PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

BORN
Ontario

Champlain Maternal Newborn Regional Program
November 17/2021

Navigating the Prenatal Genetic Screening Landscape in Ontario

Presenter: Ioana Miron (she/her/hers)
Certified Genetic Counsellor, Prenatal Screening Ontario

Learning Objectives

1. Compare the timing, components and performance of the different prenatal genetic screening modalities in Ontario

2. Identify which prenatal screening tests to offer depending on clinical circumstances

3. Describe the main differences between prenatal genetic screening and diagnostic testing

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

How to Interact

Go to menti.com and use the code 8073 1991

OR

Scan the QR code with your camera phone

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Land Acknowledgement

I would like to begin by acknowledging the land on which I am privileged to live and work, and which Region of Peel operates, is part of the Treaty Lands and Territory of the Mississaugas of the Credit. In particular, I acknowledge the territory of the Anishinabek, Huron-Wendat, Haudenosaunee and Ojibway/Chippewa peoples; the land that is home to the Métis; and most recently, the territory of the Mississaugas of the Credit First Nation who are direct descendants of the Mississaugas of the Credit.

I would like to offer my gratitude to Indigenous people for their careful stewardship of these lands in the past and acknowledge their present contributions. Thank you for joining us virtually from your territory.

Visit the Indigenous Wellness section of the BORN website to learn about BORN's efforts to develop an Indigenous data governance policy, and engagement strategy with our Indigenous partners.

What is BORN?

BORN is Ontario's maternal, newborn, and child **registry**, granted status in 2004 under the Personal Health Information Protection Act

Registry status allows BORN to collect, use and disclose personal health information without consent for the purpose of "facilitating or improving the provision of health care"

Prenatal Screening Ontario (PSO) is housed within BORN, and was launched in 2018

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Prenatal Screening Ontario Mandate

- Enhance **access** to high quality prenatal screening for all pregnant individuals in Ontario.
- Provide the **education** supports, information, and transparency needed for health care providers and pregnant individuals and their families to make informed decisions.
- Undertake ongoing **quality assurance and system performance** evaluation to support all components of the system in functioning effectively and meeting established standards.
- Facilitate the **incorporation of evolving technologies** or screening options, supporting evidence-based integration.
- Support the ongoing **alignment** of screening service provision.

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Prenatal Genetic Screening in Ontario

Multiple Marker Screening (MMS)

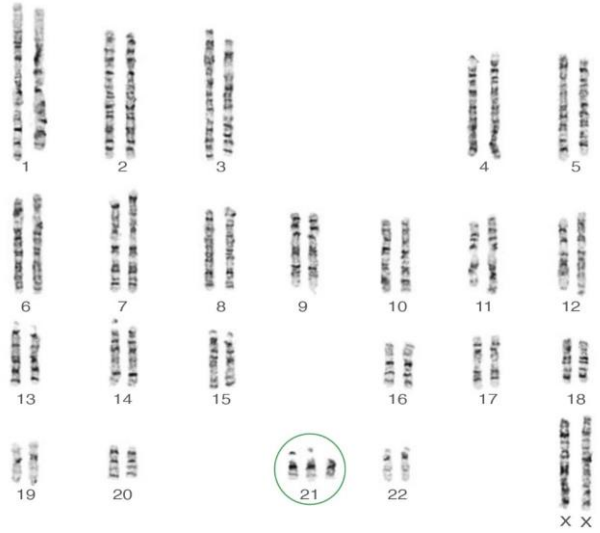
enhanced First Trimester Screening (eFTS) and Maternal Serum Screening (MSS). OHIP-funded.

Non-Invasive Prenatal Testing (NIPT)

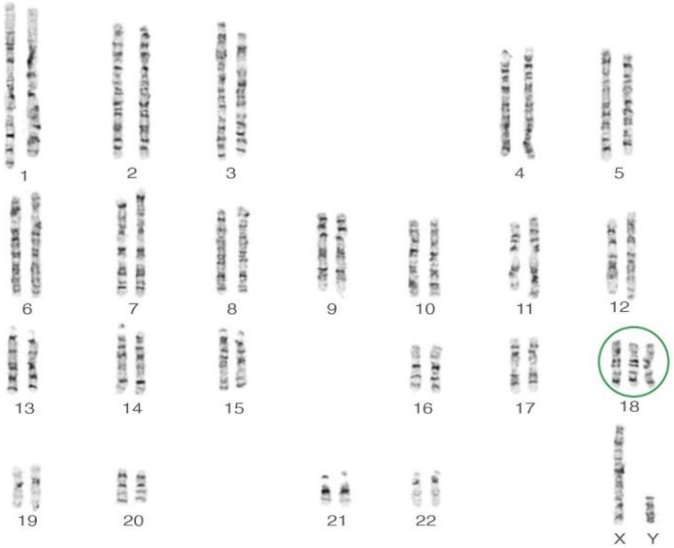
OHIP-funded when at least one of specific criteria is met.

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

What Does eFTS Screen For?



Trisomy 21
(Down syndrome)



Trisomy 18
(Edwards syndrome)

Illustrations adapted from Genetic Counseling Aids, 7th Edition, Copyright 2020, permission for use granted by Greenwood Genetic Center

Link to Chart: Chance of Chromosome Differences Based on Maternal Age

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

eFTS at a Glance

TIMING

11w2d to 13w3d gestation

COMPONENTS

Maternal age/age of oocyte provider, Nuchal Translucency ultrasound and bloodwork (hCG, PAPP-A, MS-AFP, +/-PlGF)

TURN AROUND TIME

Median TAT for multiple marker screening is 4 business days*

LOCATION

Performed at 3 Multiple Marker Screening Labs in Ontario

SCREENING THRESHOLD

1/350 – Trisomy 21
1/200 – Trisomy 18

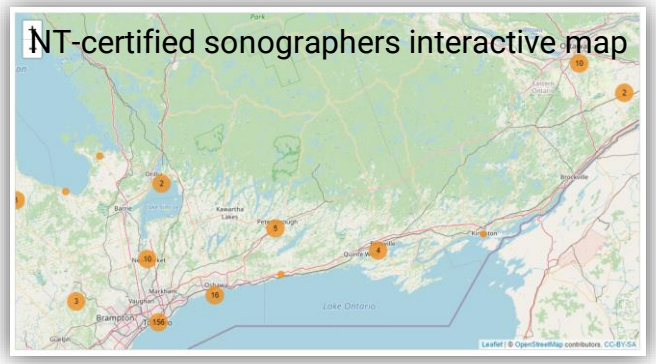
GESTATION TYPE

Singletons and twins

**Analysis was based on data from ON pregnancies with an EDD of 01-Apr-2019 to 31-Mar-2020. Only singleton pregnancies were included in this analysis*

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

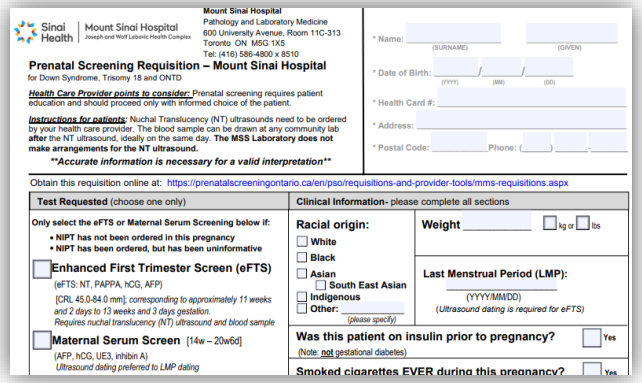
Logistics of Ordering eFTS



NT Ultrasound Requisition

NT-ultrasound requisition is center specific

LINK TO INTERACTIVE MAP



Sinai Health | Mount Sinai Hospital
Joseph and Wolf Lebovic Health Complex

Mount Sinai Hospital
Pathology and Laboratory Medicine
600 University Avenue, Room 11C-313
Toronto ON M5G 1X5
Tel: (416) 586-4800 x 8510

Prenatal Screening Requisition – Mount Sinai Hospital
for Down Syndrome, Trisomy 18 and ONTD

Health Care Provider points to consider: Prenatal screening requires patient education and should proceed only with informed choice of the patient.

