

# A Guide to Understanding Prenatal Screening Tests

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**Prenatal Screening** is an option available to all expectant parents during pregnancy. **You** can decide whether or not you would like to have prenatal screening. The guide is meant to help expectant parents decide whether or not prenatal screening is right for them.

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**Most babies are born healthy.** In Canada, about 1 in 25 (4%) babies is born with a difference, called a congenital anomaly, that may require medical or surgical intervention. The most common differences are structural heart defects, cleft lip and/or palate or a pattern of anomalies such as Down syndrome. Some risk factors, like family history or maternal age, can increase the chance that a couple will have a baby with a congenital anomaly. If you have any concerns about **your family history**, for example you have a genetic condition, there are close relatives with intellectual disability or who were born with one or more congenital anomalies, young children or babies that passed away unexpectedly, be sure to discuss that with your health care provider.

Through available **prenatal screening** and detailed second trimester ultrasound, the chance to have a baby with some specific genetic conditions and congenital anomalies can be more precisely determined.

**Prenatal screening is about risk assessment.**

## What are prenatal screening tests?

These are blood tests, sometimes accompanied by an ultrasound, that are performed early in pregnancy.

Prenatal screening determines your chance of having a baby with **Down syndrome, trisomy 18** or an **open neural tube defect**. Prenatal screening can sometimes determine the chance of other genetic conditions and congenital anomalies.

While newer screening tests can more accurately determine the **chance** your baby has one of these conditions, **only a diagnostic test can tell you for sure whether or not your baby has one of these conditions.**

Many expectant parents have a difficult time deciding whether or not to have a prenatal screening test. Some expectant parents find it helpful to read this entire guide first, before making a decision.



Prenatal screening is available to all expectant parents.

Test options vary in each region.

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# The conditions for which prenatal screening is used

## Down syndrome

Babies and children with Down syndrome are individuals who are just as unique and highly variable as anyone else. An individual with Down syndrome has an extra copy of chromosome 21 (trisomy 21).



This usually causes mild to moderate intellectual disability, which means that adults will

typically function at the level of an 8-10

year old. An individual with Down syndrome is expected to learn to read and write and to be physically active, however major developmental milestones will be delayed. Individuals with Down syndrome have a greater possibility of health conditions than the average person, such as heart, stomach, bowel, thyroid, vision and hearing problems. Treatment is available for many of these conditions. There is no way to predict how serious or mild these differences will be. People with Down syndrome generally live into their fifties. In general, about one in 1000 babies born has Down syndrome. The chance of having a child with Down syndrome increases with the mother's age (See Table 3 in [Additional Resources](#), available online). For more information on Down syndrome, visit the [Canadian Down Syndrome Society](#) website.

## Trisomy 18 (Edward syndrome)

Babies with trisomy 18 have an extra chromosome 18. Every individual with trisomy 18 is different, however serious intellectual disabilities and congenital anomalies that may affect many organ systems (e.g. heart, kidneys) are expected. Many pregnancies with trisomy 18 will miscarry. Most babies born with trisomy 18 do not survive past the first few months of life. About 10% of infants will survive up to 5 years of age, or occasionally longer. Long-term survivors are described as socially interactive with significant physical and intellectual disabilities (e.g. having few words). In general, about one in 6,000 babies born has trisomy 18. The chance of having a child with trisomy 18 increases with the mother's age. For more on trisomy 18, visit [The Trisomy 18 Foundation](#) website.

## Open Neural Tube Defects

The neural tube is a structure in the early development of the central nervous system (the spinal cord and the brain). This structure is completely formed by about 6 weeks of pregnancy. Incomplete or failed formation of the neural tube leads to congenital anomalies of the brain or spinal cord and nerves. The effects of a neural tube defect are extremely varied and depend on the location and size of the defect. Open neural tube defects are the most common and serious. The neural tube defect is closed if the defect is covered by skin and the neural tissue is not exposed to amniotic fluid. A neural tube defect involving the spinal cord is called spina bifida. **Spina bifida** causes physical disabilities such as difficulty walking, and controlling the bladder and/or bowel. People with spina bifida may also have intellectual disabilities. Treatment can help with many of the physical disabilities. A neural tube defect involving the brain is called anencephaly. A baby with anencephaly will be stillborn or die shortly after birth. In Canada, the chance of having a baby with an open neural tube defect is about one in 1000 live births. The chance does not increase with the mother's age. The chance does decrease when a prenatal vitamin with folic acid is taken. For more on spina bifida, see the [Spina Bifida & Hydrocephalus Association of Ontario](#) website. Talk to your health care provider about folic acid and prenatal vitamins.

## Additional conditions which may be screened for by prenatal screening:

### Trisomy 13 (Patau syndrome)

Babies with trisomy 13 have an extra chromosome 13. In general between 1/8,000 and 1/15,000 of babies born has trisomy 13. The chance of having a child with trisomy 13 increases with a mother's age. Every individual with trisomy 13 is different; however each individual is expected to have both serious intellectual disabilities and congenital anomalies, including differences of the brain, heart, eyes and face. Most pregnancies with trisomy 13 will miscarry. About 5-10% of infants will survive the first year of life. There are some individuals who have lived to adulthood. For information on trisomy 13, visit [Support Organization for Trisomy 18, 13 and Related Disorders \(SOFT\) website www.trisomy.org](#). See **Additional Resources** in the online version of this pamphlet for more information about genetics.

### Sex chromosome differences

Typically, each mature human cell contains 23 chromosome pairs (46 chromosomes in total). One of these chromosome pairs, the 23rd pair, is the sex chromosomes. A female cell will usually have two X chromosomes and a male cell will have one X chromosome and one Y chromosome. Some prenatal screening and diagnostic testing can identify extra or missing X and/or Y chromosomes. There are several disorders with sex chromosome differences. Generally, these types of genetic differences are quite common occurring in about 1 in 500 individuals. Expected features are variable and depend on which chromosome is extra or missing. Some features maybe as mild as tall or short size. There may be differences in development such as delayed speech or learning differences. There may be associated health issues involving puberty or the heart. For a brief overview of chromosomes and some chromosome disorder visit the Genomic Resource Centre by the World Health Organization (WHO) at [www.who.int/genomics/gender/en/index1.html](http://www.who.int/genomics/gender/en/index1.html)

## Remember...

You might decide to have prenatal screening because you want to know the chance that your baby has one of the conditions previously described.

