Murdoch Childrens Research Institute

# Your choice

## Prenatal screening tests in pregnancy

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# Introduction

This booklet is designed to help you to make decisions about prenatal screening for conditions such as Down syndrome.

This booklet will be useful to you if:

- you want to learn more about prenatal screening
- you are undecided whether or not to have screening or
- you are unsure about which test to have.

Underlined words are explained in the Glossary on page 34 and there is a Quick Summary table of screening options on page 37.

This booklet is designed to be used alongside the interactive Screening Choices web tool (see page 19). This tool will help you consider your prenatal screening options.

# Why has prenatal screening been offered to me?

Prenatal screening is offered to all pregnant women because of the small chance that a pregnancy has a chromosome condition or other physical condition. Together, these fetal conditions can sometimes be referred to as fetal abnormalities or anomalies.

While most women will have healthy babies, in about 1 in 25 pregnancies (about 4%) a baby will be born with a condition that may require medical attention. These conditions vary a lot, from very mild to very severe, and can affect physical and/or intellectual development.

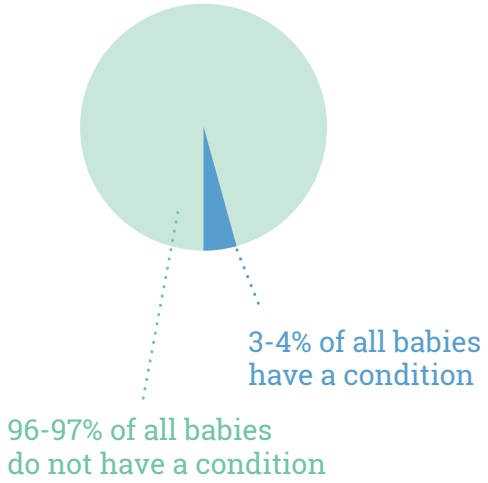



**Figure 1:** Most babies are born healthy.

Prenatal screening tests are used to identify those pregnancies with a higher chance of being affected by such conditions. No single test checks for all fetal conditions.

You can decide to have screening:

- because you want to know more about your pregnancy
- to prepare yourself for a baby with a condition
- so you have the option of terminating an affected pregnancy.

There are different types of tests available and they vary in how accurate they are, when they are performed and what information they give.

*All prenatal screening is your choice. You can decide not to have any prenatal screening.*

# What fetal conditions are tested for in pregnancy?

Prenatal screening tests look for chromosome conditions, such as Down syndrome. Some tests also look for physical conditions, such as spina bifida. It is not possible to test for all fetal conditions during pregnancy.

Knowing something about these fetal conditions can help you make a choice about whether to have prenatal screening.

*It is important to remember that most babies born will be healthy.*

## Chromosome conditions

For healthy development, humans need 46 chromosomes, or 23 pairs. Any extra or missing chromosomes, or any change in the structure or arrangement of the chromosomes, can affect normal development.

The chance of giving birth to a baby with a chromosome condition decreases as the pregnancy develops. This is because many pregnancies affected by chromosome conditions will miscarry naturally. It is not possible to predict which pregnancies will miscarry.

### Down syndrome (trisomy 21)

Down syndrome is the most common chromosome condition found during pregnancy. On average it affects 1 in every 400 pregnancies and is caused by an extra copy of chromosome 21.

The chance of giving birth to a baby with Down syndrome increases with a woman's age, but pregnancies of younger women can also be affected (Figure 2).

People with Down syndrome have characteristic physical, medical and intellectual features. Most have some degree of intellectual disability, yet are able to participate in school, work and social life.

Some can be severely intellectually disabled and require full time care. Babies with Down syndrome are also more likely to have problems with their heart and digestive system. It is not possible to predict the level of disability during pregnancy.

There is no cure for Down syndrome but early intervention, such as individualised educational programs, can support development.

For information see Down Syndrome Australia: http://www.downsyndrome.org.au

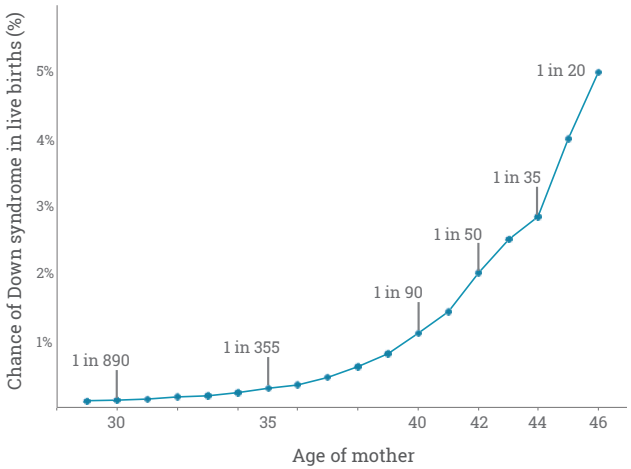



**Figure 2:** Chance of giving birth to a baby with Down syndrome by age of mother.

### Edwards syndrome (trisomy 18) & Patau syndrome (trisomy 13)

Edwards syndrome occurs approximately 1 in every 1600 pregnancies and is caused by an extra copy of chromosome 18.

Patau syndrome occurs approximately 1 in every 3400 pregnancies and is caused by an extra copy of chromosome 13.

Pregnancies affected by these conditions show many physical problems. Infants born with Edwards or Patau syndrome have severe physical and intellectual disability and survival beyond one year of age is rare.

As with Down syndrome, the chance of having a pregnancy affected by Edwards or Patau syndrome increases with a woman's age but pregnancies of younger women can also be affected.

### Sex chromosome conditions

One pair of our 46 chromosomes are called the sex chromosomes. Females usually have two X sex chromosomes (XX) and males have one X and one Y sex chromosome (XY).

Sex chromosome conditions occur when there is a missing X chromosome, an extra copy of the X chromosome or an extra copy of the Y chromosome.

Examples include:
Turner syndrome (also called monosomy X or 45,X); Klinefelter syndrome (47,XXY); triple X (47,XXX) and Jacob syndrome (47,XYY).

These conditions affect individuals in a variety of ways. Many have a normal quality of life and often remain undiagnosed in the general population.

Women of any age can have a pregnancy affected by a sex chromosome condition.

## Physical conditions

Some physical conditions can be detected by ultrasound. Women often have a 1st trimester ultrasound (nuchal translucency scan, page 13) and another between 18-22 weeks (page 17).

Scans can show some physical conditions, can confirm the due date, will identify multiple pregnancies and show the location of the placenta.

Many of the problems that are found can be treated once the baby is born. The most common physical conditions found during pregnancy include:

- Neural tube defects such as spina bifida. These occur early in pregnancy when the spine fails to form properly and the spinal cord and/or brain can be affected. Taking folate before and during early pregnancy can help prevent neural tube defects*.
- Heart conditions that affect the development of the blood vessels or the heart's structure.
- Digestive system problems such as a narrowing of the gut system.
- Kidney problems such as blockages or poor development of the kidneys.

