# Soft markers: Guidance for publicly funded Non-invasive Prenatal Testing (NIPT) eligibility

## What is the purpose of this guide?

This guide is tailored for prenatal care practitioners and describes common etiologies for two categories of soft markers **associated with trisomy 21** (Down syndrome): those with a moderate association and those with a low association. The focus is on clarifying eligibility criteria for publicly funded NIPT.

## What are soft markers?

Soft markers are findings identified at the 18-22 week (detailed anatomy) prenatal ultrasound that do not represent structural abnormalities and may be normal variants. However, they are associated with an increased chance for chromosome differences, particularly trisomy 21, and other conditions.

## Soft markers that individually have a MODERATE association with trisomy 21

| | Hypoplastic or absent nasal bone | Increased nuchal fold* (6mm or more) |
|---|---|---|
| ***Etiology*** | • normal variant<br>• trisomy 21 | |
| ***Next Steps*** | **Refer to your local Genetics/MFM centre** to discuss testing options. The presence of either soft marker meets eligibility criteria for **publicly funded NIPT**. | |

*Increased nuchal fold and enlarged nuchal translucency (NT) are two distinct markers. The NT is measured in the first trimester of pregnancy.

## Soft markers that individually have a LOW association with trisomy 21

| | Intracardiac echogenic focus/foci (IECF) | Clinodactyly | Pyelectasis | Hyperechogenic bowel | Aberrant right subclavian artery | Short femur or short humerus | Ventriculomegaly |
|---|---|---|---|---|---|---|---|
| ***Etiology*** | • normal variant<br>• trisomy 21 | • normal variant<br>• trisomy 21<br>• other genetic condition | • normal variant<br>• trisomy 21<br>• renal or urinary tract pathology | • normal variant<br>• trisomy 21<br>• other chromosome differences<br>• cystic fibrosis<br>• fetal infection<br>• gastrointestinal malformation | • normal variant<br>• trisomy 21<br>• other chromosome differences<br>• cardiac abnormalities | • normal variant<br>• trisomy 21<br>• other genetic conditions, including skeletal dysplasias<br>• fetal growth restriction | • normal variant<br>• trisomy 21<br>• central nervous system malformations<br>• fetal infection<br>• other |

***Next Steps***

### Isolated Soft Marker

The presence of an isolated soft marker from the above list **does not meet the eligibility criteria for publicly funded NIPT**. However, with the exception of intracardiac echogenic foci, each marker is associated with an increased chance of conditions other than trisomy 21, and a referral to a Genetics/MFM centre for further evaluation may still be warranted. **Consult your local Genetics/MFM centre for guidance**. For isolated intracardiac echogenic foci, no further testing is indicated if previous screening (e.g. eFTS, NIPT) has shown a low chance for trisomy 21.

### Multiple Soft Markers

If two or more of these soft markers from the list above are seen, a **referral to your local Genetics/MFM centre is recommended** to discuss testing options. The presence of any two of these markers **meets the eligibility criteria for publicly funded NIPT**.

### What About Choroid Plexus Cysts (CPCs)?

Isolated choroid plexus cysts (CPCs) are not malformations and are considered normal variants of brain development. In isolation, CPCs do not meaningfully increase the risk for trisomy 18 above the background age-related risk, and therefore their presence does not meet the eligibility criteria for publicly funded NIPT.


**References**

1. Audibert et al. No. 456 - SOGC Clinical Guideline. *J Obstet Gynaecol Can* 2024; 102694.
2. Audibert et al. No. 348-Joint SOGC-CCMG Guideline. *J Obset Gynaecol Can* 2017;39(9):805-817.
3. Audibert et al. Correction - No. 348-Joint SOGC-CCMG Guideline. *J Obset Gynaecol Can* 2018;40(8):1109.
4. Society for Maternal-Fetal Medicine et al. Society for Maternal-Fetal Medicine Consult Series #57: Evaluation and management of isolated soft ultrasound markers for aneuploidy in the second trimester. Society for Maternal Fetal Medicine 2021.


**Acronyms**

- eFTS = enhanced First Trimester Screening
- NIPT = non-invasive prenatal testing
- STS = Second Trimester Screening (previously known as Maternal Serum Screening)