Instructions for patients: Nuchal Translucency (NT) ultrasounds need to be ordered by your health care provider. The blood sample can be drawn at any community lab **after** the NT ultrasound, ideally on the same day. **The MSS Laboratory does not make arrangements for the NT ultrasound.**

****Accurate information is necessary for a valid interpretation****

* Name: (SURNAME) (GIVEN)
* Date of Birth: (YYYY) (MM) (DD)
* Health Card #:
* Address:
* Postal Code: Phone: ( )

Obtain this requisition online at: https://prenatalscreeningontario.ca/en/pso/requisitions-and-provider-tools/mms-requisitions.aspx

Test Requested (choose one only)

Only select the eFTS or Maternal Serum Screening below if:
- NIPT has not been ordered in this pregnancy
- NIPT has been ordered, but has been uninformative

☐ **Enhanced First Trimester Screen (eFTS)**
(eFTS: NT, PAPPA, hCG, AFP)
[CRL 45.0-84.0 mm]; *corresponding to approximately 11 weeks and 2 days to 13 weeks and 3 days gestation.*
Requires nuchal translucency (NT) ultrasound and blood sample

☐ **Maternal Serum Screen** [14w – 20w6d]
(AFP, hCG, UE3, inhibin A)
Ultrasound dating preferred to LMP dating

Clinical Information- please complete all sections

Racial origin:
☐ White
☐ Black
☐ Asian
☐ South East Asian
☐ Indigenous
☐ Other: (please specify)

Weight ☐ kg or ☐ lbs

Last Menstrual Period (LMP):
(YYYY/MM/DD)
(*Ultrasound dating is required for eFTS*)

Was this patient on insulin prior to pregnancy? ☐ Yes
(Note: not gestational diabetes)

Smoked cigarettes EVER during this pregnancy? ☐ Yes

Multiple Marker Screening Requisition

Each of the three MMS laboratories has a specific catchment area. Which MMS requisition you use is dependent on your location.

LINK TO MMS REQUISTIONS

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

HOW TO GET enhanced FIRST TRIMESTER SCREENING (eFTS)

WHAT IS eFTS? eFTS is an optional prenatal genetic screening test that can tell you the chance for having a baby with trisomy 21 (Down syndrome) or trisomy 18 (Edwards syndrome).

WHEN IS eFTS DONE? eFTS is done in the first trimester of pregnancy, usually between 11 weeks 2 days to 13 weeks 3 days gestation. Knowing the gestational age of your pregnancy is key for timing eFTS. Discuss this with your healthcare provider.

HOW DO I GET eFTS? eFTS is arranged through your healthcare provider. You will first have a nuchal translucency (NT) ultrasound, which measures the fluid-filled pocket at the back of the neck of the developing baby. The ultrasound is followed by a blood test.

STEP 1 BOOK NT ULTRASOUND

- Your provider will fill out a requisition for your NT ultrasound.
- The NT ultrasound will be booked by you or your healthcare provider.
- If you are booking the ultrasound yourself, the contact information for the ultrasound facility will be on the requisition given to you by your provider. Some ultrasound facilities have multiple locations.

WHERE CAN I GET THE NT ULTRASOUND DONE?

- Your healthcare provider may recommend a hospital or clinic for your NT ultrasound.
- If needed, you can search the interactive map on our website to locate a NT ultrasound facility in your area.

STEP 2 ATTEND NT ULTRASOUND

A section of the Prenatal Screening Requisition (also known as the Multiple Marker Screening Requisition) will be filled out at the ultrasound facility.

STEP 3 GET BLOOD TEST

Take the Prenatal Screening Requisition to any blood collection laboratory, such as LifeLabs® or Dynacare®. Visit their websites for the most up-to-date information on available locations and how to plan for your visit.

WHILE SAME DAY BLOOD COLLECTION IS PREFERRED, IT IS NOT ESSENTIAL. THE BLOOD TEST CAN BE DONE ANY TIME AFTER THE ULTRASOUND, UP UNTIL APPROXIMATELY 13 WEEKS 3 DAYS GESTATION.

STEP 4 OBTAIN RESULTS

The results from the eFTS will be sent to your healthcare provider within 5 business days. Make a plan with your provider about how and when the results will be given to you.

PRENATAL SCREENING DÉPISTAGE PRÉNATAL ONTARIO

HOW DO I GET MORE INFORMATION?

Visit our website to read more about eFTS and other screening options

Speak to a Genetic Counsellor

Ontario

www.prenatalscreeningontario.ca 1-833-351-6490 pso@bornontario.ca

Rev. July 2021

Logistics of Getting eFTS

🔗 Link to Patient Leaflet

PRENATAL SCREENING DÉPISTAGE PRÉNATAL ONTARIO

eFTS Performance

Chromosome Difference	Detection Rate % (95% CI)	False Positive Rate % (95% CI)
trisomy 21	88.29 (85.52,90.69)	6.34 (6.24,6.44)
trisomy 18	83.96 (77.90,88.91)	0.24 (0.22,0.27)

Notes:
1. Singleton pregnancies with an EDD of 01-Sep-2016 to 30-Jun-2020 were included in this analysis
2. "eFTS" includes both 4-marker and 5-marker eFTS
3. Outcome data for autosomes screened (chromosomes 21, 18, and 13) were supplemented using data from the BORN information system (BIS) for negative results only, where the outcomes for pregnancies with no cytogenetic outcome were set to test-negative when their corresponding BIS record had no indication for the disorder during the perinatal period

Detection rate: Probability that a pregnancy *with* a chromosome difference will get a “screen positive” result

False positive rate: Probability that a pregnancy *without* the chromosome difference will get a “screen positive” result

Multiple Marker Screening

	eFTS	MSS
TIMING	11w2d to 13w3d	14w0d to 20w6d
SCREENED CHROMOSOME DIFFERENCES	trisomy 21, trisomy 18	trisomy 21, trisomy 18
COMPONENTS	Maternal age, NT ultrasound, bloodwork (hCG, PAPP-A, MS-AFP +/- PIGF)	Maternal age, bloodwork (MS-AFP, uE3, DIA, hCG)
THRESHOLD (trisomy 21)	1/350	1/200 (temporarily changed to 1 in 350)
GESTATION TYPE	Singletons and twins	Singletons only

eFTS is the preferred screening modality.
MSS is performed when eFTS is not available.

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

No. 348-Joint SOGC-CCMG Guideline

Update on Prenatal Screening for Fetal Aneuploidy, Fetal Anomalies, and Adverse Pregnancy Outcomes

- Discussion of risks, benefits and alternatives of the various prenatal diagnosis and screening options, including option of no testing should be undertaken with **all** patients prior to any prenatal screening
- Patients should be offered:
  - No aneuploidy screening
  - Standard prenatal screening based on locally offered paradigms
  - Invasive testing when appropriate indications are present
  - Maternal plasma cell-free DNA screening where available, with the understanding that it my not be provincially funded (II-B)

Link to No. 348-Joint SOGC-CCMG Guidelines

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

NIPT Overview

NIPT analyzes cell-free DNA originating from the placenta, circulating the bloodstream of the pregnant individual

More accurate screen than eFTS/MSS

Can be performed as a first tier test after 9-10 weeks gestation, or subsequent to eFTS/MSS

OHIP-funded or private pay

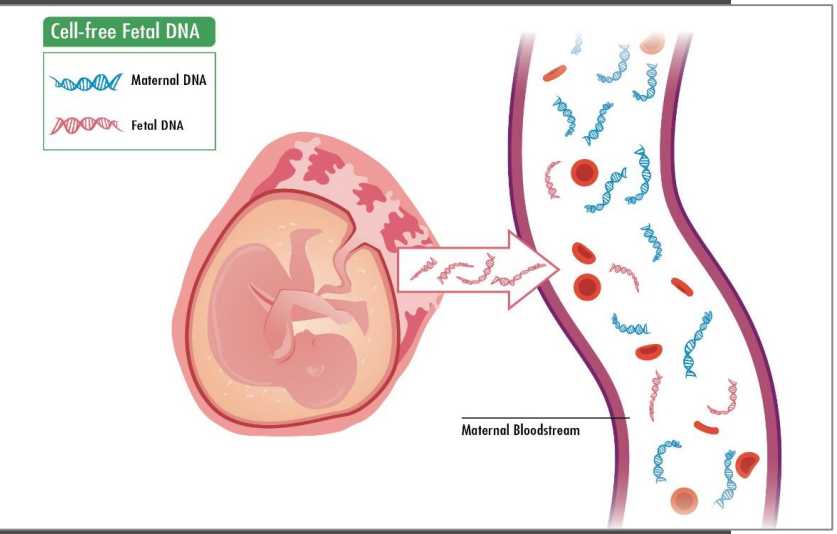


Illustration adapted from Genetic Counseling Aids, 7th Edition, Copyright 2020, permission for use granted by Greenwood Genetic Center