*It is important to remember that most babies born, regardless of a mother's age, do not have any of these problems.*

**For further information go to the websites of the Public Health Association of Australia and the Spina Bifida Foundation of Victoria: http://www.phaa.net.au/policy/folate and http://www.sbfv.org.au*

# Types of prenatal tests for chromosome conditions

Prenatal tests fall into two groups: screening tests and diagnostic tests.

**Screening tests**
These tests give an estimate of the chance that a pregnancy is affected by a certain condition (they are not diagnostic tests).

If the screening test shows a high chance, a diagnostic test is offered. This will confirm if a condition is present or will reassure that the pregnancy is not affected.

Screening tests require a blood sample from the mother and/or an ultrasound scan. They are available to women of all ages.

**Diagnostic tests**
Diagnostic tests will give a definitive (yes or no) answer. They can confirm if a condition is present or reassure that the pregnancy is not affected.

Diagnostic tests are performed on samples of the placenta or amniotic fluid from around the developing baby. These samples are collected by two procedures: chorionic villus sampling (CVS) and amniocentesis.

As these procedures have a very small risk of miscarriage (above the natural miscarriage rate), diagnostic tests are usually offered to women who have a greater chance of having an affected pregnancy (e.g. advanced maternal age, family history, or have received a high chance screening result).

This booklet and the web tool focus on screening tests. More information about diagnostic testing can be found on page 28.

*Examples of screening tests:*

- Combined first trimester screening (cFTS)
- 2nd trimester maternal serum screening (2TMSS)
- Cell-free DNA testing (cfDNA) or non-invasive prenatal testing (NIPT)
- Ultrasound

*See pages 12-16.*

## Combined first trimester screening (cFTS)

Combined first trimester screening adds different measures together to provide an estimate of the chance a pregnancy is affected by Down syndrome, Edwards syndrome or Patau syndrome.

cFTS is not diagnostic, but it can predict Down syndrome in 85-90% of cases. cFTS does not identify neural tube defects.


**Figure 3:** Detection rate of Down syndrome using combined first trimester screening.

The measures are:

1. Maternal blood, taken between 9-13 weeks gestation to measure chemicals PAPP-A and free beta-hCG.
2. A nuchal translucency ultrasound (NT scan) (11 to 13 weeks).
3. Maternal age, weight and gestation.

In some cases, an additional measurement, called the nasal bone, is included. The presence or absence of the nasal bone (seen on ultrasound) is added to the combined score.

*Combined first trimester screening does not give a 'yes' or 'no' answer. Based on the result however, a decision can be made about diagnostic testing.*

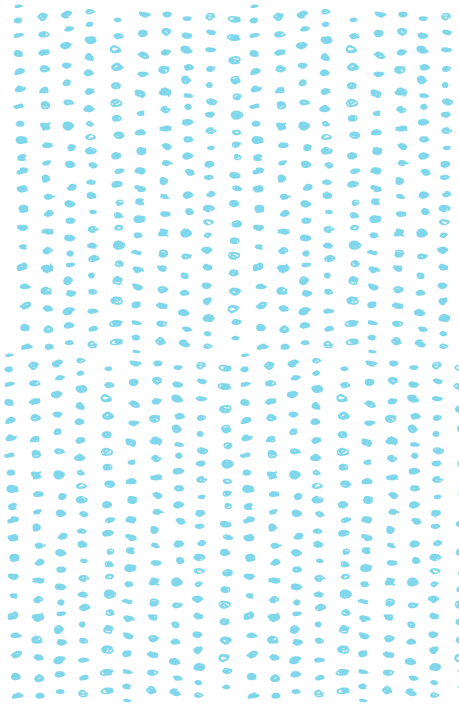
For information about how combined first trimester screening test results are reported, see page 21.

**Nuchal Translucency ultrasound (NT scan)**
The NT scan is performed between 11-13 weeks gestation. Sound waves are used to produce an image of the developing baby. This scan measures the thickness of the fluid filled space at the back of the baby's neck. An enlarged NT measurement may mean an increased chance for certain conditions, such as Down syndrome.

An NT scan alone is not able to accurately diagnose Down syndrome. A larger than normal NT measurement means that follow-up diagnostic testing is needed to confirm the presence of a condition or to reassure that the pregnancy is unaffected.

This early ultrasound can also:

- Confirm the due date.
- Identify twins.
- Identify if a miscarriage has occurred.
- Identify some physical features.



## Second trimester maternal serum screening (2TMSS)

Second trimester maternal serum screening is a single blood test, between 14-20 weeks of gestation (best done between 15-17 weeks).

2TMSS provides an estimate of the chance a pregnancy is affected by Down syndrome, Edwards syndrome, or neural tube defects such as spina bifida.

2TMSS is not diagnostic, but it can predict between 75-80% of pregnancies affected with Down syndrome.