Prenatal screening uses the age of the mother/egg, blood test(s) and/or ultrasound of the baby to determine a more accurate chance.



## Are prenatal screening tests right for me?

It is **your** choice whether or not to have a prenatal screening test. There is not a right or wrong choice.

To help your decision-making, here are some questions expectant parents may ask themselves and discuss with a partner, health care provider, spiritual leader, family or friends.

1. **Do I want to know** the chance of my baby having Down syndrome, trisomy 18 or open neural tube defect?
2. **What would I do** with this information?

## Consider...

- What could you **do** with this information:
  - **Pregnancy management:** If you are found to be at increased risk for one of these conditions, your health care provider may suggest additional tests (e.g. **diagnostic testing** (page 15), more ultrasounds) and/or suggest changes to how your pregnancy is managed or the way your baby is delivered
  - **Reproductive choice:** *If I have a child with intellectual and/or physical disabilities, how might this affect my life, my other children, and my relationship with my partner and my extended family?* Some expectant parents have screening because they would like the information before birth to help with decision-making in the pregnancy. If their baby was found to have one of these conditions they would:
    - prepare for a child with special needs (See point 5 for more)
    - consider giving the baby up for adoption
    - consider ending the pregnancy
- Some expectant parents **choose to not** have screening because they would not:
  - have a **diagnostic test** (page 15) under any circumstance because of the small risk of miscarriage
  - change the course of their pregnancy by choosing to end the pregnancy

**Remember** that most babies are born healthy, however 1 in 25 babies in Canada is born with a difference at birth requiring medical intervention (*congenital anomaly*). Prenatal screening does not screen for all possible congenital anomalies. There is no cure for Down syndrome, trisomy 18 or open neural tube defect

3. How will this information affect **my feelings** throughout the pregnancy?

A low risk (*screen negative*) result is the most common outcome and those expectant parents are likely to feel reassured.

*Consider...* how would I feel if I received an increased chance (*screen positive*) for one of these conditions? Many expectant parents experience anxiety and worry when their test results say that the chance of having a baby with one of these conditions is higher than expected.

4. If your screening test result says there is an increased chance (*screen positive*) your baby has Down syndrome, trisomy 18 or open neural tube defect, you will need to decide if you want **diagnostic testing**. A screening test can only tell you the chance (probability) that your baby has one of these conditions. A diagnostic test can tell you for sure whether or not your baby does have the condition. Prenatal diagnostic testing for Down syndrome or trisomy 18 consists of amniocentesis or chorionic villus sampling (CVS) (see page 15). In the case of open neural tube defects, diagnostic testing will include a detailed ultrasound, amniocentesis or other investigation.

Would I **pursue diagnostic testing** in the event of a screen positive result?

*Consider...*

- **Diagnostic testing** will tell you if your baby has or does not have one of these conditions, **but** with amniocentesis and chorionic villus sampling (CVS) procedures there is a small chance of miscarriage (less than 1%).
  - *Would I be willing to take that risk to have this information?*
- **Diagnostic testing** can also detect conditions for which you were not known to be at increased risk, such as another chromosome difference.
  - *Would I want this additional information about my baby?*
- If **diagnostic testing** confirms a baby has the condition, expectant parents need to decide if they want to continue the pregnancy or if they will end the pregnancy.
  - *If more testing shows that my baby has a condition for sure, what will I do with the information?* (See points 1, 2 and 5 for more)

5. If you know that you would not end a pregnancy for any reason, prenatal screening may be an option for you. With a prenatal diagnosis you can: plan for the birth of your child; find out from others what it is like to raise a child with this condition; learn about resources available in your community; meet with various health care teams who may be involved with your child's care; or look into adoption.

*Consider...*

- Before the baby is born, to know for sure if a baby has one of these conditions, a **diagnostic test** like amniocentesis or chorionic villus sampling (CVS) is needed. Remember diagnostic tests are invasive and have a small chance of causing miscarriage.
- **Diagnostic testing** for a chromosome difference can be performed on a blood sample once a baby is born. This is a non-invasive option for expectant parents who would not change the course of their pregnancy based on such a diagnosis
- *Would this information be helpful to me before the birth or can I wait until my baby is born?*

## I have decided...

### A. I do not want to have prenatal screening, now what?

Your health care provider will follow you as in any other pregnancy and make sure that both you and your baby are in the best possible health. Where available, you may be offered an ultrasound in the late first trimester (around 11-14 weeks gestation) for more accurate dating of your pregnancy, determination of twins, and early detection of major congenital anomalies. You may be offered an ultrasound in the second trimester at around 18-20 weeks gestation to look at the baby's growth and anatomy.

### B. I do not want to have prenatal screening but rather *diagnostic testing*, now what?

Your access to diagnostic testing will vary depending on where you live. If you, or in the case of a donor, the egg, will be 40 years or older at the time of birth you will likely have the option to choose diagnostic testing without prenatal screening. Talk to your health care provider about next steps. See page 15 for more on diagnostic testing, and for more on available genetic tests see [Additional Resources](#) online.