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

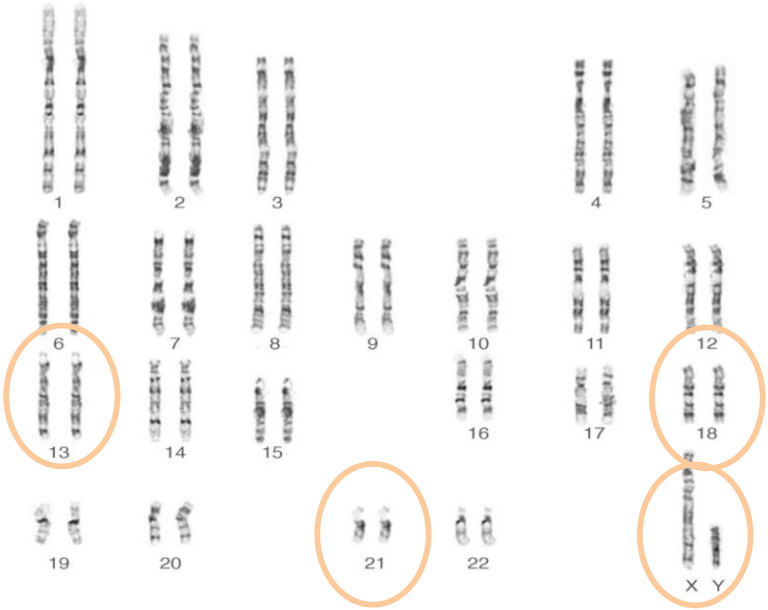


Illustration adapted from Genetic Counseling Aids, 7th Edition, Copyright 2020, permission for use granted by Greenwood Genetic Center

What Does NIPT Screen For?

- Trisomy 21
- Trisomy 18
- Trisomy 13
- Triploidy (LifeLabs)
- +/- Sex Chromosome Differences

Screening for additional chromosome differences (e.g. microdeletion syndromes) is possible BUT this testing is not funded by MOH and not endorsed in Ontario.

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

The mission of AXYS is to help individuals with one or more extra X or Y chromosomes and their families to live fuller and more productive lives.

AXYS serves individuals and families affected by Sex Chromosome Aneuploidy including:

- 47,XXY (Klinefelter syndrome)
- 47,XYY (Jacobs syndrome)
- 47,XXX (Trisomy X)
- 48,XXYY and 48,XXXY

Donate to AXYS

AXYS is a 501c3 organization. It relies on donations to fund our important support, advocacy and education work. Please consider making a tax deductible, online donation to AXYS at

www.genetic.org/donate/

Services Available to the X and Y Variations Community

- Helpline helpline@genetic.org or 888-999-9428
- Online library of publications
- Educational webinars
- Support groups
- The AXYS Clinic and Research Consortium, a network of specialized clinics in the US
- Professional directory
- Research recruitment
- AXYS Family Conference

Visit AXYS at www.genetic.org

P.O. Box 659, Paoli, PA 19301
info@genetic.org

axys

X and Y Chromosome Variations

(Sex chromosome aneuploidy)

What are Sex Chromosome Differences?

- Refers an variation from the typical number of sex chromosomes (e.g. 45,X; 47,XXY; 47,XXX)
- Incidence: 1/500 – 1/1000
- Wide variation in symptoms and severity
- Features include: tall or short stature, infertility, delayed puberty, hypotonia, learning and social difficulties, anxiety and other psychiatric challenges

Link to AXYS patient leaflet

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

NIPT for Sex Chromosome Differences

- The **NIPT performance is lower** for sex chromosome differences than for trisomy 21, 18, 13*.
- If diagnostic testing is desired following a “high risk” NIPT result, amniocentesis is preferred over CVS.
- Can “opt out” through Harmony (Dynacare), but not Panorama (LifeLabs)

Pregnant individuals need to balance the need to know with the risk for unnecessary procedures, unnecessary anxiety, stressful decision-making given the relatively milder presentation.

*No. 348-Joint SOGC-CCMG Guidelines

NIPT Performance

Chromosome Difference	Detection Rate % (95% CI)	False Positive Rate % (95% CI)
Trisomy 21	99.49 (98.71,99.86)	0.07 (0.05,0.10)
Trisomy 18	96.26 (99.44,98.48)	0.03 (0.02,0.05)
Trisomy 13	90.91 (80.05,96.98)	0.04 (0.03,0.07)

Notes:
1. Singleton pregnancies with an EDD of 01-Sep-2016 to 30-Jun-2020 were included in this analysis
2. No-call and missing data screening results were excluded from this analysis
3. Uninterpretable, inconclusive, mosaic and partial cytogenetic results were excluded from this cohort.
4. Outcome data for autosomes screened (chromosomes 21, 18, and 13) were supplemented using birth outcome data for negative results only, where the outcomes for pregnancies with no cytogenetic outcome were set to test-negative when their corresponding birth record had no indication for the disorder during the perinatal period.

Detection rate: Probability that a pregnancy *with* a chromosome difference will get a "high risk" result

False positive rate: Probability that a pregnancy *without* the chromosome difference will get a "high risk" result

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Criteria for OHIP-funded NIPT

Category I criteria – to be ordered by any physician or nurse practitioner for singletons, and temporarily[1] for twin pregnancies

- a positive prenatal screening result from MMS for this pregnancy
- the maternal age / age of oocyte provider will be 40 years or older at the expected date of delivery[2]
- the nuchal translucency (NT) measurement is ≥3.5 mm
- there is a personal history of a previous pregnancy or child with trisomy 21, 18 or 13
- exceptional funding due to COVID-19 pandemic for any twin pregnancy where either
  - NT ultrasound is unavailable OR
  - when the maternal age / age of oocyte provider will be 35 years or older at the expected day of delivery[2]

Category II criteria - must be ordered by a genetics or maternal fetal medicine specialist for singletons and twin pregnancies

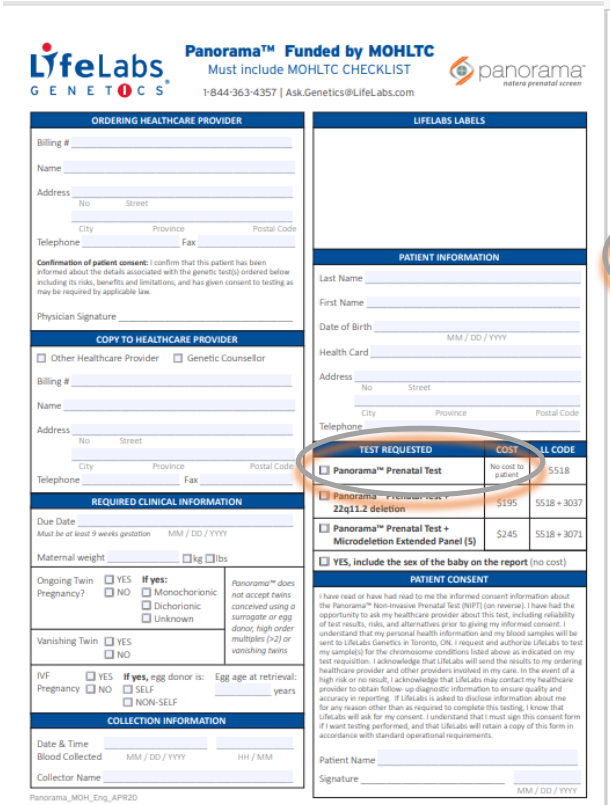
- there are findings on ultrasound which are associated with an increased chance for trisomy 21, trisomy 18 or trisomy 13
- there is chance for a sex-linked genetic condition
- the ultrasound shows findings suggestive of a sex chromosome difference
- the ultrasound shows findings suggestive of a disorder of sex determination

[1] Temporary guidelines came into effect as a response to the COVID-19 pandemic and are applicable until March 31, 2022

[2] In the context of IVF, the maternal age is guided by the age at egg retrieval (whether own egg or donor egg)

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

How to Order OHIP-funded NIPT



LifeLabs GENETICS

Panorama™ Funded by MOHLTC
Must include MOHLTC CHECKLIST
1-844-363-4357 | Ask.Genetics@LifeLabs.com

panorama natera prenatal screen

ORDERING HEALTHCARE PROVIDER

Billing #
Name
Address
No Street
City Province Postal Code
Telephone Fax

Confirmation of patient consent: I confirm that this patient has been informed about the details associated with the genetic test(s) ordered below including its risks, benefits and limitations, and has given consent to testing as may be required by applicable law.

