Fact sheet 65

REPRODUCTIVE CARRIER SCREENING (RCS)

This fact sheet describes an optional genetic test carried out before pregnancy (or in early pregnancy) called reproductive carrier screening (RCS). The test can identify a couple's chance of having a child with certain genetic conditions and can help them make informed choices about planning their family. This is a screening test and is also known as pre-pregnancy or preconception carrier screening.

NOTE: RCS is different to screening tests undertaken during pregnancy, such as non-invasive prenatal testing (NIPT), which assess the chances of a baby having Down syndrome or other chromosome conditions.

IN SUMMARY

- RCS is an optional blood or saliva test carried out prior to pregnancy or in early pregnancy. It looks for variations in a person's genes.
- RCS can identify a couple's chance of having a child with specific serious inherited genetic conditions.
- Couples found to have an increased chance of having a child with a genetic condition will be given information about their reproductive options.
- There are different RCS tests available through different laboratories. The difference between tests may include the number of conditions included, price and turn-around time.
- Some RCS tests are covered by Medicare (items 73451 and 73452), others may have "out-of-pocket" costs.

WHAT IS REPRODUCTIVE CARRIER SCREENING (RCS)?

RCS is a blood or saliva test that looks at a person's genes to check for variants which we know can cause certain genetic conditions. RCS can determine if one or both parents are genetic carrier(s) of some genetic conditions(s). These conditions can affect the health and development of any children they may have together.

WHO MIGHT WANT TO HAVE RCS?

RCS might be useful for anyone who is planning a pregnancy, or in the early stages of a pregnancy (recommended before 12 weeks' gestation), and would like to be more informed about their chance of having a child affected by certain genetic conditions.

RCS is available for all couples, however those with a known family history of a genetic condition may have a higher chance and should be referred to their local genetic service.

Our body is made up of billions of cells, and in each cell there are two copies of all our DNA. This is packaged into 46 chromosomes, arranged into 23 pairs. One pair is made up of the sex chromosomes called X and Y. People born male usually have one X chromosome and one Y chromosome. People born female usually have two copies of the X chromosome.

Chromosomes contain genes, which provide instructions for our body to grow and function. We all have variation in our genes which is normal and makes us unique and different. Some gene variations, however, may mean that the gene does not work properly or works in a different way that is harmful. A variation that causes a health or developmental condition is called a pathogenic variant or mutation.

Gene variants may be inherited from a parent or happen for the first time in a person. Once you have a gene variant, however, it may be passed on to future generations. This is referred to as genetic inheritance.

WHAT IS A GENETIC CARRIER?

We all have two copies of each gene. We inherit one copy from our mother and one copy from our father. A genetic carrier is a person who has a variant in only one copy of a gene. The other copy of the gene does not have a variant and is said to be 'working'.

In most cases, genetic carriers do not have any associated health concerns, as the presence of the working copy of the gene is sufficient to keep them healthy. Genetic carriers are typically unaffected by the condition.

Males and females can be genetic carriers of a recessive condition, or females can be genetic carriers of an X-linked condition.

HOW DOES A CHILD INHERIT A GENETIC CONDITION FROM UNAFFECTED PARENTS?

RCS can screen for both recessive and X-linked genetic conditions, which are inherited in different ways:

1. **Recessive conditions occur when both parents are genetic carriers of variants in the same gene (Figure 1)**

   For each pregnancy that this couple have together, there is a 1 in 4 (or 25%) chance that the baby will inherit both non-working copies of the gene and be affected by the genetic condition. This applies for either daughters or sons.

   Examples of conditions like this include:

   - **cystic fibrosis** (affects the lungs and digestive system and is a life-limiting condition)
   - **spinal muscular atrophy Type 1** (progressive muscular weakness that leads to early childhood death without a cure)

2. **X-linked conditions occur in males when they inherit a variant from their mother who is a carrier of a variant on one of her X chromosomes (Figure 2)**

   Females have two X chromosomes, and males have one X and one Y chromosome. If there is a gene change on the X chromosome, it can cause a genetic condition.