### C. I do want to have prenatal screening, now what?

Once you have decided to proceed with prenatal screening, the next step is for you and your health care provider to choose which testing option is right for you. The following two tables compare available screening tests. Some factors that affect which prenatal screening tests you can choose from are:

- Where you live
  - Screening choices vary according to where you live. Your health care provider will discuss what is available.
- How far along you are in the pregnancy
  - Accurate dating of your pregnancy, determined by a first trimester ultrasound, is important for accurate screening results. Dating based on last menstrual period (LMP) is not ideal, but if a first trimester ultrasound is not available this dating can be used.
  - If the first prenatal visit with your health care provider is *before* 14 weeks (3-1/2 months) of pregnancy, options that may be presented to you include:
    - First Trimester Screening (FTS)
    - Enhanced First Trimester Screening (eFTS)
    - Integrated Prenatal Screening (IPS)
    - Serum Integrated Prenatal Screening (SIPS)
    - Non-Invasive Prenatal Testing (NIPT)
  - If the first prenatal visit with your health care provider is *after* 14 weeks (3-1/2 months) and before 21 weeks (~5 months) of pregnancy, options that may be presented to you include:
    - Maternal Serum Screening (MSS)
    - Non-Invasive Prenatal Testing (NIPT)
- The age of the mother (or the egg in the case of a donated egg) when the baby is born
  - If the mother/egg will be 40 years of age or older at the time of birth, prenatal testing options include all screening tests above, in addition to the option of [diagnostic testing](#) (page 15)
  - If the mother/egg will be 39 years of age or younger at the time of birth, prenatal options include all of the screening tests above, however NIPT would have to be paid for out of pocket and is not covered by Ontario Health Insurance Plan (OHIP). Diagnostic testing would not typically be offered at this time.

In addition to blood work, many screening tests also include an ultrasound measurement called the **nuchal translucency (NT)**. What is the NT measurement?



- The nuchal translucency (NT) is a fluid filled space at the back of every baby's neck (see image left)
- A larger NT measurement is associated with an increased chance for chromosome disorders like Down syndrome and some other genetic and non-genetic issues like congenital heart defect
- An ultrasound to measure NT is performed between 11 and 14 weeks of pregnancy and should be done at a *certified* ultrasound site. Your health care provider will tell you where an NT ultrasound can be obtained.
- An NT measurement of 3.5mm or bigger is considered significant and would be a *screen positive*. A referral for genetic counselling will likely be offered.

**Table 1** (page 8) has an overview of the prenatal screening tests available in Ontario and how they compare to each other. Not all test options are available in all areas.

First Trimester Screening (FTS) and Integrated Prenatal Screening (IPS) are the most commonly offered prenatal screening tests. Both screen for Down syndrome and trisomy 18. IPS also screens for open neural tube defects. Results from FTS are available earlier in pregnancy.

Prenatal screening is moving toward results available earlier in pregnancy, allowing expectant couples more time for decision making and access to additional services. Already many centres are offering **enhanced FTS (eFTS)**. This improved test performs better than traditional FTS with a higher detection rate and lower false positive rate. eFTS is expected to be just as good as IPS, but with results available earlier in pregnancy.

When access to a *certified* ultrasound site to measure the nuchal translucency is not possible, Serum Integrated Prenatal Screening (SIPS) may be offered.

A woman who presents to her first prenatal visit at a later gestational age (after 14 weeks) may be offered Maternal Serum Screening (MSS).

An ultrasound is recommended for all pregnant women at about 18-20 weeks of pregnancy to look at the baby's growth and anatomy, regardless of prenatal screening results. While most babies are born healthy, 1 in 25 babies in Canada will be born with a difference that may require medical intervention. It is important to remember that no test can detect every type of congenital anomaly.

If you are expecting twins, prenatal screening is available but in general is not as good as for pregnancies with one baby. Also, not all screening options will be available for a twin pregnancy. Talk to your health care provider for more about screening in a twin pregnancy.

### *Remember...*

Your health care provider will help you choose the right prenatal screening test. Factors that affect what is available are: where you live, gestational age of the pregnancy at the time of the first prenatal visit, maternal age/egg age at the time of birth.

The nuchal translucency (NT) can only be measured between 11 and 14 weeks of pregnancy at a certified ultrasound centre. This is a normal fluid filled space in every baby. You will likely be offered a referral to your local genetics centre if the NT measurement is greater than 3.5mm.

**Table 1. Prenatal screening tests available and how they compare.**

	<b>First Trimester Screening (FTS)</b>	<b>Integrated Prenatal Screening (IPS)</b>	<b>Non-Invasive Prenatal Testing (NIPT)/cfDNA screening</b>	<b>Serum Integrated Prenatal Screening (SIPS)</b>	<b>Maternal Serum Screening (MSS)</b>
<b>Components of test</b> All screens use maternal age in risk assessments u/s = ultrasound NT = nuchal translucency see page 7 for more	<ul style="list-style-type: none"> <li>One maternal blood test for pregnancy related hormones</li> <li>u/s for NT</li> </ul>	<ul style="list-style-type: none"> <li>Two maternal blood tests for pregnancy related hormones</li> <li>u/s for NT</li> </ul>	One maternal blood test for cell-free (cf) DNA	Two maternal blood tests for pregnancy related hormones	One maternal blood test for pregnancy related hormones
<b>Gestational age at first trimester blood test</b>	11 – 13 weeks + 6 days	11 – 13 weeks + 6 days	9-10 weeks onward	11 – 13 weeks + 6 days	Not applicable
<b>Gestational age at the NT ultrasound</b>	11 – 13 weeks + 6 days	11 – 13 weeks + 6 days	Not applicable	Not applicable	Not applicable
<b>Gestational age at second trimester blood test</b>	Not applicable	15 - 20 week + 6 days	Not applicable	15 - 20 week + 6 days	15- 20 week + 6 days
<b>Detection rate</b>	<i>Meaning, how many pregnancies where the baby really does have Down syndrome will be flagged as increased risk (screen positive) by this test?</i>				
	75-90%	85-90%	99%	80-90%	80%
<b>False positive rate</b>	<i>Meaning, how many pregnancies will this test flag as increased risk (screen positive) BUT the baby does NOT really have Down syndrome?</i>				
	about 3-9%	about 2-4%	Less than 0.1%	about 2-7%	about 5%
<b>Conditions screened for</b>	<ul style="list-style-type: none"> <li>Down syndrome</li> <li>Trisomy 18</li> </ul>	<ul style="list-style-type: none"> <li>Down syndrome</li> <li>Trisomy 18</li> <li>Open neural tube defects</li> </ul>	<ul style="list-style-type: none"> <li>Down syndrome</li> <li>Trisomy 18</li> <li>Trisomy 13</li> <li>Sex chromosome differences</li> </ul>	<ul style="list-style-type: none"> <li>Down syndrome</li> <li>Trisomy 18</li> <li>Open neural tube defects</li> </ul>	<ul style="list-style-type: none"> <li>Down syndrome</li> <li>Trisomy 18</li> <li>Open neural tube defects</li> </ul>
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# Non-invasive prenatal testing by cell-free DNA: the latest in prenatal screening

## What is non-invasive prenatal testing by cell-free DNA?

**Non-Invasive Prenatal Testing (NIPT)** is a screening test to estimate the chance that the unborn baby has Down syndrome or another chromosome condition (trisomy 18, trisomy 13 or an extra or missing sex chromosome). Normally **genetic information (DNA)** is contained within a cell (see the **Additional Resources** section online for an introduction to genetics). When a cell dies it releases its contents into the blood stream and the DNA is broken up into tiny pieces. This DNA is called **cell-free DNA (cfDNA)**.