Physician Signature

COPY TO HEALTHCARE PROVIDER

☐ Other Healthcare Provider ☐ Genetic Counsellor

Billing #
Name
Address
No Street
City Province Postal Code
Telephone Fax

REQUIRED CLINICAL INFORMATION

Due Date
Must be at least 9 weeks gestation MM / DD / YYYY
Maternal weight ☐ kg ☐ lbs

Ongoing Twin Pregnancy? ☐ YES ☐ NO
If yes: ☐ Monochorionic ☐ Dichorionic ☐ Unknown

Vanishing Twin ☐ YES ☐ NO

Panorama™ does not accept twins conceived using a surrogate or egg donor, high order multiples (>2) or vanishing twins

IVF Pregnancy ☐ YES ☐ NO
If yes, egg donor is: ☐ SELF ☐ NON-SELF
Egg age at retrieval: ____ years

COLLECTION INFORMATION

Date & Time Blood Collected MM / DD / YYYY HH / MM
Collector Name

LIFELABS LABELS

PATIENT INFORMATION

Last Name
First Name
Date of Birth MM / DD / YYYY
Health Card
Address
No Street
City Province Postal Code
Telephone

TEST REQUESTED	COST	LL CODE
☐ **Panorama™ Prenatal Test**	No cost to patient	5518
☐ Panorama™ Prenatal Test + **22q11.2 deletion**	$195	5518 + 3037
☐ **Panorama™ Prenatal Test + Microdeletion Extended Panel (5)**	$245	5518 + 3071

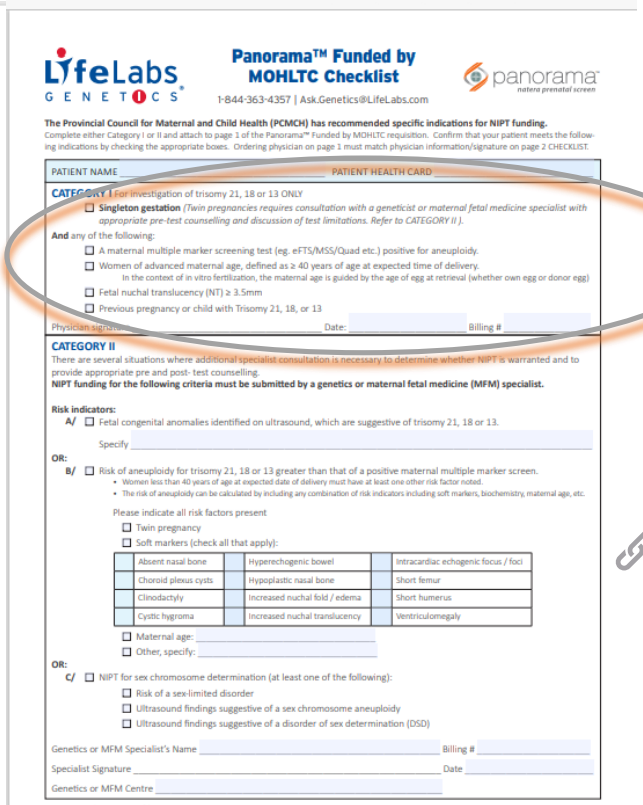
☐ **YES, include the sex of the baby on the report** (no cost)

PATIENT CONSENT

I have read or have had read to me the informed consent information about the Panorama™ Non-Invasive Prenatal Test (NIPT) (on reverse). I have had the opportunity to ask my healthcare provider about this test, including reliability of test results, risks, and alternatives prior to giving my informed consent. I understand that my personal health information and my blood samples will be sent to LifeLabs Genetics in Toronto, ON. I request and authorize LifeLabs to test my sample(s) for the chromosome conditions listed above as indicated on my test requisition. I acknowledge that LifeLabs will send the results to my ordering healthcare provider and other providers involved in my care. In the event of a high risk or no result, I acknowledge that LifeLabs may contact my healthcare provider to obtain follow- up diagnostic information to ensure quality and accuracy in reporting. If LifeLabs is asked to disclose information about me for any reason other than as required to complete this testing, I know that LifeLabs will ask for my consent. I understand that I must sign this consent form if I want testing performed, and that LifeLabs will retain a copy of this form in accordance with standard operational requirements.

Patient Name
Signature MM / DD / YYYY

Panorama_MOH_Eng_APR20



LifeLabs GENETICS

Panorama™ Funded by MOHLTC Checklist
1-844-363-4357 | Ask.Genetics@LifeLabs.com

panorama natera prenatal screen

The Provincial Council for Maternal and Child Health (PCMCH) has recommended specific indications for NIPT funding.
Complete either Category I or II and attach to page 1 of the Panorama™ Funded by MOHLTC requisition. Confirm that your patient meets the following indications by checking the appropriate boxes. Ordering physician on page 1 must match physician information/signature on page 2 CHECKLIST.

PATIENT NAME PATIENT HEALTH CARD

CATEGORY I For investigation of trisomy 21, 18 or 13 ONLY

☐ **Singleton gestation** *(Twin pregnancies requires consultation with a geneticist or maternal fetal medicine specialist with appropriate pre-test counselling and discussion of test limitations. Refer to CATEGORY II).*

And any of the following:

☐ A maternal multiple marker screening test (eg. eFTS/MSS/Quad etc.) positive for aneuploidy.
☐ Women of advanced maternal age, defined as ≥ 40 years of age at expected time of delivery.
In the context of in vitro fertilization, the maternal age is guided by the age of egg at retrieval (whether own egg or donor egg)
☐ Fetal nuchal translucency (NT) ≥ 3.5mm
☐ Previous pregnancy or child with Trisomy 21, 18, or 13

Physician Signature Date: Billing #

CATEGORY II

There are several situations where additional specialist consultation is necessary to determine whether NIPT is warranted and to provide appropriate pre and post- test counselling.
NIPT funding for the following criteria must be submitted by a genetics or maternal fetal medicine (MFM) specialist.

Risk indicators:

A/ ☐ Fetal congenital anomalies identified on ultrasound, which are suggestive of trisomy 21, 18 or 13.
Specify

OR:

B/ ☐ Risk of aneuploidy for trisomy 21, 18 or 13 greater than that of a positive maternal multiple marker screen.
- Women less than 40 years of age at expected date of delivery must have at least one other risk factor noted.
- The risk of aneuploidy can be calculated by including any combination of risk indicators including soft markers, biochemistry, maternal age, etc.

Please indicate all risk factors present

☐ Twin pregnancy
☐ Soft markers (check all that apply):

☐	Absent nasal bone	☐	Hyperechogenic bowel	☐	Intracardiac echogenic focus / foci
☐	Choroid plexus cysts	☐	Hypoplastic nasal bone	☐	Short femur
☐	Clinodactyly	☐	Increased nuchal fold / edema	☐	Short humerus
☐	Cystic hygroma	☐	Increased nuchal translucency	☐	Ventriculomegaly

☐ Maternal age:
☐ Other, specify:

OR:

C/ ☐ NIPT for sex chromosome determination (at least one of the following):

☐ Risk of a sex-limited disorder
☐ Ultrasound findings suggestive of a sex chromosome aneuploidy
☐ Ultrasound findings suggestive of a disorder of sex determination (DSD)

Genetics or MFM Specialist's Name Billing #
Specialist Signature Date
Genetics or MFM Centre

Panorama_MOH_Eng_APR20

Link to NIPT Requisitions for OHIP-funded NIPT (Dynacare and LifeLabs)

PRENATAL SCREENING DÉPISTAGE PRÉNATAL ONTARIO

How to Order NIPT – Step by Step

STEP 1
Discussion with Patient

Provide information, **and** explore patient values and attitudes

STEP 2
Provide Requisition

NIPT is available through Dynacare or LifeLabs. Ensure the appropriate requisition is used (private pay versus OHIP-funded).