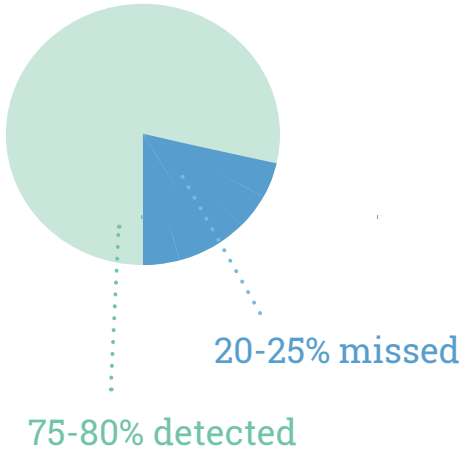


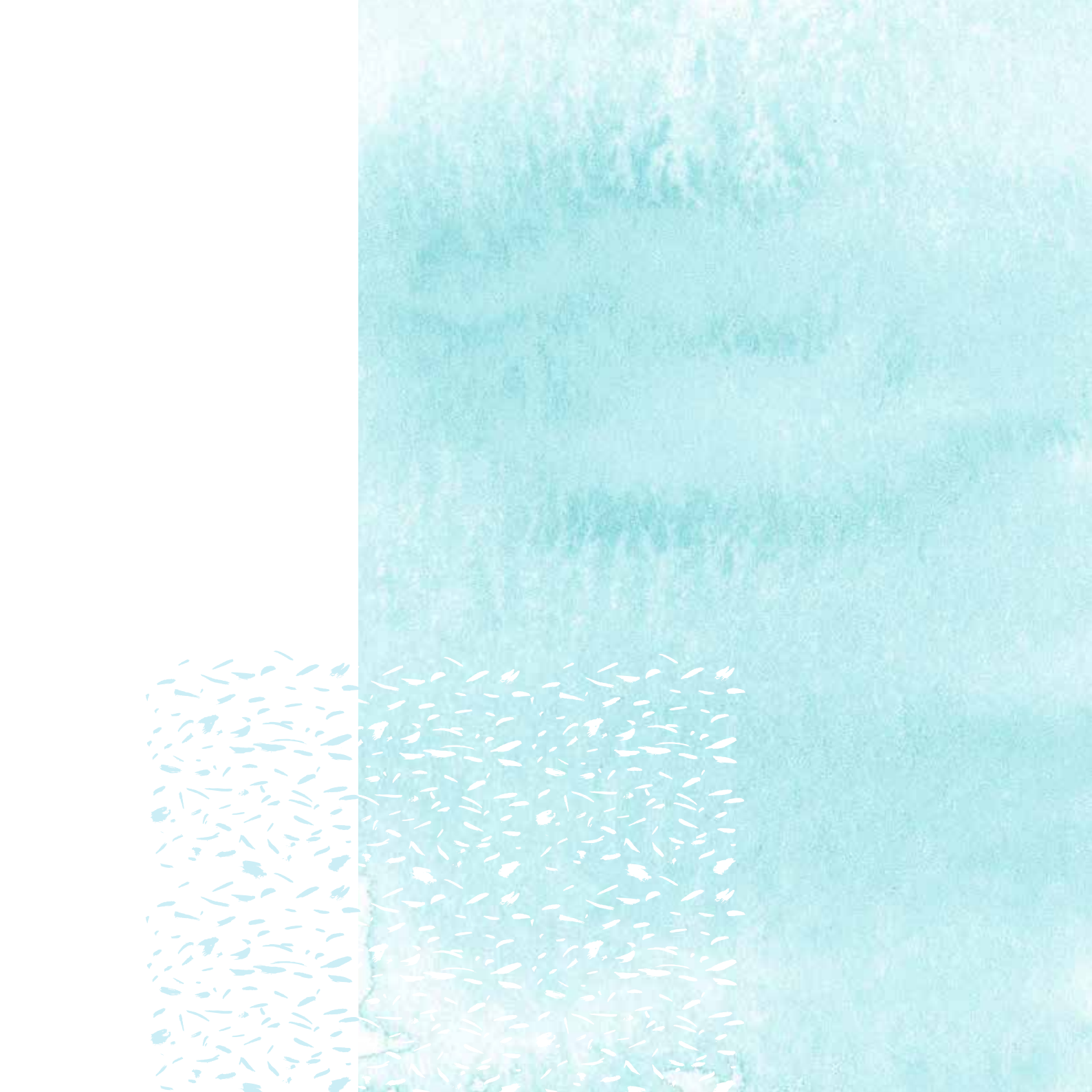

**Figure 4:** Detection rate of Down syndrome using second trimester maternal serum screening.

This test measures the level of four chemicals: alpha-feto protein, unconjugated estriol, free beta hCG and dimeric inhibin A. These are combined with maternal age, weight and gestation.

Women can have either combined first trimester screening or second trimester maternal serum screening depending on their gestation. It is not recommended that women have both screening tests. If you've had first trimester screening, you won't be offered second trimester screening.

*Second trimester screening does not give a 'yes' or 'no' answer. Based on the result however, a decision can be made about diagnostic testing.*

For information about how second trimester screening risk results are reported, see page 22.



## Cell-free DNA prenatal testing (cfDNA)

*(also known as non-invasive prenatal testing or NIPT)*

Cell-free DNA prenatal tests give an estimate of the chance that a pregnancy is affected by Down syndrome, Edwards syndrome, Patau syndrome or sex chromosome conditions.

Some cfDNA tests can also identify the baby's sex, reveal secondary findings and can include microdeletion syndromes (see page 36).

Most cfDNA tests have a detection rate of over 99% for Down syndrome. This means that if a pregnancy is affected by Down syndrome, it will almost certainly be detected. The detection rate is not as high for the other conditions.

*While cfDNA tests are more accurate than other screening tests, they are not 100% diagnostic and do not replace diagnostic testing.*

Blood for cfDNA testing can be taken any time from 10 weeks gestation onwards.

It is also recommended that an NT ultrasound scan (page 13) is performed alongside the cfDNA test. This scan may identify physical conditions that the cfDNA test can't.

**How is cfDNA different to the other prenatal screening tests?**

Combined first trimester and second trimester maternal serum screening look at various chemicals in mum's bloodstream to predict fetal abnormalities (biochemistry). cfDNA however, looks at short pieces of DNA from the placenta (genetic), which are found in mum's blood (Figure 5).