NIPT is also known as **cfDNA screening**. NIPT/cfDNA screening detects, reads and counts cfDNA in a pregnant woman's blood stream. Although this cfDNA is not directly from the baby, it is from the placenta and usually represents the genetic profile of the baby.

## What are the benefits of NIPT/cfDNA screening?

- **Accuracy:** NIPT/cfDNA screening is more accurate than conventional screening tests, detecting more than 99% of pregnancies where the baby has Down syndrome (versus 75-90% by other screening methods). See Table 1 on page 8 for more on conventional prenatal screening.
- **Timing:** The result from NIPT/cfDNA screening is available earlier than other types of prenatal screening. NIPT/cfDNA screening is just one blood test and can be done as early as 9 weeks, with results available about 1-2 weeks after that. Having screening results earlier in pregnancy allows expectant parents more time for decision-making and potentially offers them more options.

## What are the limitations of NIPT/cfDNA screening?

- **Screening test:** While NIPT/cfDNA screening is an excellent test, it cannot tell for sure whether or not your baby has any of the chromosome conditions mentioned above. It is a screening test that provides a risk assessment (high risk or low risk). If the result comes back as high risk for one of the conditions, **a diagnostic test** such as amniocentesis or chorionic villus sampling (CVS) is recommended before any final decision is acted upon. (See page 15 for more on Diagnostic tests)
- **NIPT/cfDNA screening does not screen for all possible conditions:** A negative NIPT/cfDNA screening result does not guarantee a healthy baby. A late first trimester ultrasound at 11 to 14 weeks may be offered, where available. An ultrasound at 18-20 weeks gestation is recommended for all pregnancies, regardless of screening results.
- **Possibility of re-draw or no results:** About 1-8% (1 to 8 in 100) or less of women will need to have their blood drawn a second time because the test fails. About half the time a result will be available after this second try. There are various reasons why a test may fail including technical issues with the sample, or not enough cfDNA from the pregnancy (**low fetal fraction**). Factors that may result in a low fetal fraction are: too early in the pregnancy, chromosome disorder, maternal obesity.
- **Incidental findings:** NIPT/cfDNA screening also screens for differences in other chromosomes, like the sex chromosomes. Additionally, because this test is also looking at the mother's cfDNA, occasionally a genetic difference in the mother may be identified.

## Who should have NIPT/cfDNA screening?

NIPT/cfDNA screening is available to all pregnant women. NIPT/cfDNA screening can be used as a second screen (i.e. after receiving a positive First Trimester Screening result or if specific ultrasound differences have been found) or as a first screening test (e.g. before any other screening). Ontario Health Insurance Plan (OHIP) will pay for NIPT/cfDNA screening for women in Ontario who meet certain criteria.

Women who do not meet the criteria (see below) can pay for NIPT/cfDNA screening themselves. Prices vary by company, the average cost being around 500\$.

OHIP will fund NIPT/cfDNA screening for women who:

- 🚩 Have a positive prenatal screening result such as First Trimester Screening or other conventional screening methods described in Table 1 (page 8).
- 🚩 Are over the age of 40 at the expected date of delivery.
- 🚩 Have had a previous pregnancy or child with a chromosome condition.
- 🚩 Have findings on ultrasound which are associated with an increased risk for Down syndrome, trisomy 18 or trisomy 13.

### Who offers NIPT/cfDNA screening?

The Ministry of Health and Long Term Care (MOHLTC) has an agreement with two companies to provide NIPT/cfDNA screening in Ontario (Table 2). The technology each company uses to calculate the risk of a chromosome condition is different, but the accuracy of the tests is comparable. If you choose to have NIPT/cfDNA, the company you and your health care provider choose may vary depending on factors listed in Table 2.

**Table 2.** Non-Invasive Prenatal Testing (NIPT) in Ontario. *Last updated April 2017.*

	<b>Harmony™ by Ariosa</b>	<b>Panorama™ by Natera</b>
Where is my blood drawn for this test?	<u>DynaCare Next</u>	<u>LifeLabs Genetics</u>
How early can I have this test?	10 weeks gestation	9 weeks gestation
When would results be available?	10 business days	10 business days
Will this test work if this pregnancy:		
• Was conceived by <i>in vitro fertilization</i> (IVF)?	Yes	Yes
• Was conceived by IVF with a donor egg (not self)?	Yes	No
• Is being carried by a surrogate?	Yes	No
• Is twins?	Yes	No
What proportion of the pregnancies where the baby <i>has</i> Down syndrome will be detected? (Detection rate)	>99%	>99%
What proportion of the pregnancies where the baby <i>does not have</i> Down syndrome will be falsely called high risk? (False positive rate)	About 1 in 1,000 (0.1%)	About 1 in 1,000 (0.1%)

**Talk to your health care provider if you are interested in NIPT/cfDNA screening.**

## What about the other genetic conditions screened for by NIPT/cfDNA screening?

You may have read that the NIPT/cfDNA screening can suggest other genetic conditions, such as *microdeletion* and *microduplication* syndromes. These are rare genetic conditions, occurring in about 1 in 5,000 to 1 in 50,000 pregnancies. They are caused by very tiny extra or missing pieces of chromosomes.