STEP 3
Blood Draw

SOGC guidelines recommend blood draw >10 weeks*

STEP 4
Results

7-10 business days. Results are reported as high risk or low risk. Rarely, NIPT can fail.

*Link to No. 348-Joint SOGC-CCMG Guidelines

Dynacare (“Harmony”) $495
LifeLabs (“Panorama”) $550

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Misleading Use of Statistics

ABORTION, FERTILITY AND TECHNOLOGY

A FALSE SENSE OF SECURITY: FALSE POSITIVES FROM PRENATAL TESTING LEAD TO ABORTIONS OF HEALTHY BABIES

FEBRUARY 21, 2015 ALEXANDRA CHRETIEN 5 COMMENTS

BBC Sign in Home News Sport Reel Worklife

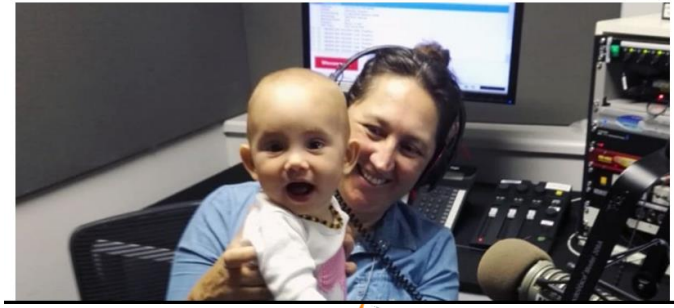
NEWS

Home | Coronavirus | Video | World | US & Canada | UK | Business | Tech | Science | Stories | Entertainment

Stories

'I nearly aborted my baby because of an unreliable test'

8 February 2019



PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

“High Risk” Result

How likely is it that the baby has the condition = Positive Predictive Value?

Chromosome Difference	Detection Rate % (95% CI)	False Positive Rate % (95% CI)	Positive Predictive Value % (95% CI)	Negative Predictive Value % (95% CI)
Trisomy 21	99.49 (98.71,99.86)	0.07 (0.05,0.10)	95.50 (93.86,96.82)	99.99 (99.98,100.00)
Trisomy 18	96.26 (99.44,98.48)	0.03 (0.02,0.05)	92.31 (87.63,95.63)	99.99 (99.97,99.99)
Trisomy 13	90.91 (80.05,96.98)	0.04 (0.03,0.07)	S	99.99 (99.98,100.00)

Notes:

1. Singleton pregnancies with an EDD of 01-Sep-2016 to 30-Jun-2020 were included in this analysis
2. No-call and missing data screening results were excluded from this analysis
3. Uninterpretable, inconclusive, mosaic and partial cytogenetic results were excluded from this cohort.
4. Outcome data for autosomes screened (chromosomes 21, 18, and 13) were supplemented using birth outcome data for negative results only, where the outcomes for pregnancies with no cytogenetic outcome were set to test-negative when their corresponding birth record had no indication for the disorder during the perinatal period.
5. S = data supressed due to a confidence interval >20%

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

“Low Risk” Result

How likely is it that the baby does not have the condition = Negative Predictive Value?

Chromosome Difference	Detection Rate % (95% CI)	False Positive Rate % (95% CI)	Positive Predictive Value % (95% CI)	Negative Predictive Value % (95% CI)
Trisomy 21	99.49 (98.71,99.86)	0.07 (0.05,0.10)	95.50 (93.86,96.82)	99.99 (99.98,100.00)
Trisomy 18	96.26 (99.44,98.48)	0.03 (0.02,0.05)	92.31 (87.63,95.63)	99.99 (99.97,99.99)
Trisomy 13	90.91 (80.05,96.98)	0.04 (0.03,0.07)	S	99.99 (99.98,100.00)

Notes:

1. Singleton pregnancies with an EDD of 01-Sep-2016 to 30-Jun-2020 were included in this analysis
2. No-call and missing data screening results were excluded from this analysis
3. Uninterpretable, inconclusive, mosaic and partial cytogenetic results were excluded from this cohort.
4. Outcome data for autosomes screened (chromosomes 21, 18, and 13) were supplemented using birth outcome data for negative results only, where the outcomes for pregnancies with no cytogenetic outcome were set to test-negative when their corresponding birth record had no indication for the disorder during the perinatal period.

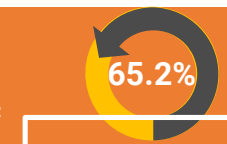
"High Risk" Result

WHAT DOES IT MEAN?

There is a significant chance the baby has the condition

NEXT STEPS

Offer referral for genetic counselling. Options include invasive diagnostic testing and ultrasounds



65.2% of Ontario pregnancies with a "high risk" NIPT result for trisomy 21 had follow up PND*

Link to genetics clinics in ON.

PND = prenatal diagnosis

"Low Risk" Result

WHAT DOES IT MEAN?

The chance that a low risk result for trisomy 21, trisomy 18 or trisomy 13 is a true result is generally >99.9%

NEXT STEPS

Routine care if no other pregnancy concerns

*Dougan, S et al (2021): DOI: https://doi.org/10.1503/cmaj.202456

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

No NIPT Result

WHAT DOES IT MEAN?

Causes range from technical issues to maternal (e.g. high BMI) and fetal/placental factors (e.g. twin pregnancy, IVF pregnancy, early GA, chromosome difference in placenta and/or fetus)

NEXT STEPS

Options include repeat NIPT blood draw, alternative screening testing (eFTS/MSS), detailed anatomy ultrasound, referral for genetic counselling

2.2% of pregnancies that underwent OHIP-funded NIPT had a “no call” result (including multiple attempts)*

*Dougan, S et al (2021): DOI: https://doi.org/10.1503/cmaj.202456

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Multiple Gestation Pregnancy

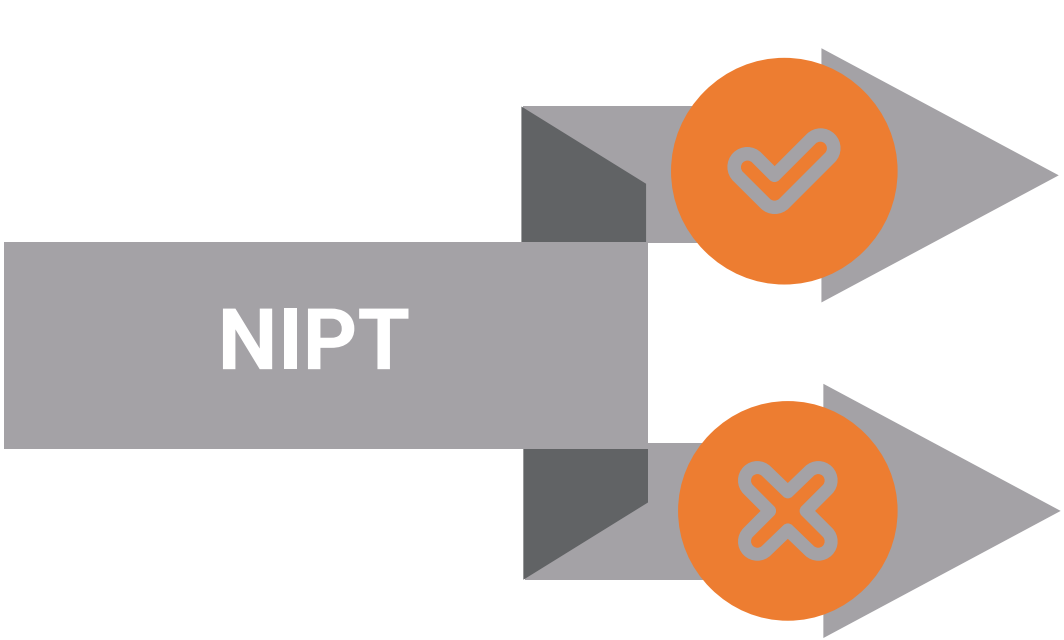
	NT Only	eFTS	MSS	NIPT
Twins	X	X		X
Higher Order Multiples[1] (e.g. triplets, quadruplets)	X			
"Vanishing" twin	X		X 8 weeks post demise[2]	

[1]In higher order multiples, screening is limited to NT in combination with maternal (or donor egg) age