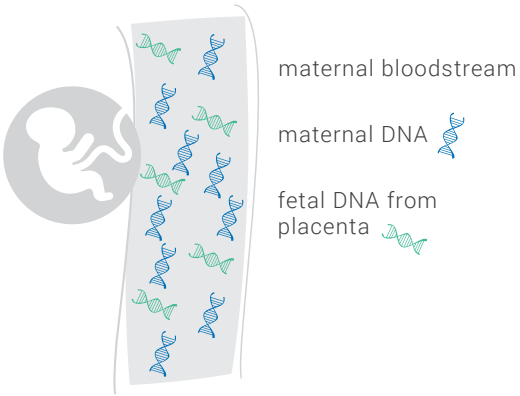



**Figure 5:** Cell-free DNA from the placenta found in the maternal bloodstream

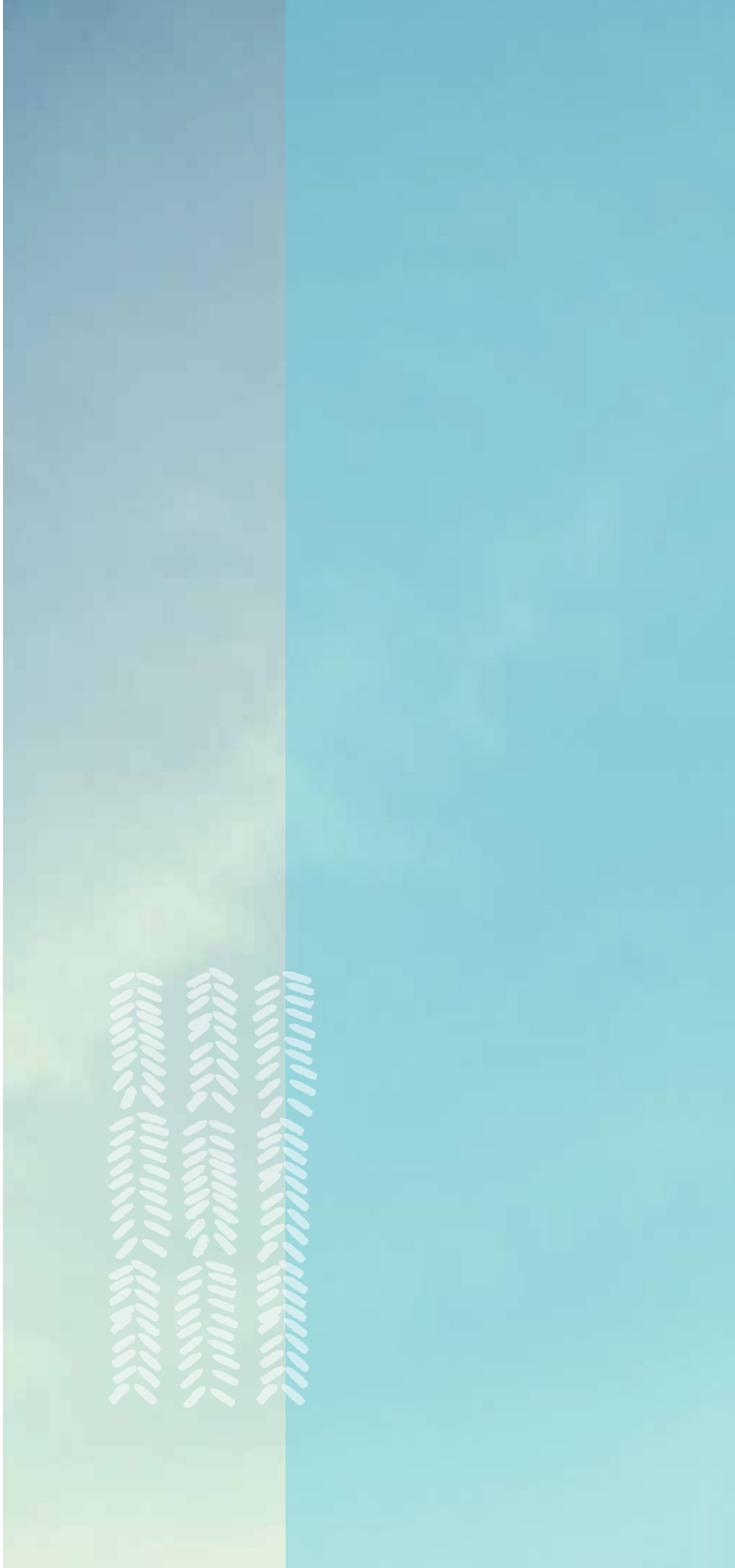
## 18-22 week ultrasound

This scan can detect a number of physical conditions, such as major heart problems and spina bifida.

This later gestation scan can also detect 'soft markers'*. These are risk factors which may mean a greater chance of a chromosome condition being present. A diagnostic test may be required to exclude the presence of a chromosome condition. In many cases, these markers are not significant.

By itself, ultrasound is not a reliable test for Down syndrome. It does however, provide information about the growth and well-being of the baby, along with the health and position of the placenta.

**Soft markers (e.g. head shape) are often non-specific findings. They don't always mean there is a problem and can also be found in normal, healthy pregnancies.*



# Making a decision about prenatal screening tests

# Screening Choices web tool

We have designed a web tool to help you make decisions about whether prenatal screening may be helpful to you.

The web tool can be found at:
www.mcri.edu.au/screening-choices

This is version 1 of the web tool and we'd appreciate any feedback or suggestions.
screeningchoices@mcri.edu.au

*Remember, all prenatal screening is your choice. You can decide not to have any screening.*

**Worksheet 1:**
**Will prenatal screening give me useful information?**

In this worksheet, we have listed some of the things women think about when deciding whether or not to have a prenatal screening test.

Indicate how you feel about each of these statements and based on your answers, the tool will give you an idea of whether a screening test may or may not be useful for you.

**Worksheet 2:**
**Which option is right for me?**

Worksheets 2 and 3 look at the screening test options available to you, based on your gestation.

For women less than 14 weeks, worksheet 2 compares combined first trimester screening and cell-free DNA testing.

For women 14 weeks or more, worksheet 3 compares second trimester maternal serum screening and cell-free DNA testing.

# Further information about prenatal screening & diagnostic tests

# Reporting of screening test results

### Combined first trimester screening

Results for combined first trimester screening will be reported as words (screen positive/high/increased risk or screen negative/low risk) and numbers (e.g. 1 in 300).

Two results are often reported. One is based on maternal age alone and the other, the combined result. The combined result takes into account the blood test and NT ultrasound, along with the mothers age, weight and gestation.

A high chance (screen positive) result does not mean the pregnancy is definitely affected by a particular condition; it means the pregnancy has an increased chance of having a condition. In most cases, the pregnancy **will not** be affected. A diagnostic test is the only way to confirm if a condition is present, or to provide reassurance that the pregnancy is not affected.

A low chance (screen negative) result means it is very unlikely the pregnancy is affected. A low chance does not mean 'no chance'. There is no test that can rule out all conditions and sometimes, affected pregnancies will be missed by screening. A low chance result means that diagnostic testing will not usually be offered.

| Chromosome condition | high chance (screen positive) | low chance (screen negative) |
|---|---|---|
| Down syndrome (T21) | 1 in 2 - 1 in 300 | 1 in 301 - 1 in 20,000 |
| Edwards syndrome (T18) | 1 in 2 - 1 in 175 | 1 in 176 - 1 in 20,000 |
| Patau syndrome (T13) | 1 in 2 - 1 in 100 | 1 in 101 - 1 in 20,000 |

**Figure 6:** Breakdown of result categories for combined first trimester screening. Note that categories do vary from place to place.

### Second trimester maternal serum screening

The test result will be reported as words (screen positive/high/increased risk or screen negative/low risk) and numbers (e.g. 1 in 300).

A high chance (screen positive) result does not mean the pregnancy is definitely affected by a particular condition; it means the pregnancy has an increased chance of having a condition. In most cases, the pregnancy **will not** be affected. A diagnostic test is the only way to confirm if a condition is present, or to provide reassurance that the pregnancy is not affected. Where the AFP level is 2.5 MoM or above, an 18 week ultrasound is recommended.

A low chance (screen negative) result means it is very unlikely the pregnancy is affected. Low chance does not mean 'no chance'. There is no test that can rule out all conditions and sometimes, affected pregnancies will be missed by screening. A low chance result means that diagnostic testing will not usually be offered.

| Chromosome condition | high chance (screen positive) | low chance (screen negative) |
|---|---|---|
| Down syndrome (T21) | 1 in 2 - 1 in 250 | 1 in 251 - 1 in 20,000 |
| Edwards syndrome (T18) | 1 in 2 - 1 in 200 | 1 in 201 - 1 in 20,000 |
| Neural tube defects | AFP ≥ 2.5 MoM | AFP < 2.5 MoM |

**Figure 7:** Breakdown of result categories for second trimester serum screening. AFP = alfa-feto protein. MoM = multiple of the median.

**Cell-free DNA tests**

Results for cfDNA tests are usually reported as:

Low chance/no condition detected
Most results are reported as low chance. This means it is very unlikely your pregnancy is affected by the specific conditions being screened for. However, other conditions not identified by the cfDNA test may be present.

High chance/condition detected-suspected
High (or increased) chance for the chromosome condition reported. However, other conditions not identified by the cfDNA test may be present. A diagnostic test will usually be offered.

No result/no call
In some cases, no result is obtained. This is very uncommon (less than 1% of samples) and can be caused by having your blood sample collected prior to 10 weeks.

**What does a high chance cfDNA result mean?**
While the overall detection rate for Down syndrome is very high with cfDNA screening, the likelihood that an individual high chance result is a true positive (pregnancy is actually affected), depends on a number of factors, including maternal age and how common the condition is in the population. This is known as the positive predictive value or PPV.