   For each pregnancy the female genetic carrier has, there is a 1 in 4 (or 25%) chance that the baby is a boy affected by the genetic condition.

   Sometimes, females who carry X-linked gene changes may be affected by the condition, although this is usually milder.

   An example of a condition that is inherited in this way is **fragile X syndrome** (the most common inherited cause of intellectual disability in boys; girls can also be mildly affected).

Figure 1:
Autosomal recessive inheritance when both parents are unaffected genetic carriers for the condition. The non-working copy of the gene containing a recessive variant is represented by 'r'; the working copy of the gene by 'R'.

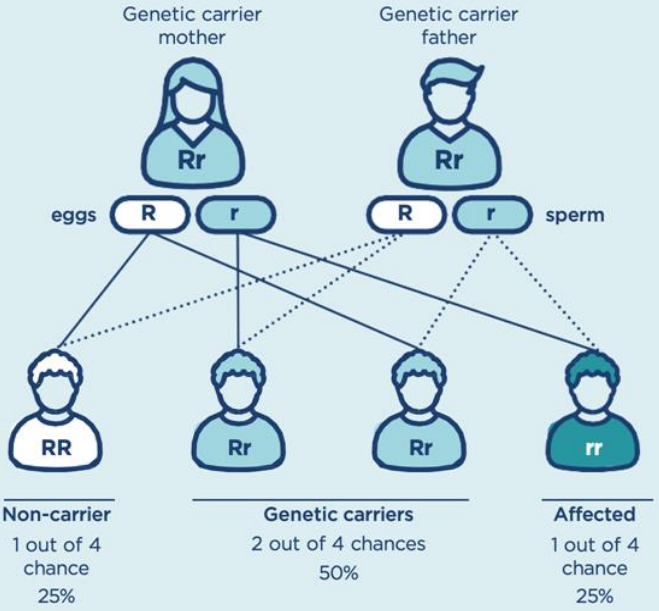
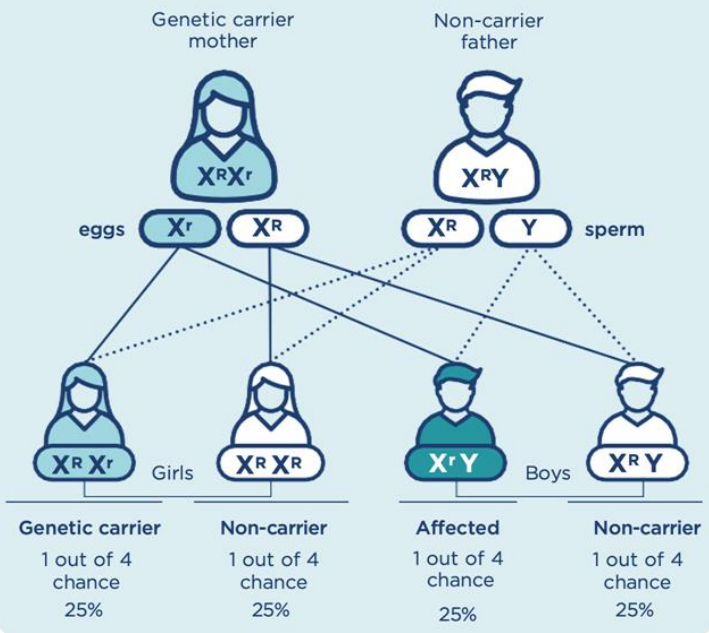


Figure 2:
X-linked recessive inheritance where the mother is a carrier of the non-working copy of the X-linked gene. The X-linked recessive non-working gene copy is represented by 'r'; the working copy by 'R'.



Usually, male children are more severely affected by X-linked conditions than females, because they only have one X chromosome (inherited from their mother).

Female children who inherit a non-working copy of a gene on an X-chromosome may be healthy genetic carriers who do not show any symptoms of the health condition. This is because they have a second working copy of the gene from the other X chromosome.

WHAT CONDITIONS DOES RCS TEST FOR?