[2]"Vanishing" twin scenario**: NT + MSS if available**. It is recommended that the bloodwork be drawn at least 8 weeks post-demise

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Screening after First-Tier NIPT



NT ULTRASOUND

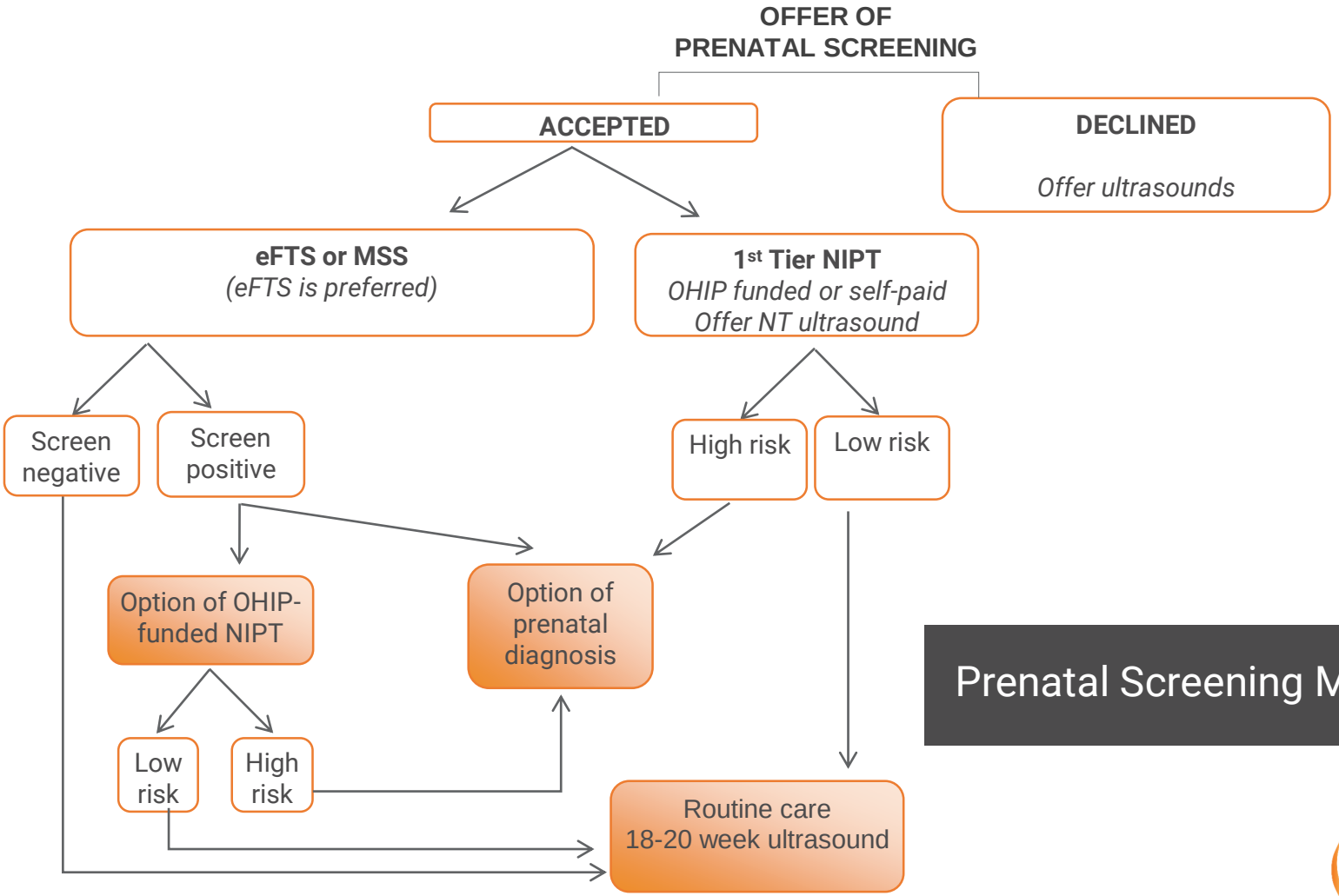
An increased NT has been associated with: normal variation, chromosome differences, single gene disorders, structural abnormalities

eFTS or MSS

- A positive screen after a low risk NIPT can cause anxiety
- Universal screening for adverse pregnancy outcomes using maternal serum markers is not recommended[1]

[1]No. 348-Joint SOGC-CCMG Guidelines

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO



Prenatal Screening Model

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Prenatal Screening Model

OFFER OF PRENATAL SCREENING

ACCEPTED

DECLINED

Offer ultrasounds

eFTS or MSS
(eFTS is preferred)

