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# First Trimester Screening

## Updates on Prenatal Screening

Prenatal screening programs have traditionally been focused on the common autosomal aneuploidies (Trisomy 21, 13 and 18). This is because they are major causes of perinatal morbidity and mortality and are amenable to prenatal diagnostic tests such as CVS or amniocentesis. With advancing technology, prenatal screening has evolved over the last decade. In broad terms, one can divide prenatal screening into chromosomal, genetic, structural and preterm pre-eclampsia.

**Prenatal screening can be categorised into the following groups;**

1. **Fetal chromosome abnormalities**
   a. combined first trimester screening
   b. cell-free DNA (cfDNA/NIPT)
2. **Early structural scan**
3. **Preterm Pre-eclampsia screening**
4. **Reproductive Carrier Screening (+pre-conception)**

## Fetal Chromosome Abnormalities

### Combined first trimester screening

**What does it involve?**

- Maternal age, ultrasound measurement of fetal nuchal translucency and presence of nasal bone, maternal serum markers (PAPPA-A, BHCG)

**When can it be performed?**

- 11 to 13+6 weeks of gestation
- Crown rump length – 45 to 84mm

**Test characteristics for Trisomy 21**

- Sensitivity 85%
- Specificity 95%
- Positive predictive value 7-10%

**Can it provide additional information?**

- Detection of structural abnormalities (similar to early structural scan)
- PAPP-A – <0.4 MoM – associated with low birth weight, preterm birth
- BHCG - <0.2 MoM or >5 MoM – associated with adverse maternal and fetal outcomes and atypical chromosomes
- Chorionicity of multiple pregnancies, pre-eclampsia screening

**Cost - $200 to $400**

### Cell-free DNA/NIPT

**What does it involve?**

- Uses DNA sequencing or array based technology to detect aneuploidy in placental tissues by measuring cfDNA in maternal plasma

**When can it be performed?**

- After 10 weeks of gestation

**Test characteristics for Trisomy 21**

- Sensitivity 99%
- Specificity 99%
- Positive predictive value 45%

**Can it provide additional information?**

- Fetal sex, sex chromosome aneuploidy – less accurate compared with T21, T13, T18
- 22q11.2 deletion, other microdeletion syndromes, genome-wide chromosomes abnormalities – limited clinical performance data compared with T21

**Cost - $400 to $1000**

## Early Structural Scan

**What does it involve?**

- Ultrasound of the fetal head, chest, abdomen and four limbs
- Often performed in conjunction with NIPT

**When can it be performed?**

- After 11 weeks, usually between 11 to 14 weeks

**What can it detect?**

- Detection rate
  - Major structural conditions 40-50%
  - Lethal conditions 75%
- Anencephaly, alobar holoprosencephaly, abdominal wall defects, univentricular heart, megacystitis, body stalk anomalies

**Can it provide additional information?**

- Chorionicity of multiple pregnancies, pre-eclampsia screening

**Cost - $300 to $500**

Sensitivity – the proportion of people with the target condition who test positive
Specificity – the proportion of people without the target condition who test negative
Positive predictive value – the proportion of those with a positive index who have (or will go on to develop) the target condition

## Preterm Pre-eclampsia screening

- RANZCOG recommends offering routine screening in early pregnancy for preterm preclampsia to all women

### What does it involve?

- Clinical history, blood pressure (MAP), ultrasound with mean artery pulsatility index (UtPI) and maternal serum biochemical markers (PAPP-A and PIGF)

### When can it be performed?

- 11 to 14 weeks

### What can it detect, what to do and why?

- Risk cut off of 1:100 i.e. >1:100 = increased risk
- For women at increased risk of preeclampsia, low dose Aspirin (at least 100mg) to start before 16 weeks (Number needed to treat 27)
- Preterm pre-eclampsia may result in substantial morbidity for both mother and neonate thus early identification is important to reduce the burden of pre-eclampsia

### Can it provide additional information?

- Risk of small for gestational age fetus

**Cost – performed at the same time with cFTS or early structural scan. Cost of bloods around $50.**

## Reproductive Carrier Screening

### What does it involve?

- Maternal blood test

### When can it be performed?

- Pre-conception, first trimester

### What can it detect, what to do and why?

- Screening for common inherited conditions i.e. cystic fibrosis, fragile X syndrome and spinal muscular atrophy

**Cost – Medicare**

**(Note that there is expanded genetic carrier screening which tests for 1000 recessive and X-linked genes. This is not covered by Medicare.**

| | Number of people who are carriers | Number of people with the condition |
|---|---|---|
| **Cystic Fibrosis** | 1 in 25 | 1 in 2,500 |
| **Fragile X Syndrome** | 1 in 250 | 1 in 4000 |
| **Spinal Muscular Atrophy** | 1 in 40 | 1 in 6000 – 1 in 10,000 |

It is essential to acknowledge that not every patient will want to undergo prenatal testing. It is also important to recognise that the tests are not mutually exclusive for example preterm pre-eclampsia screening can be performed at the same as time as cFTS or early structural scan.

### References


1. RANZCOG. Prenatal screening for fetal genetic or structural conditions. July 2019.
2. RANZCOG. Prenatal screening and diagnostic testing for fetal chromosomal and genetic conditions. July 2018.
3. RANZCOG. Prenatal assessment of fetal structural conditions. March 2018.
4. RANZCOG. Early pregnancy screening and prevention of preterm preeclampsia and related complications. April 2024.


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