Most of these conditions occur by chance, meaning that they tend to not run in families and can occur out of the blue. The risk of these conditions is not associated with the mother's age, as it is for Down syndrome and trisomy 18 (conditions caused by extra whole chromosomes).

The addition of these rare conditions to NIPT/cfDNA screening increases the false positive rate. This means that more women would receive a positive (high risk) screen result even though the baby does not actually have the condition. This would result in more women having diagnostic tests, with associated risk of miscarriage. Current recommendations **do not** support the routine inclusion of screening for microdeletion and microduplication syndromes in NIPT/cfDNA screening.

### *Remember...*

Non-Invasive Prenatal Testing (NIPT), also known as cfDNA screening, is a test to estimate the chance that the baby a woman is carrying has Down syndrome and other specific genetic conditions.

NIPT/cfDNA screening is available to all pregnant women. Ontario Health Insurance Plan (OHIP) will pay for NIPT/cfDNA screening for women in Ontario who meet certain eligibility criteria. Women who do not meet these criteria can self-pay for NIPT/cfDNA screening. Prices vary by company, the average cost being around 500\$.

**Benefits:** NIPT/cfDNA screening is much better at detecting Down syndrome and other specific genetic conditions than conventional prenatal screening (e.g. Integrated Prenatal Screening, First Trimester Screening). NIPT/cfDNA screening has a lower false positive rate than conventional prenatal screening. Higher detection and lower false positive rates mean that fewer women will need to have follow-up invasive testing which is associated with a small risk of pregnancy loss.

**Limitations:** NIPT/cfDNA screening is **not** diagnostic, meaning that it cannot tell with certainty whether or not the baby a woman is carrying has Down syndrome or another genetic condition. A woman who receives a high risk or positive NIPT/cfDNA screening result will be offered diagnostic testing by amniocentesis or chorionic villus sampling to confirm or rule out the diagnosis. NIPT/cfDNA screening cannot detect all possible genetic conditions. There is no screening or diagnostic test which can guarantee a healthy baby. A woman who receives a low risk NIPT/cfDNA screening result may still be offered additional counselling or testing depending on why she was originally offered NIPT/cfDNA screening.

## What do my screening results mean?

### A: Screening results using First Trimester Screening as an example:

First Trimester Screening (FTS) calculates the chance that the baby has Down syndrome or trisomy 18. It does not screen for open neural tube defects or any other condition. FTS uses the age of the mother/egg at the time of delivery, the size of the nuchal translucency (NT) on a first trimester ultrasound, and the levels of certain hormones in the mother's blood that are being produced by the current pregnancy. A risk is then calculated estimating the chance that the baby has either condition. Generally, for FTS, a risk greater than 1/350 (~0.3%) is considered *screen positive* and any risk lower than this is a *screen negative*. For more on FTS see Section [I have decided. I do want to have prenatal screening, now what?](#) on page 6.

### What if my FTS result is a screen NEGATIVE?

This is reassuring. This means that the chance that your baby has Down syndrome or trisomy 18 is LOWER than the screening cut-off (for example less than 0.3% or 1/350). Note that the screening cut-off may vary by laboratory and condition.

#### What do I do next?

Remember FTS is only intended to screen for Down syndrome and trisomy 18. FTS is not intended to screen for any other conditions. An ultrasound is recommended for [all pregnant women](#) at about 18-20 weeks of pregnancy to look at the baby's growth and development, regardless of prenatal screening results. While most babies are born healthy, 1 in 25 babies in Canada will be born with a difference that may require medical or surgical intervention. It is important to remember that no test can detect every type of congenital anomaly.

### What if my FTS result is a screen POSITIVE?

This means that the chance of your baby having Down syndrome or trisomy 18 is HIGHER than the screening cut-off (for example greater than 0.3% or 1/350). This result does not necessarily mean that your baby has one of these genetic conditions. Remember that most babies are born healthy.

A [nuchal translucency \(NT\) measurement](#) (page 7) greater than 3.5mm is an automatic screen positive for Down syndrome [and](#) certain other disorders and should prompt a referral for genetic counselling.

### Is an FTS screen POSITIVE result accurate?

FTS will identify most (about 80- 90%) pregnancies where the baby has Down syndrome.

FTS does not perform as well when detecting trisomy 18, however it will identify most pregnancies with trisomy 18.

While FTS is excellent at identifying most pregnancies where the baby has Down syndrome or trisomy 18, most screen positive results turn out to be false. This is called a FALSE POSITIVE and is identified either by diagnostic testing or by the birth of a baby who does not have the condition.

FTS does not screen for open neural tube defect.

FTS is not meant to screen for any other disorders.

#### What do I do next?

See the section [What are the next steps if my prenatal screening test is POSITIVE?](#) on page 14 for more.

## **B: Screening results using non-invasive prenatal testing (NIPT) as an example:**

NIPT/cfDNA screening is a newer and more accurate way to screen for Down syndrome, trisomy 18, trisomy 13 and sex chromosome differences in a pregnancy. NIPT examines DNA in the mother's blood that comes from the pregnancy.

### **What if my NIPT/cfDNA screening result is NEGATIVE?**

This is very reassuring. Generally, an NIPT/cfDNA screen NEGATIVE result is reported as LOW RISK (*less than 1 in 10,000 chance*). The chance that your baby has Down syndrome, trisomy 18, trisomy 13 or a sex chromosome difference is LOWER than that. NOTE: In twin pregnancies, it is not possible to screen for sex chromosome differences.

#### **What do I do next?**

Remember NIPT/cfDNA screening is only intended to screen for Down syndrome, trisomy 18, trisomy 13 and sex chromosome differences. You may be offered a late first trimester ultrasound (11-14 weeks). Additionally, an ultrasound is recommended for all pregnant women at about 18-20 weeks of pregnancy to look at the baby's growth and anatomy, regardless of prenatal screening results. While most babies are born healthy, 1 in 25 babies in Canada will be born with a difference that may require medical intervention. It is important to remember that no test can detect every type of congenital anomaly.

### **What if the risk number reported is not less than 1 in 10,000?**

If you received a risk result other than less than 1 in 10,000 (e.g. another low risk value or a borderline risk) you should discuss this result with your health care provider or genetic counsellor. This test is still relatively new and additional follow up testing and/or counselling may be needed.