A high chance result does not mean your baby definitely has a condition. False positive results are possible with all screening tests. This is why diagnostic testing is recommended for all women with a high chance result, especially if they might consider ending the pregnancy.

*Detection rate, positive predictive value and false positives are described on pages 26-27.*

# Understanding results

For all screening results it is important to understand what the numbers are telling us about the chance of a fetal condition as well as the chance of not having a fetal condition.

If we think of a result for Down syndrome such as 1 in 100, this also means a chance that 99 out of 100 pregnancies **will not** be affected. This may be easier to understand by looking at the diagrams.

Screening results are based on a cut-off level to determine whether or not a diagnostic test will be offered.

For example, the cut-off used to define a high chance result for Down syndrome using combined first trimester screening is 1 in 300. If a result is higher than this (e.g. 1 in 200), then a diagnostic test will be offered.

If the result is below the cut-off (e.g. 1 in 400), it does not mean there is no chance of having a fetal condition, but it does mean that diagnostic testing will not be offered.

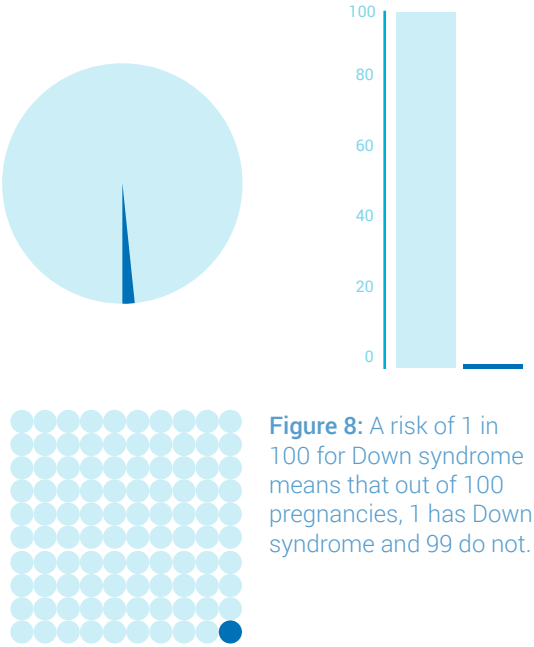



**Figure 8:** A risk of 1 in 100 for Down syndrome means that out of 100 pregnancies, 1 has Down syndrome and 99 do not.

# Characteristics of prenatal screening tests

Screening tests are available to all women, regardless of age. Screening tests do not increase the risk of miscarriage. Screening tests give an estimate of the chance that a pregnancy is affected by a chromosome condition, not a definite diagnosis. They are used to separate women into 'high chance' or 'low chance' categories.

### Terms related to screening tests:

**False positive & false negative**

False positive = when a screening test gives a high chance result, but the pregnancy is not affected.

False negative = when the screening test gives a low chance result, but the pregnancy is actually affected.

**Detection Rate (DR)**

The detection rate of a test describes how good the test is at identifying a particular condition.

Detection rate answers the question: *If my baby has Down syndrome, what is the likelihood I will get a high chance result (screen positive)?*

As an example, the detection rate for Down syndrome with first trimester combined screening (cFTS) is 90%. If we screen 100 women whose pregnancies are affected by Down syndrome, the test will give a high chance (screen positive) result in 90 of them. It will miss the condition in 10 of these affected pregnancies.

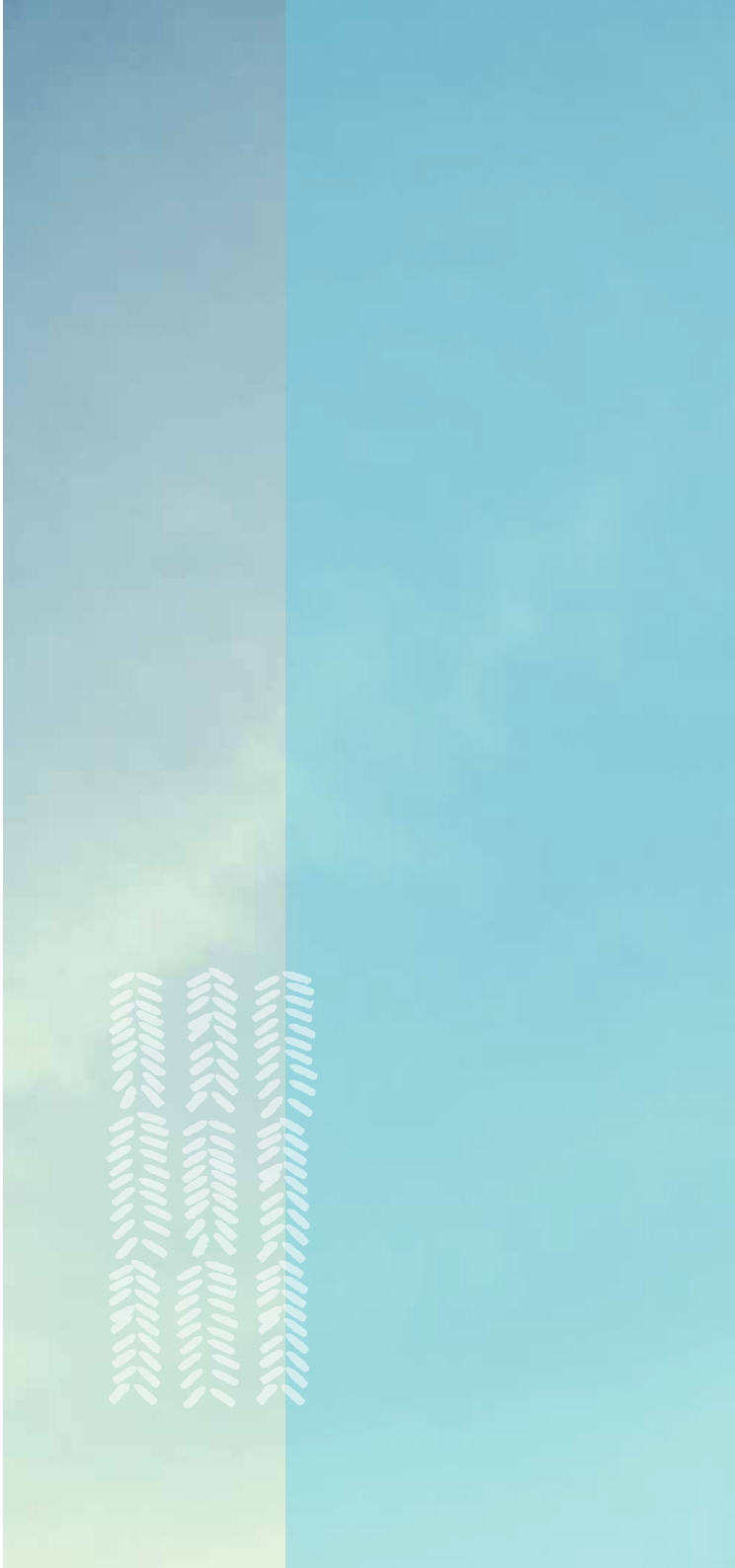
A related question: *If my screening test gives a high chance result (screen positive), what is the likelihood my baby has Down syndrome?*

To answer this question, we need to consider Positive Predictive Value.