1st Tier NIPT
OHIP funded or self-paid
Offer NT ultrasound

Screen negative

Screen positive

High risk

Low risk

Option of OHIP-funded NIPT

Option of prenatal diagnosis

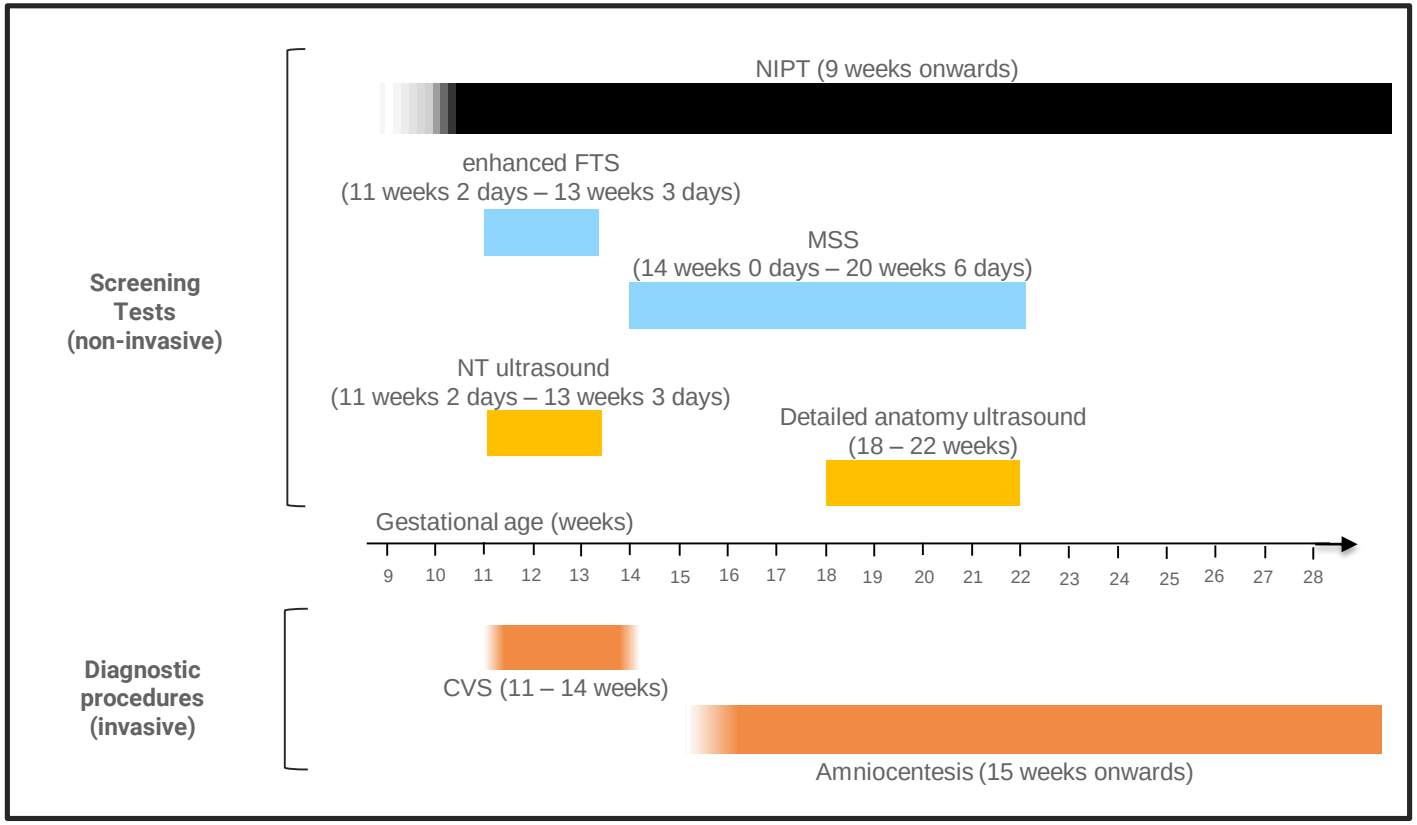
Low risk

High risk

Routine care
18-20 week ultrasound

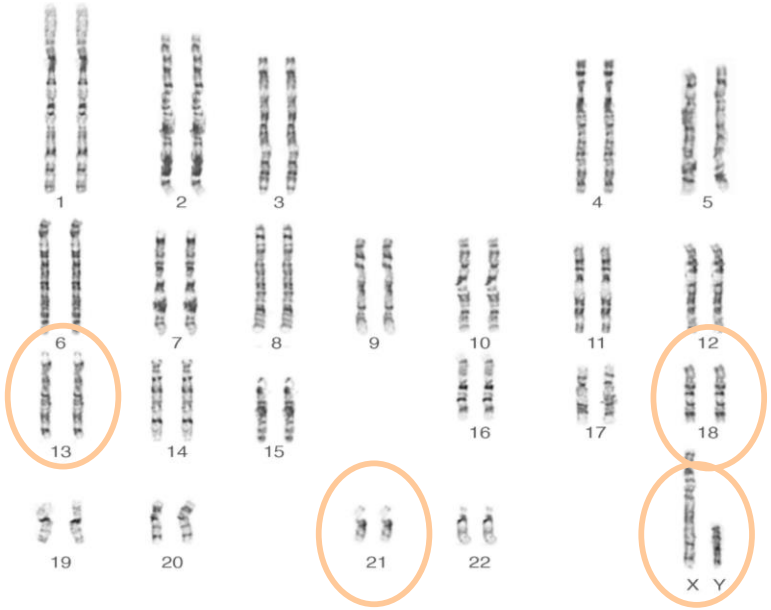
PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

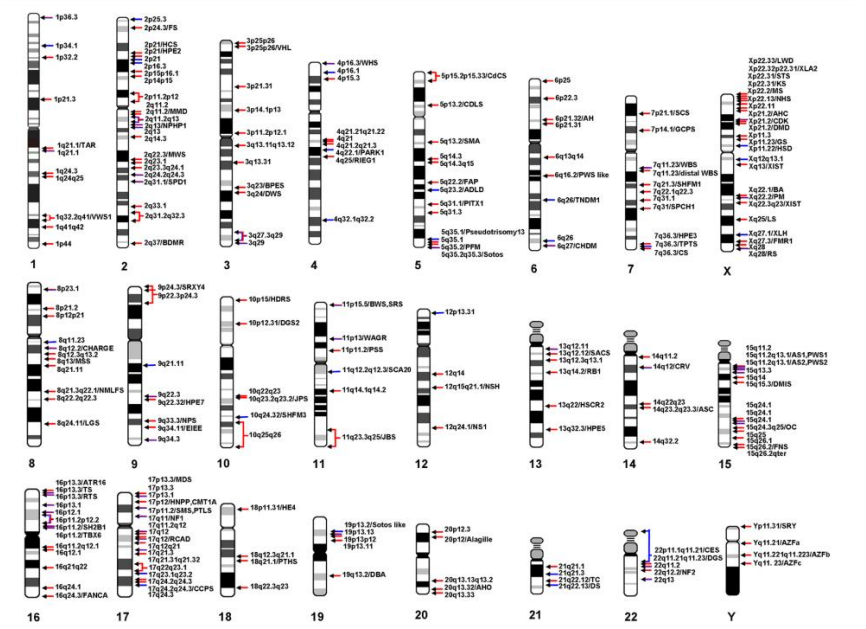
Prenatal Testing Timeline



An adapted pdf version of this slide is available on PSO website: www.prenatalscreeningontario.ca. There is some variability in gestational age requirements for testing.

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO





NIPT

Trisomies 21, 18, 13 +/- sex chromosome differences (7-10 business days)

Prenatal Diagnosis

1. Rapid test: trisomies 21,18,13, sex chromosome differences (2-4 business days)
2. Microarray analysis (2-3 wks)[1]
3. Single gene testing if indicated

[1]may only be available for certain indications at some centres

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

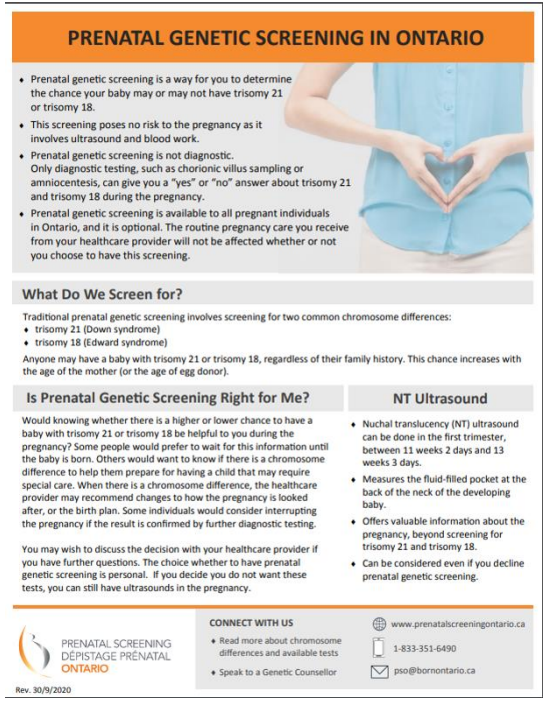
NIPT versus Prenatal Diagnosis

	NIPT	INVASIVE DIAGNOSTIC TESTING
BENEFITS	• Non-invasive • Can be done earlier	• Diagnostic • Can be more comprehensive
LIMITATIONS	• Screen • Does not screen for all chromosome differences • Fails in a small percentage of pregnancies • Cannot be done for vanishing twins, higher order multiples	• Risk of pregnancy loss CVS 1/455 (0.22%); Amnio 1/909 (0.11%)[1] • CVS: small chance for confined placental mosaicism • Has to be organized through genetics/MFM • Can get inconclusive result / variant of unknown significance

[1]Akolekar et al (2015) – meta-analysis

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Resources



PRENATAL GENETIC SCREENING IN ONTARIO

- Prenatal genetic screening is a way for you to determine the chance your baby may or may not have trisomy 21 or trisomy 18.
- This screening poses no risk to the pregnancy as it involves ultrasound and blood work.
- Prenatal genetic screening is not diagnostic. Only diagnostic testing, such as chorionic villus sampling or amniocentesis, can give you a "yes" or "no" answer about trisomy 21 and trisomy 18 during the pregnancy.
- Prenatal genetic screening is available to all pregnant individuals in Ontario, and it is optional. The routine pregnancy care you receive from your healthcare provider will not be affected whether or not you choose to have this screening.

What Do We Screen for?

Traditional prenatal genetic screening involves screening for two common chromosome differences:
- trisomy 21 (Down syndrome)
- trisomy 18 (Edward syndrome)

Anyone may have a baby with trisomy 21 or trisomy 18, regardless of their family history. This chance increases with the age of the mother (or the age of egg donor).

Is Prenatal Genetic Screening Right for Me?

Would knowing whether there is a higher or lower chance to have a baby with trisomy 21 or trisomy 18 be helpful to you during the pregnancy? Some people would prefer to wait for this information until the baby is born. Others would want to know if there is a chromosome difference to help them prepare for having a child that may require special care. When there is a chromosome difference, the healthcare provider may recommend changes to how the pregnancy is looked after, or the birth plan. Some individuals would consider interrupting the pregnancy if the result is confirmed by further diagnostic testing.

You may wish to discuss the decision with your healthcare provider if you have further questions. The choice whether to have prenatal genetic screening is personal. If you decide you do not want these tests, you can still have ultrasounds in the pregnancy.

NT Ultrasound

- Nuchal translucency (NT) ultrasound can be done in the first trimester, between 11 weeks 2 days and 13 weeks 3 days.
- Measures the fluid-filled pocket at the back of the neck of the developing baby.
- Offers valuable information about the pregnancy, beyond screening for trisomy 21 and trisomy 18.
- Can be considered even if you decline prenatal genetic screening.