### **What if my NIPT/cfDNA screening test fails?**

Occasionally NIPT/cfDNA screening may fail and no result is reported. There are various reasons why a test may fail, see page 9 for more. In this event, you may be asked for a new blood sample. Most of the time a result will be available after this second try. This can delay results. If the second try is also unsuccessful you may be offered genetic counselling to discuss this and additional testing options.

### **What if my NIPT/cfDNA screening result is POSITIVE?**

An NIPT/cfDNA screen POSITIVE result is generally reported as HIGH RISK (*greater than 99% chance*). NIPT/cfDNA screening has a very low false positive rate meaning that further testing is expected to confirm the diagnosis and most screen positives will be true positives.

However, NIPT/cfDNA screening is **not** a diagnostic test and there is still a small chance that a high risk result is false. In the event of a screen positive NIPT/cfDNA result, diagnostic testing is recommended prior to any permanent action (e.g. choosing to end the pregnancy). Information gained from diagnostic testing is also helpful for future counselling about recurrence risks in future pregnancies. If expectant parents would continue the pregnancy regardless of diagnostic results, chromosomal testing can be arranged after the baby is born.

#### **Is an NIPT/cfDNA screen POSITIVE result accurate?**

NIPT/cfDNA screening will identify about 99% of pregnancies (99 out of 100) where the baby has Down syndrome. Studies have shown that NIPT/cfDNA screening is at least 10-20 times better than IPS at accurately identifying babies who have Down syndrome. NIPT/cfDNA screening does not perform as well when detecting trisomy 18 and even less so when detecting trisomy 13 and sex chromosome differences, however it is still considered a superior screen to traditional prenatal screening (Table 1) for these conditions.

## What do I do next?

See the next section [What are the next steps if my prenatal screening test is POSITIVE?](#) on this page for more.

## What are the next steps if my prenatal screening test is POSITIVE?

If your prenatal screening result is reported as **positive** or **high risk** for a chromosome disorder (i.e. Down syndrome, trisomy 18), you are likely to be offered an appointment with a genetic counsellor. There you will discuss what this result means and your options, including no further testing, or a **diagnostic test** (page 15) such as amniocentesis or chorionic villus sampling (CVS). Genetic counsellors can help you understand your options and make the decision that is right for you. They will support your decision no matter what you decide.

If your result is screen positive for a neural tube defect, you may have the option of a detailed ultrasound at 18 to 20 weeks *instead of* amniocentesis. This will vary depending on where you live.

There are many factors that influence expectant parents' decision to choose one option over another following a positive prenatal screening result. Some important considerations are:

- What information from diagnostic testing may be used for
  - reassurance
  - reproductive planning e.g. planning for a future with a child with special needs, or adoption or choosing to end the pregnancy
  - see [Are prenatal tests right for me?](#) (page 4) for more
- How far along the pregnancy is
  - time is an important consideration in pregnancy decisions
  - in Canada, while there are no legal restrictions on ending a pregnancy by medical termination, the availability is different in each city. Typically, before 22 weeks of pregnancy, medical termination can be accessed. After this, special arrangements may need to be made. Your health care provider and/or genetic counsellor will be able to help you learn what is available to you.
- The risk reported by the screening test
  - a screen positive risk score of 1/200 (0.5%) versus a screen positive risk score of 1/2 (50%) may weigh differently on expectant parents' decision

When deciding about whether or not you wish to proceed with diagnostic testing you should consider what you might do in the event that the results say your baby does have the condition. You do not have to decide before testing what you would do in the event a diagnosis is confirmed; however preparing yourself to make such a decision can be important. Your health care provider will also discuss your choices with you. You may want to discuss this with your partner, friends, family, spiritual leader or other supports.



**Consider...** Based on the risk number you have been given, whether it is a 1 in 10 (10%) or a 1 in 100 (1%), can you continue your pregnancy with that level of uncertainty or do you need to know for sure?

## What if diagnostic testing has been offered to me?

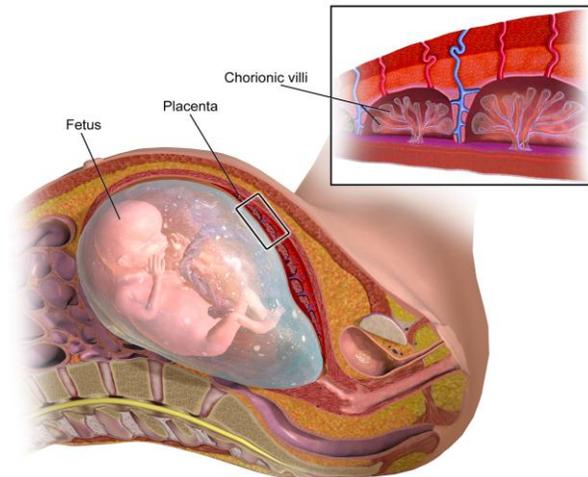
### Diagnostic tests

Where screening tests calculate a risk (*what is the chance*), a **diagnostic test** will rule in or rule out for sure whether or not a baby has one of the conditions. There are two common **diagnostic tests** that are offered: **chorionic villus sampling (CVS)** and **amniocentesis**. Whereas prenatal screening tests are considered *non-invasive* as they pose no risk to a pregnancy, diagnostic tests are considered *invasive* because they are associated with a small procedural risk – an increased chance to lose the pregnancy (miscarriage).

### Chorionic villus sampling (CVS)

#### What is chorionic villus sampling?

Chorionic villus sampling (CVS) is a procedure where a small piece of the placenta is taken and tested. Chorionic villi (see image on the right) attach the placenta to the uterus wall. The placenta is made from the fertilized egg and is expected to have the same genetic information as the baby. CVS is not available in all regions. Talk to your health care provider to see if this is an option for you. CVS cannot detect open neural tube defects.



#### When is a CVS carried out?

CVS is usually performed between 11 and 13 weeks of pregnancy.