**Positive Predictive Value (PPV)**
PPV is the likelihood that a pregnancy will be affected if you receive a high chance screening result. PPV looks at how common the condition is in the general population, maternal age (because age influences the chance you will have a baby with Down syndrome) and the false positive rate (there will always be false positives with a screening test).

Question:
*Some non-invasive prenatal tests are marketed as being 99% accurate. If i receive a high chance result, does that mean they are 99% certain my baby has Down syndrome?*

No, they are not 99% certain your baby has Down syndrome. The detection rate of the test is 99%, but the PPV is not 99%. PPV varies with age and will be higher for older women. For younger women, the PPV will be lower (meaning a high chance screening result is more likely to be a false positive).



# Prenatal diagnostic tests

A prenatal diagnostic test can confirm (give a yes or no answer) whether a pregnancy is, or is not, affected by a chromosome or other condition.

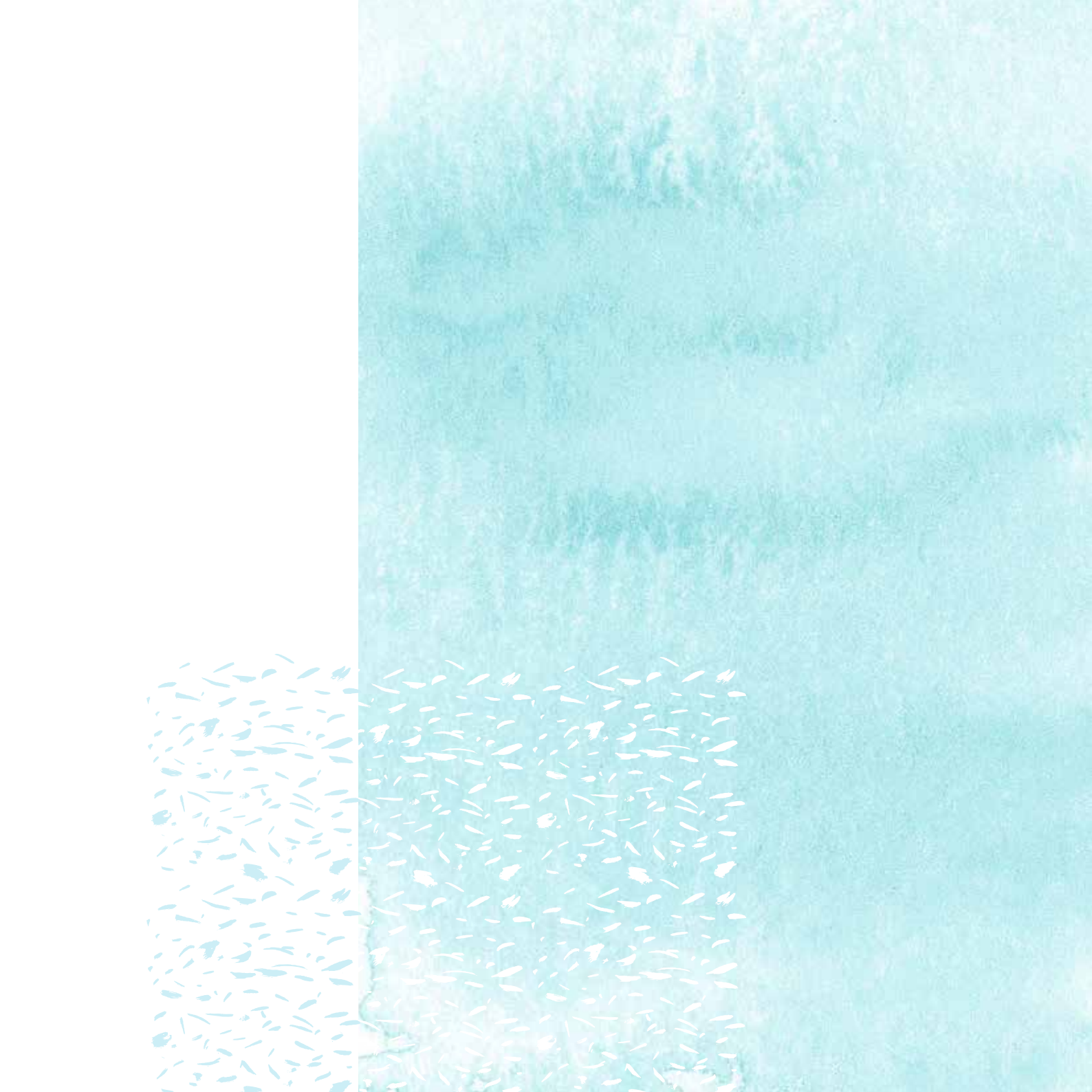
A diagnostic test is not offered to every pregnant woman. They are usually only offered if a woman has a high chance screening result, a previous family history of a fetal condition, is of advanced maternal age (more than 35-37 years, depending on where you live), or if both parents are carriers of a particular condition (e.g. thalassaemia or cystic fibrosis).

To perform a diagnostic test, a sample of the placenta or amniotic fluid is required. To obtain these samples, there are two diagnostic procedures available: chorionic villus sampling (CVS) and amniocentesis.

A CVS is performed to collect a sample of the placenta between 11 and 13 weeks. Risk of miscarriage with a CVS is often reported as 1 in 100, but recent evidence suggests it could be as low as 1 in 500*.

Amniocentesis is performed to collect a sample of the amniotic fluid after 15 weeks. Risk of miscarriage associated with an amniocentesis is often reported as 1 in 200, with research suggesting it could be as low as 1 in 1000*.

* Akolekar.R et al. 2015. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol*, 45:16.



# Diagnostic Procedures
(collecting a fetal sample)

**Chorionic villus sampling (CVS) @ 11-13 weeks**

The procedure is performed by skilled doctors, under ultrasound guidance. A fine needle is inserted through the abdomen and cells from the early placenta are collected and sent to the laboratory for testing.

If the placenta cannot be reached from a needle through the abdomen, a CVS may be performed through the vagina.

On very rare occasions there can be problems interpreting the results, and another sample may need to be collected.

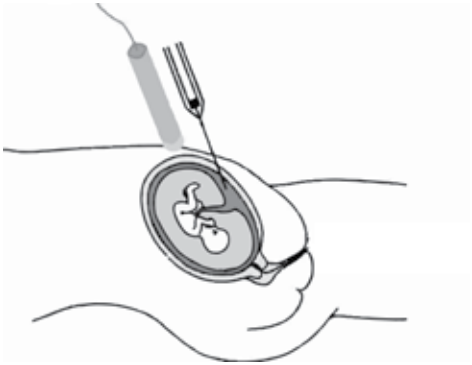


**Figure 9:** Chorionic villus sampling: sample of the placenta

**Amniocentesis @ 15+ weeks**

The procedure is performed by skilled doctors, under ultrasound guidance. A fine needle is inserted through the abdomen and a sample of the amniotic fluid around the baby is collected and sent to the laboratory for testing.

