Who is offered the option for NIPT?

Patients who have a high risk for Down syndrome in the pregnancy after routine screening and ultrasound assessment will be counselled about this option. These patients will be seen by Medical Genetics or Maternal-Fetal Medicine specialists for counselling about all test options. For patients who are at increased risk, NIPT will be offered as an alternative to diagnostic testing (CVS or amniocentesis).

Can I have NIPT even if my pregnancy is not at high risk for Down syndrome?
Patients who are not at high risk for Down syndrome, but want to have NIPT, can pay to have the testing done privately.
Your health care provider can help you understand your risk, and all options of screening or testing that are available to you.

Before paying for this test, you should understand the limitations:
1. NIPT tests only for the genetic conditions stated; it does not give information about any other genetic conditions in the fetus or family
2. NIPT is a ***screening test***

- a reassuring result does not completely eliminate the possibility of Down syndrome in the fetus
- a high-risk result is very likely to be true, but some of these may be found to be normal when a diagnostic test is done.

3. NIPT has a small risk of test failure, and a second sample may be required
4. Performance of NIPT is not as good in twin pregnancies

Speak with your health provider about these limitations before getting NIPT

INFORMATION FOR HEALTHCARE PROVIDERS

Non-Invasive Prenatal Testing (NIPT): Information for Care Providers

What is NIPT?

NIPT (or NIPS) for Trisomy's 13, 18, 21 (Down Syndrome), and sex chromosome aneuploidy is a maternal blood test that involves analyzing cell-free DNA (derived from the placenta) from a maternal serum sample to provide a risk assessment. NIPT can be performed as early as 10 weeks gestation. The detection rate for Down syndrome is greater than 99% with a false positive rate of less than 0.1%.

Should I discuss NIPT with my patient?

According to the Joint Canadian College of Medical Geneticists (CCMG)/Society Obstetricians and Gynecologists of Canada (SOGC) guidelines, "patients should be offered… maternal plasma cell-free DNA screening [NIPT] where available, with the understanding that it may not be provincially funded" [JOGC 39(9): 805-817].

Is NIPT funded in Nova Scotia?

Patients in Nova Scotia will be offered funded NIPT under the following circumstances:

- Women with a previous pregnancy affected with Trisomy 13, 18 or 21 are eligible for funded NIPT in the first trimester, as early as 10 weeks gestation. This is in lieu of standard screening using the MST and nuchal translucency assessments. In order to access funded NIPT, these patients must be referred to Medical Genetics or a Maternal-Fetal Medicine Specialist.
- Women who have undertaken standard screening and are found to be at **increased risk** of Down syndrome based on the results of standard screening, will be seen by either Medical Genetics or Maternal-Fetal Medicine Specialists and offered the option of funded NIPT in lieu of diagnostic testing (CVS or amniocentesis). A referral is not necessary.

Patients meeting specific eligibility criteria as noted above will be provided pre-test counselling, test co-ordination, result reporting, and additional counselling as needed.

NIPT is not offered to patients who are **not at increased risk** of Down syndrome either before or after standard screening tests.

Can patients pay for NIPT if they are not high risk?

If a patient wishes to have NIPT either in lieu of standard screening, or after receiving a low risk result after standard screening, they have the option to independently pay for the test.

Do patients still need to do maternal serum screening if they choose to pay for NIPT?

NO. If the patient chooses NIPT (either through eligibility for funded NIPT with Medical Genetics

or a Maternal Fetal Medicine Specialist or through self-pay NIPT), then they should NOT have any further maternal serum testing.

What are the key points for counselling the patient about this test?

Description

NIPT is a test used to screen primarily for Trisomy 21 (Down syndrome). NIPT analyzes cell-free DNA from the placenta that is detected in the mother's blood to predict if the fetus may be affected. NIPT is considered a **screening test** and does not perform with diagnostic accuracy. This test can also provide information about Trisomy 13, Trisomy 18, and sex chromosome aneuploidy.

Benefits

- NIPT can be done as early as 10 weeks gestation in a documented viable pregnancy.
- NIPT is much more sensitive and specific than standard screening tests for aneuploidy.
- NIPT is a blood test on the mother, and therefore the risk of pregnancy loss is not increased.

Limitations

- NIPT is a screening test
- False positive rate of 0.3% (one in 350 women will mistakenly have a high-risk result)
- In a high-risk population, a positive test result is true more than 90% of the time
- In a low risk population, a positive test result is true about 60-70% of the time
- Although the test approaches diagnostic accuracy, a reassuring result does not completely exclude the possibility of Down syndrome (or the other genetic conditions screened for) in the fetus. For instance, about one in 1000 pregnancies with Trisomy 21 will mistakenly have a reassuring result. NIPT tests only for the genetic condition(s) specified; it does not give information about any other genetic conditions in the fetus or family.
- NIPT has a small risk of test failure of approximately 1%. Test failure can be related to the relative amount of cell-free DNA found in the maternal serum (fetal fraction). Factors that decrease the fetal fraction include multiple fetuses (twins or higher multiples) and maternal obesity.

What is the test performance of NIPT for common aneuploidies?

	Sensitivity	Specificity
Trisomy 21	99.9 %	99.2 %
Trisomy 18	99.9 %	96.3 %
Trisomy 13	99.9 %	91.0 %
Monosomy X	99.8 %	90.3 %

What is the positive predictive value (PPV) for a positive NIPT result for Trisomy 21?

Positive predictive value is the probability that a patient with a positive NIPT screening test

result will actually have an affected pregnancy. The following table of the PPV for Trisomy 21 was derived using the NIPT Predictive Calculator created by the Perinatal Quality Foundation and the National Society of Genetic Counselors (https://www.perinatalquality.org/Vendors/NSGC/NIPT/).

Maternal Age in years	Age related risk for Trisomy 21	Probability of having a positive NIPT result for Trisomy 21	PPV of a positive NIPT result for Trisomy 21*
20	1/1177	~1/500	48%
35	1/296	~1/250	79%
40	1/86	~1/80	93%

*The PPV for Trisomy 21 of a high-risk standard screening result ranges from <1% to 20%.

Following NIPT test results, how should pregnancies be managed?

- Following a negative NIPT result, the risk of aneuploidy would be greatly reduced and diagnostic testing would not be indicated, and **NO FURTHER** maternal serum testing should be done.
- Following a positive NIPT result, genetic counselling and diagnostic testing should be offered to confirm the diagnosis.
    - Diagnostic testing is optional, but not required if the patient is choosing expectant management of the pregnancy.
    - Diagnostic testing must be done if the patient is considering an interruption of pregnancy.
    - A referral for genetic counselling through the Maritime Medical Genetic Service can be faxed to (902) 470-8709.
- Patients who privately pay for NIPT should still be offered a 20-week ultrasound examination to assess fetal growth and development, placentation, and amniotic fluid volume. This can be arranged in their local Diagnostic Imaging unit unless there is another indication for assessment in the high-risk Fetal Assessment and Treatment Centre (FATC) clinic at the IWK.

How can self-pay NIPT be arranged?

The patient or Health Care Provider (HCP) must obtain a collection kit from the vendor of choice. The HCP is responsible for counselling the patient regarding benefits and limitations of the test and obtaining patient consent for the test. The HCP must complete all paperwork and identify a method for the blood collection. This can be done in the office, or through an outpatient blood collection service. The HCP must verify that the outpatient lab chosen is able to provide this service prior to sending the patient for blood draw.