#### What is the risk associated with CVS?

Both CVS and amniocentesis have been associated with a slightly increased chance of losing the baby following the procedure (miscarriage). The chance of miscarriage after a CVS or an amniocentesis is 0.5 to 1% (about 1 in 100 or less).

Because of the nature of the sample, there is a small chance that the result is difficult to interpret and additional testing, like amniocentesis, may be recommended.

#### What should I expect at my CVS appointment?

CVS is an outpatient procedure, meaning that you will not need to stay overnight in the hospital. You will be told to have a full bladder. There are two methods to collect a sample from the placenta; either through the vagina or the abdomen. Both methods use ultrasound as a guide the entire time.

Through the vagina, using ultrasound, a speculum is inserted (just like a Pap test). Then a very thin, plastic tube is inserted up the vagina and into the cervix. The tube is guided up to the placenta and a small sample is removed.

To collect a sample through the abdomen, a thin needle is inserted through the woman's abdominal wall, using ultrasound to guide the needle tip to the placenta.

#### Will it be painful?

Most women describe the procedure as uncomfortable rather than painful. In general, no medication or anesthetic is given. Through the vagina, the discomfort is similar to that with a Pap test. Through the abdomen, the pain from the needle is similar to having a blood sample drawn. The needle is a bit thicker and a numbing cream may be applied to the skin prior to the procedure. You can expect to experience some cramping during the procedure.

## Amniocentesis

### What is amniocentesis?

Amniocentesis is a procedure where a small sample of **amniotic fluid** (*the fluid that surrounds the baby*) is removed and tested. Usually only about 1-2 tablespoons are taken. Amniotic fluid contains fetal cells: skin cells and others cells that are naturally shed by the baby.

### When is an amniocentesis carried out?

The ideal timing is between 15 and 18 weeks to allow opportunity for the procedure, results and decision making. An amniocentesis can, however, be performed any time after 15 weeks.

### What is the risk associated with amniocentesis?

Both CVS and amniocentesis have been associated with a slightly increased chance of losing the baby following the procedure (miscarriage). The chance of miscarriage after a CVS or an amniocentesis is 0.5 to 1% (about 1 in 100 or less).

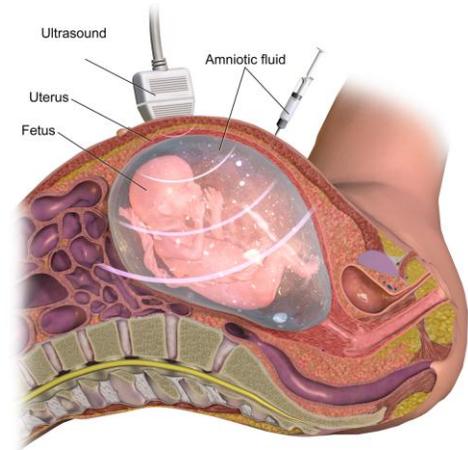
### What should I expect at my amniocentesis appointment?

Amniocentesis is an outpatient procedure, meaning that you will not need to stay overnight in the hospital. You may be told to have a full bladder, but this will likely depend on how far along in pregnancy you are.

To collect a sample of amniotic fluid, using ultrasound guidance the entire time, a thin needle is inserted through the woman's abdominal wall into a pocket of fluid (not near the baby) and fluid is extracted.

### Will it be painful?

Most women describe the procedure as uncomfortable rather than painful. In general, no medication or anesthetic is given. The pain from the needle is similar to that when having a blood sample drawn. You can expect to experience some cramping during the procedure.



### *Remember...*

Amniocentesis and chorionic villus sampling (CVS) are procedures where a sample from the pregnancy is obtained for prenatal diagnostic genetic testing.

Through a diagnostic test, you can learn for sure whether or not your baby has the condition tested positive for by prenatal screening (Down syndrome, trisomy 18, trisomy 13, sex chromosome difference, open neural tube defect).

\*CVS cannot detect neural tube defects. Closed neural tube defects may not be detected by amniocentesis.\*

These tests are associated with a small chance to lose the pregnancy (miscarriage).

Other genetic conditions can also be detected by these tests.

Your genetic counsellor or prenatal care provider will discuss these testing options with you in more detail and help you to understand the right test for you.