On very rare occasions there can be problems interpreting the results, and another sample may need to be collected..

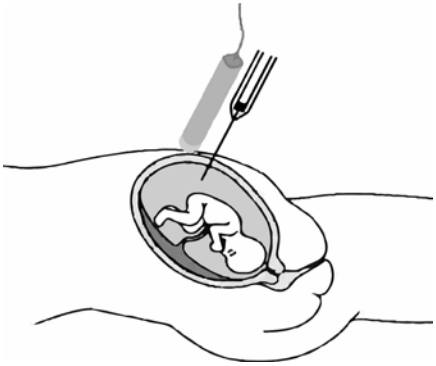


**Figure 10:** Amniocentesis: sample of the amniotic fluid

# Diagnostic Testing
(testing the fetal sample)

There are a few different laboratory tests that are used to look at the fetal cells (containing the chromosomes) collected by either CVS or amniocentesis.

## Early detection tests

**FISH or qf-PCR**
Using fluorescent dyes or tags, FISH and qf-PCR can quickly identify whether the fetal cells contain the right number of chromosomes. These tests can determine whether a pregnancy is affected by Down syndrome, Edwards syndrome or Patau syndrome. These are preliminary tests that will provide results in 1-2 working days.

## Confirmatory tests

**Karyotype**
A karyotype is used to look at the size, shape and number of chromosomes in the sample of fetal cells. This means any extra, missing or large change in the chromosomes can be identified. This test will provide results in 10-14 working days.

**Chromosome microarray (molecular karyotype)**
A chromosome microarray is a detailed test that gives lots of information about a baby's chromosomes. Instead of counting the chromosomes to make sure there is the right number, a microarray looks at the content of the chromosomes (the DNA) to identify smaller changes or variations. These are known as copy number variants or CNVs *(see page 36)*.

A variation is a small segment of missing or extra DNA. Some of these variations can affect health, while others may not have any impact on health and/or development.

Results from a microarray are available in about 10-14 working days.

*Depending on the clinical situation and family history, other DNA testing can also be done at this stage to identify specific genetic conditions, such as cystic fibrosis or Duchenne muscular dystrophy (see genetic conditions on page 36). These conditions are not routinely tested for. Please discuss with your doctor or genetic counsellor for more information.*

# What happens after a diagnostic test?

Early detection test results can be available in 1-2 working days, while a karyotype and/or microarray results can take up to two weeks.

Waiting for these results can be an anxious time. It's advisable to ask your doctor:

- When you should expect to get the results.
- Who will let you know the results and how (i.e by letter or phone call).
- If genetic counselling is available.

If no conditions are detected then no further testing is required.

**What if a fetal condition is found?**

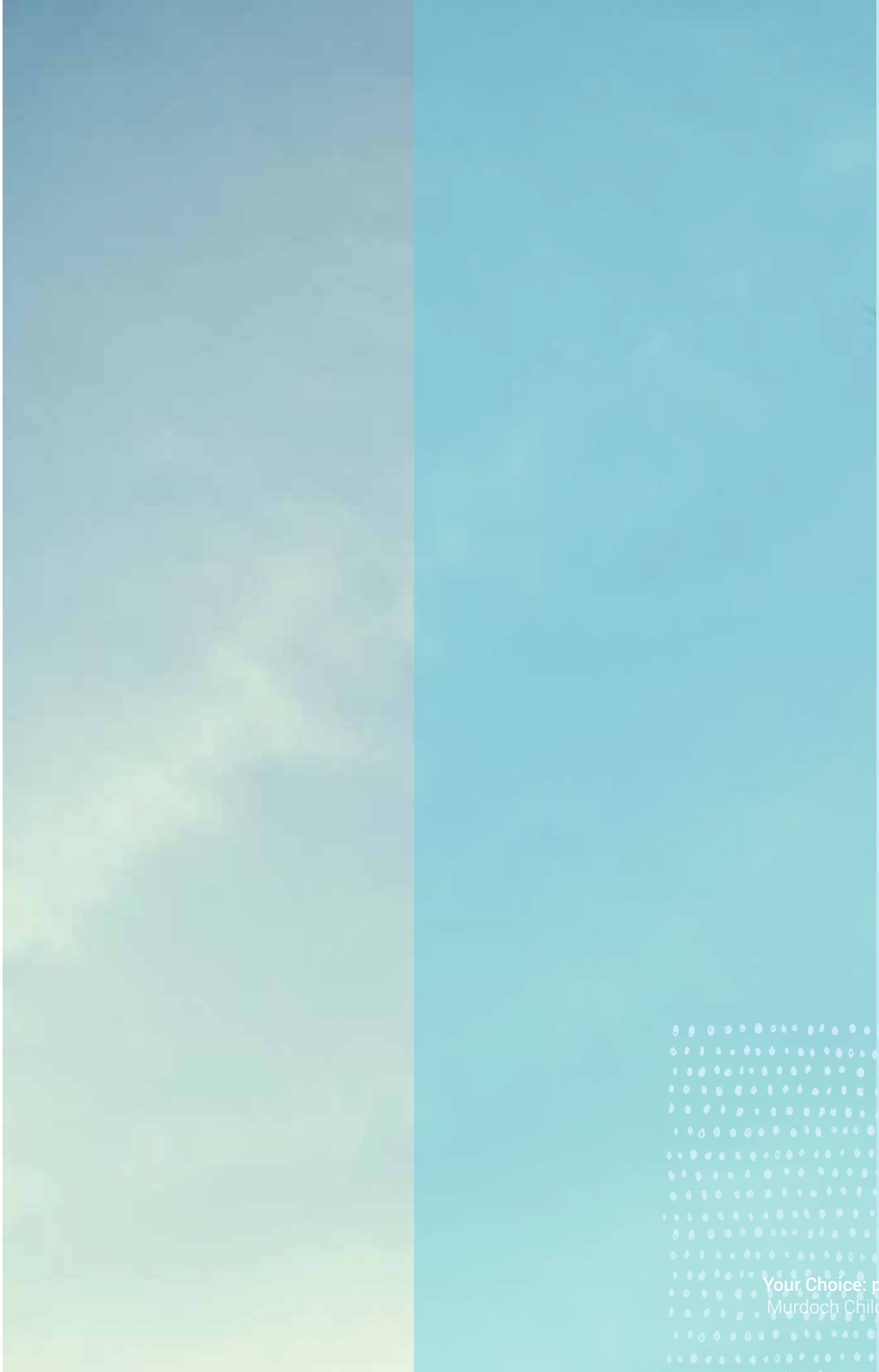
If a condition is found you can choose to continue the pregnancy, or to terminate the pregnancy. Your health care provider will offer specialist genetic counselling and refer you to a high risk pregnancy service.

Your choice to continue the pregnancy, or to terminate, will be respected and supported.