PRENATAL SCREENING DÉPISTAGE PRÉNATAL ONTARIO

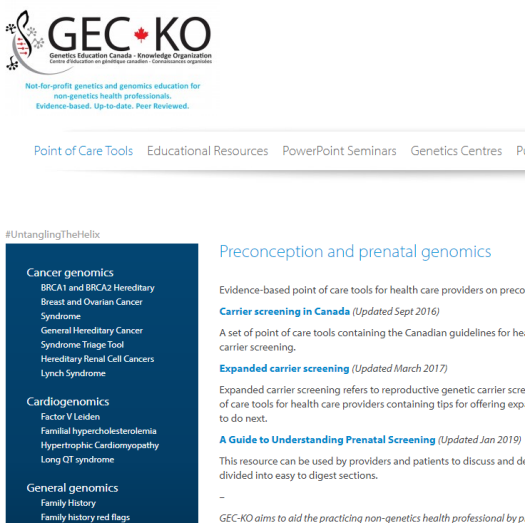
CONNECT WITH US
- Read more about chromosome differences and available tests
- Speak to a Genetic Counsellor

www.prenatalscreeningontario.ca
1-833-351-6490
pso@bornontario.ca

Rev. 30/9/2020

🔗 Link to prenatal screening leaflet

www.prenatalscreeningontario.ca



GEC-KO
Genetics Education Canada - Knowledge Organization
Centre d'éducation en génétique canadien - Connaissances organisées

Not-for-profit genetics and genomics education for non-genetics health professionals.
Evidence-based. Up-to-date. Peer Reviewed.

Point of Care Tools | Educational Resources | PowerPoint Seminars | Genetics Centres | P

#UntanglingTheHelix

Cancer genomics
- BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer Syndrome
- General Hereditary Cancer Syndrome Triage Tool
- Hereditary Renal Cell Cancers
- Lynch Syndrome

Cardiogenomics
- Factor V Leiden
- Familial hypercholesterolemia
- Hypertrophic Cardiomyopathy
- Long QT syndrome

General genomics
- Family History
- Family history red flags

Preconception and prenatal genomics

Evidence-based point of care tools for health care providers on preco

Carrier screening in Canada *(Updated Sept 2016)*

A set of point of care tools containing the Canadian guidelines for he carrier screening.

Expanded carrier screening *(Updated March 2017)*

Expanded carrier screening refers to reproductive genetic carrier scre of care tools for health care providers containing tips for offering exp to do next.

A Guide to Understanding Prenatal Screening *(Updated Jan 2019)*

This resource can be used by providers and patients to discuss and d divided into easy to digest sections.

–

GEC-KO aims to aid the practicing non-genetics health professional by p

www.geneticseducation.ca

OMama

About Us Feedback Glossary

Pre-Pregnancy | Early Pregnancy | Mid Pregnancy | Late Pregnancy | Lal

Trusted information, when and where you need it

BORNOntario - RT @DrMWalkerMD: Amazing report on the utility of Whole Exome Sequencing in

www.omama.com

Website and App

PRENATAL SCREENING DÉPISTAGE PRÉNATAL ONTARIO

Connect With Us

www.PrenatalScreeningOntario.ca

PSO@BORNontario.ca

Toll free: 1-933-351-6490
613-737-2281

Follow us on Twitter: @OntarioPSO

PSO has on-call genetic counsellors to answer questions about prenatal screening

Mon - Fri / 9 am - 3 pm

PRENATAL SCREENING
DÉPISTAGE PRÉNATAL
ONTARIO

Q&A

Q1. Is the timing (gestational age) for prenatal genetic screening based on the ultrasound date or last menstrual period?
Answer: The timing of the enhanced First Trimester Screening is based on ultrasound measurements. Specifically, the timing of the NT ultrasound has to occur when the CRL is between 45 and 84 mm. Regarding Maternal Serum Screening (MSS), ultrasound is not required (LMP can be used) but a dating ultrasound is recommended to improve the accuracy of the screening result (the hormone levels measured through MSS vary based on gestational age).

Q2. Are your patient handouts/resources available in French?
Answer: At the moment, our leaflets are only available in English. We are in the process of having some of our main leaflets translated into French.

Q&A

Q3. What is the added value of NT with NIPT if they are going to have a complete morphology scan in a couple of weeks?
Answer: An increased NT measurement (3.5 mm or higher) is not only associated with an increased risk for structural defects that may be picked up through a detailed anatomy scan, but it is also associated with an increased chance for chromosome differences (microdeletions/microduplications) and other genetic conditions (e.g. Noonan syndrome) that are not covered by NIPT. A key point is that not all babies with one of these other genetic conditions have findings on a prenatal ultrasound. An increased NT measurement prompts the offer of diagnostic testing (CVS/amniocentesis) to look for those microdeletions/microdeletions, as well as Noonan syndrome testing.

In addition, an increased NT measurement would prompt many genetics/MFM centers to offer an early anatomy ultrasound (prior to the standard 18-20 weeks ultrasound). If there was a structural abnormality present, an early ultrasound would provide the opportunity for this information to be known sooner in pregnancy.

Lastly, an increased NT measurement would often prompt a referral for a fetal echocardiogram which may detect cardiac abnormalities that are missed through regular imaging.

Q&A

Q4. Which NIPT do you recommend – Harmony or Panorama?
Answer: There are some benefits and limitations to each one. For instance, with Harmony, patients can choose not to screen for sex chromosome differences. With Panorama, that option does not exist – sex chromosome differences are automatically included along with the screening for trisomy 21, trisomy 18 and trisomy 13. On the other hand, Panorama offers zygosity testing for twin pregnancies which may help with pregnancy management. See below for a full comparison chart.

Factors	Harmony™ by Ariosa	Panorama™ by Natera
Where is the blood drawn for this test?	Dynacare	LifeLabs Genetics
Cost (if self-pay)	$495	$550
How early can blood be drawn?	10 weeks gestation	9 weeks gestation
Twins	Yes	Yes – zygosity testing available
Higher order multiples	No	No
In-Vitro Fertilization (IVF)	Yes	Yes
IVF with donor egg (not self)	Yes	Yes – only singletons
Surrogate	Yes	Yes – only singletons
Triploidy	No	Yes
Vanishing twin	No	No
Sex chromosome aneuploidy (singletons only)	Opt-in for: monosomy X, sex chromosome aneuploidy	Screening for sex chromosome aneuploidy is standard – cannot opt out

Q&A

Q5. Any talk of NIPT becoming the gold standard for genetic testing and OHIP funded (like eFTS is now)?
Answer: Offering NIPT to all pregnant individuals as a primary screening method is not fiscally feasible in most provinces currently, including Ontario.

Q6. Will midwives be able to order NIPT in the future?
Answer: PSO is in full support of that, and we are in the process of making a written recommendation to MOH to extend the provision of cfDNA screening to registered midwives. In the end, the decision lies with the MOH in terms of making the required legislative change.

Q7. Can you comment or give us some insight into some of the less expensive prenatal testing that is being promoted?
Answer: OHIP-funded NIPT can only be ordered through LifeLabs and Dynacare. With regards to the private pay options, there is an increasing number of additional commercial laboratories that provide this type of screening outside of Canada at different price points. We are not able to endorse one company over another. On our website, we are suggesting factors for patients and providers to take into account as they consider the private-pay NIPT route: https://prenatalscreeningontario.ca/en/pso/about-prenatal-screening/non-invasive-prenatal-testing.aspx. We can appreciate cost is a large consideration for patients, and we are encouraging patients to have a discussion with their provider to help them choose the best test for them.

Q&A

Q8. I struggle to explain a positive eFTS result to a patient and what exactly it means. Should I discuss the exact number? What is the chance the baby is normal with a positive result?
Answer: It may help to start by explaining that the threshold for this screen is 1 in 350 and anyone who gets a risk figure higher than this is screen positive. However, most babies who screen positive do not actually end up having a baby with Down syndrome or trisomy 18.

And yes, you can discuss the exact number on the report, irrespective whether it is a screen positive or screen negative result. A result of 1 in 300, for instance, can be explained as a 0.3% chance that the baby has Down syndrome, and a 99.7% chance that the baby does not have Down syndrome. Or, out of 300 pregnant people who get this result, 1 will have a baby with Down syndrome and the other 299 will not.

If it is a screen positive result, the options include: no further screening, NIPT (which is a more accurate form of screening) and diagnostic testing.