## A word about unexpected news

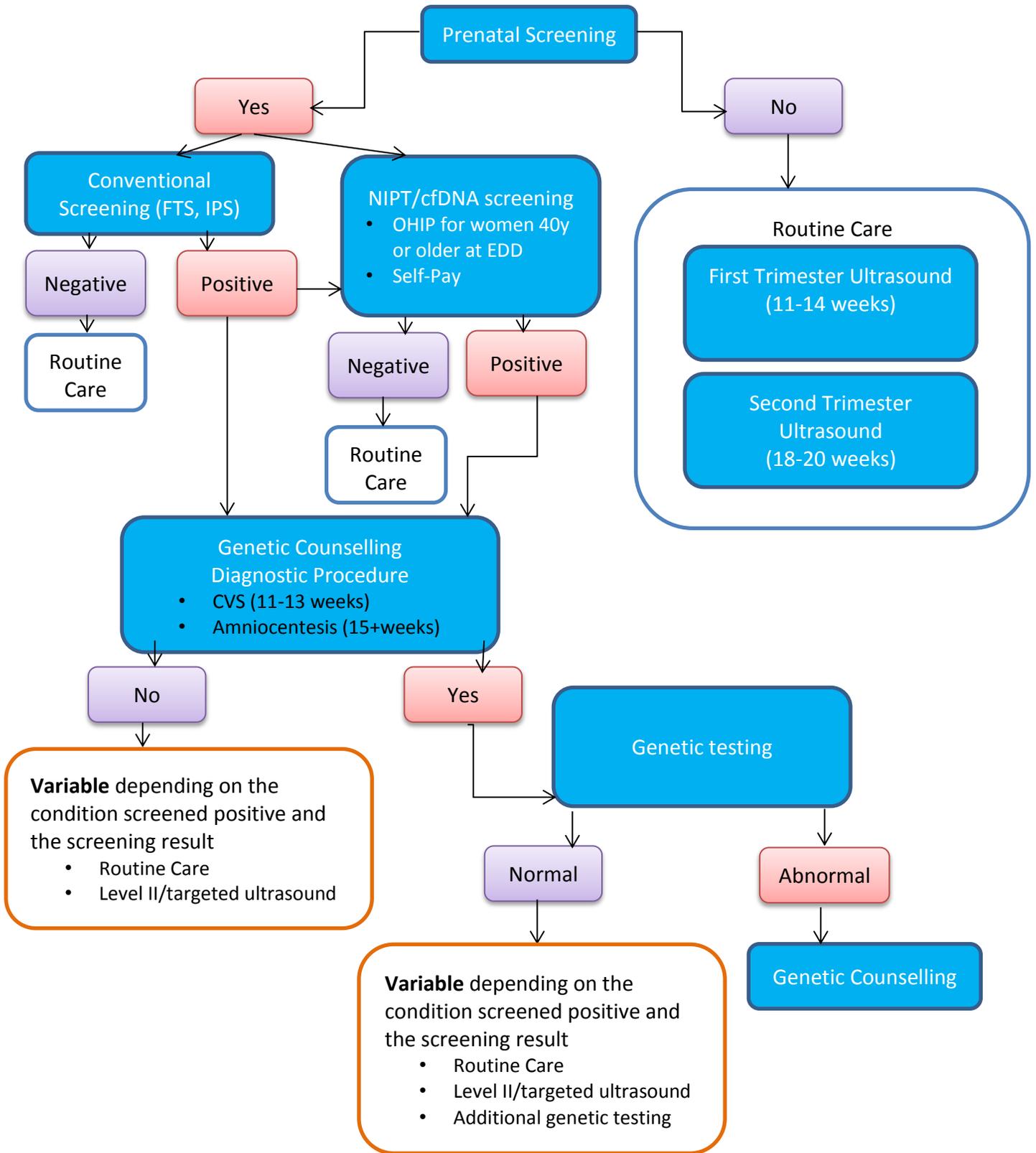
If you have diagnostic testing and the results confirm that your baby has Down syndrome, trisomy 18 or open neural tube defect, genetic counsellors are available to help you discuss your options: continuing the pregnancy, adoption or choosing to end the pregnancy.

Making a decision is not easy. Genetic professionals can help you find resources, such as support groups, that may be helpful to you during and after your decision-making. There are health care providers available to help you and offer support no matter what decision you make.

The choice is yours.



# A prenatal screening process map



## Online resources

This guide and additional resources including an introduction to genetics, diagnostic tests (more on what testing may be offered following a diagnostic procedure), and a prenatal testing process map can all be found online at [www.geneticseducation.ca](http://www.geneticseducation.ca)

For more resources on an **Introduction to Genetics**, try:

- [My46.org](http://www.my46.org) by the University of Washington
  - <https://www.my46.org/intro/what-is-genetics>
- [Health Centre for Genetics Education](http://www.genetics.edu.au/) by New South Wales government
  - <http://www.genetics.edu.au/>
- [Education materials](https://www.genome.gov/10000002/education/) by the National Human Genome Research Institute
  - <https://www.genome.gov/10000002/education/>

For more resources on **the conditions** screened for by prenatal screening, try:

- Canadian Down Syndrome Society
  - <http://www.cdss.ca> or 1-800-883-5608
- The Trisomy 18 Foundation
  - <http://www.trisomy18.org> or call 1-810-867-4211
- Support Organization for Trisomy 18, 13 (S.O.F.T.) and Related Disorders:
  - <http://www.trisomy.org> or call 1-800-716-7638 or 585-594-4621
- Spina Bifida and Hydrocephalus Association of Canada
  - <http://www.sbhac.ca> or call 1-800-565-9488
- The Genetics Home Reference - for more on these and other genetic conditions
  - <http://www.ghr.nlm.nih.gov>
- Genomic Resource Centre by the World Health Organization (WHO)
  - [www.who.int/genomics/gender/en/index1.html](http://www.who.int/genomics/gender/en/index1.html)

For an appointment with a genetic counsellor at **your local genetics centre**, you will most likely need a referral from your primary care provider or pregnancy care provider. To locate the nearest centre to you, see Genetics Education Canada – Knowledge Organization (GEC-KO) [www.geneticseducation.ca](http://www.geneticseducation.ca) > Genetics Centres [http://geneticseducation.ca/genetics-centres/canada/canadian\\_clinics/](http://geneticseducation.ca/genetics-centres/canada/canadian_clinics/)

For more on **non-invasive prenatal testing (NIPT)/cfDNA screening** in Ontario, see:

- Harmony™ by Ariosa
  - <https://www.dynacare.ca/healthcare-providers-and-hospitals/patient-wellness-management/prenatal-testing.aspx>
  - Blood samples are collected through DynaCare Next
  - <https://www.dynacare.ca/> or call 800.565.5721
- Panorama™ by Natera
  - <http://www.lifelabsgenetics.com/non-invasive-prenatal-testing/>
  - Blood samples are collected through LifeLabs
  - <http://www.lifelabsgenetics.com/> or call 1-84-GENE HELP (1-844-363-4357)

For more on **Ontario provincial screening programs**, see:

- Mount Sinai Hospital, Sinai Health Systems
  - First Trimester Screening
    - <http://womensandinfantshealth.ca/tests/first-trimester-combined-screening-fts/>
  - Integrated Prenatal Screening
    - <http://womensandinfantshealth.ca/tests/integrated-prenatal-screening-ips/>
  - Maternal Serum Screening
    - <http://womensandinfantshealth.ca/tests/maternal-serum-screening/>
  - Phone: 416-586-4457
- North York General Hospital
  - <http://www.nygh.on.ca/Default.aspx?cid=1366&lang=1>
  - Phone: 416-756-6345
- Trillium Health Partners (formerly Credit Valley Hospital)
  - <https://trilliumhealthpartners.ca/patientservices/genetics/Pages/requisitions-forms.aspx>
  - Phone: 905-813-4104

All images are open-source. Links to their original site are attached to each photo.

## Acknowledgements:

This guide was written by a multidisciplinary team and with input from new parents.