A termination before 14 weeks is usually a surgical procedure. A termination after this time will most likely require the induction of labour.

Termination of pregnancy laws and services vary across Australia. Your doctor will be able to provide more detailed information.

This resource from the UK might be useful: http://www.arc-uk.org/for-parents/decision-making



# Glossary

**Chromosome**
A chromosome is a structure that stores our DNA. DNA is short for deoxyribonucleic acid. It is the chemical that carries all our genetic information (our genome).Humans have 46 chromosomes in total (23 from mum and 23 from dad), and most cells in our body contain chromosomes. Parents pass their DNA to their offspring via chromosomes found in sperm and eggs.

**Chromosome conditions**
There are two basic types of chromosome conditions: numerical (missing or extra chromosomes) and structural (where parts of chromosomes are deleted, duplicated or turned upside down).

**Detection rate** - see page 26.

**False positive & false negative** - see page 26.

**Fetal abnormality/anomaly**
A condition that can affect the healthy development of the fetus. This could be caused by a change in the chromosomes or it could be a physical/structural problem.

**Genetic counselling (Genetic counsellors)**
Genetic counsellors are trained to help people understand complicated genetic information. They are available to support people in making informed decisions that are consistent with their circumstances, beliefs and values.

If you receive a high chance screening result, you can be referred to a genetic counsellor. A counsellor can also arrange further testing and/or help you work through complicated results or difficult information.

**Multiple of the median (MoM)**
The MoM score measures how far an individual test result is from the expected result. It is simply a way for scientists to be able to compare test results and determine what is normal and what isn't normal.

**Nuchal translucency (NT)**
This is the fluid filled space at the back of the neck of the baby that can be seen during the 1st trimester ultrasound.

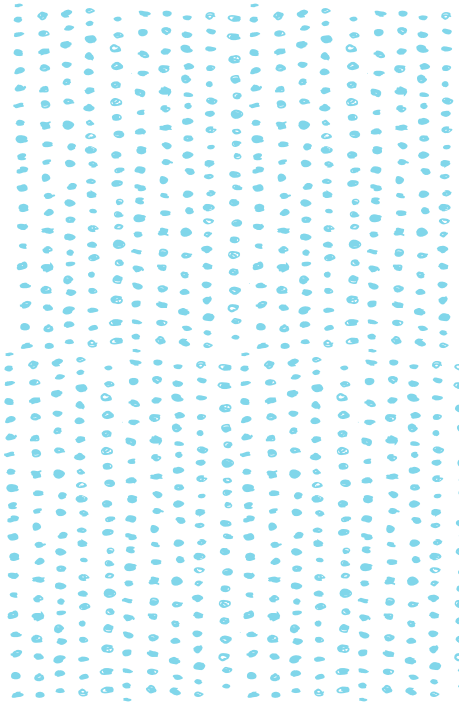
**Positive predictive value (PPV) -** see page 27.

**Prenatal screening test**
A screening test is designed to identify pregnant women who may have a greater chance of having a baby affected by a condition, such as Down syndrome. They are not diagnostic (not 100% correct), but are used to classify women into high or low chance categories.

**Prenatal diagnostic test**
A diagnostic test will provide a definitive yes or no answer as to whether a pregnancy has a particular condition (they are 100% correct).

**Sex chromosome**
One pair of the 46 chromosomes are known as the sex chromosomes because they determine the sex of the baby. Females have two X chromosomes while males have one X and one Y chromosome.

**Syndrome**
A syndrome is a group of features that when found together, are associated with a particular condition. For example, people with DiGeorge syndrome often have heart problems and/or characteristic facial features and/or hearing loss and/or learning difficulties.



# Conditions that can be identified with diagnostic prenatal testing

**Chromosome conditions**
Down syndrome (trisomy 21); Edwards syndrome (trisomy 18); Patau syndrome (trisomy 13)

**Sex chromosome conditions**
Turner syndrome (also called monosomy X or 45,X); Klinefelter syndrome (XXY); triple X (47,XXX); Jacob syndrome (47,XYY)

**Neural tube defects**
Spina bifida; anencephaly

**Physical conditions seen by ultrasound**
Heart conditions, digestive system problems, limb and kidney conditions.

**Copy number variants (CNVs)**
These variations are small segments of missing or extra DNA. Some have been linked with disease and disability, while others represent normal human variation. The affect on health of some CNVs is currently unknown or uncertain.

**Microdeletion syndromes**
Microdeletion syndromes are caused by small segments of missing DNA. Examples include: 1p36 deletion syndrome; Wolf-Hirschhorn syndrome (4p); Cri-du-chat syndrome (5p); Langer-Giedion syndrome (8q); Jacobsen syndrome (11q); Angelman/Prader-Willi syndromes (15q); DiGeorge syndrome (22q)

**Genetic conditions**
Many genetic conditions can be specifically tested for during pregnancy. These include single gene disorders such as cystic fibrosis and Duchenne muscular dystrophy, Huntington disease and thalassaemia. Specific gene mutations (e.g. BrCa for breast cancer or HNPCC for colon cancer) can also be tested for during pregnancy, though such testing is not routine and will depend on the clinical situation and/or family history.

**Secondary findings**
A secondary or incidental finding is an unintentional or unrelated finding found during testing. The test wasn't looking for this information, but it was found. For cfDNA tests, incidental findings are maternal or fetal conditions other than those being tested for. Conditions that have been found include problems with maternal chromosomes (e.g. sex chromosome conditions), maternal cancers and fetal chromosome conditions other than those affecting chromosomes 21, 18, 13, X and Y, e.g. trisomy 16.

**Sex**
XX – female
XY – male.

# Quick summary of tests

| Test Characteristics | Screening | | | Diagnostic |
|---|---|---|---|---|
| | combined first trimester (cFTS) | second trimester screening (2TMSS) | cell-free DNA (cfDNA) | CVS & amniocentesis |
| T21 detection rate | 90% | 75-80% | 99% | 99.99% |
| Medicare rebate available | Blood test - yes<br>U/sound - yes | Blood test - yes | No Medicare rebate | Yes |
| What can be detected | T21,T18, T13, structural problems on u/sound | T21,T18,<br>neural tube defects | T21, T18, T13,<br>sex chromosome conditions, | Many chromosome & genetic conditions. Neural tube defects (amnio only). |
| False positive rate for T21 | 3-5% | 7-8% | Less than 1% | Less than 1% |
| Test failure rate | Less than 1% | Less than 1% | 1-5% | Less than 1% |
| Timing of test | Blood @ 9-13 weeks<br>U/sound @ 11-13 weeks | 14 weeks + | Anytime from<br>10 weeks onwards | CVS @ 11-13 weeks<br>Amnio @ 15+ weeks |
| Type of test | Maternal Blood test + ultrasound | Maternal Blood test | Maternal Blood test | Sample of of fetal cells |
| Risk to pregnancy | None | None | None | Small increase in risk of miscarriage (see page 18) |

**Figure11:** Quick summary of screening tests.
T21 - Down syndrome; T18 - Edwards syndrome; T13 - Patau syndrome