RCS can test for different genetic conditions from the same single test. The number of conditions tested for can vary depending on the test being used by your healthcare provider. Usually, the tests are carried out in one of the following ways:

- A **3-gene carrier screen** that tests for three genetic conditions that have a serious impact on the health of an affected individual: cystic fibrosis (CF), spinal muscular atrophy (SMA) and fragile X syndrome. This test is covered by Medicare.
- **Expanded carrier screening** can test for many different genetic conditions (sometimes tens or hundreds) most of which are rare. The expanded carrier screening test will usually look for the 3 common conditions: CF, SMA and fragile X syndrome, as well as many others that are severe and can start early in life. This test is **not** currently covered by Medicare.

Couples should be aware that RCS does not screen for every genetic condition. It is important to talk to your healthcare provider about the specific conditions that can be identified through different RCS tests.

WILL RCS PROVIDE INFORMATION ABOUT MY HEALTH?

RCS tests for variants which usually have little or no impact on your own health but may have significant health implications for future children. For some genetic conditions, there might be health implications for you. Your healthcare provider can give you more information.

HOW COMMON ARE THESE CONDITIONS?

The chance of a child being born with a genetic condition can vary depending on the ethnicity of the population. The numbers of carriers and affected individuals for the more common conditions are shown in Table 1.

It is not unusual to be identified as a carrier of a genetic condition. People are often healthy carriers of several genetic conditions, though they are usually unaware. The chance of having a child affected by a condition is increased only when both members of a reproductive couple are found to be carriers of the same recessive condition.

Table 1.
Frequencies for more common genetic conditions*

Condition	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 4,000
Spinal muscular atrophy	1 in 40	1 in 6,000 – 1 in 10,000

**Note: Due to available population data, frequencies listed above are representative for Caucasian populations*

HOW IS RCS DONE?

RCS tests require a blood or saliva sample from one or both reproductive partners. There are two pathways for undertaking RCS:

- **Individual testing:** An individual is tested first (usually the female reproductive partner), and if they are found to be a genetic carrier, the other partner is then tested to determine their chance as a couple. If the female reproductive partner is tested first then the testing can also include X-linked conditions. Male partners do not need to be tested for X-linked conditions (assuming they are unaffected).
- **Couple testing**: Both male and female reproductive partners are tested at the same time to see if they are genetic carriers for the same recessive genetic condition. The female partner may also be tested for X-linked conditions. **If the couple is already pregnant,** couple testing may be the preferred approach to avoid delays in receiving results.

  Depending on the type of test and laboratory, RCS results may be reported for each individual, or for a couple jointly. If you change reproductive partners, refer to the section *"Do I*

need to have RCS every time I have a baby".

WHEN SHOULD RCS BE DONE?

The ideal time for testing is before becoming pregnant. This gives couples time to consider the results and make informed choices about their reproductive options.

Reproductive genetic carrier screening can also be performed in early pregnancy (before 12 weeks). There will be fewer options available to the couple, depending on the stage of the pregnancy.

HOW DO I ARRANGE SCREENING?

If you are thinking about RCS, you can discuss this with a healthcare provider (e.g. your GP, midwife or obstetrician, genetic counsellor).

WHAT ARE THE COSTS?

At present, only the 3-gene carrier screen is covered by Medicare (items 73451 and 73452). Depending on which test you choose, your healthcare provider will tell you if there are out of pocket costs.

HOW ACCURATE IS RCS?

RCS is a **screening test**. It will provide information about the chance that your baby will inherit a certain genetic condition, based on your genetic carrier status as an individual or couple. You will receive an increased chance or low chance result.

- An **increased chance result** means that one parent carries an X-linked condition or both parents carry the same recessive genetic condition. When both parents carry the same recessive condition, there is a 25% (1 in 4) chance of having a baby with that condition. When a parent carries an X-linked condition the chance will depend on the condition and the result. Your health professional will discuss this more with you.
- A **low chance result** means that the test did not identify any X-linked conditions and the parents are not carriers of the same recessive genetic conditions. This does not guarantee a healthy baby but it means there is a very low chance of having a child with any of the genetic conditions you were screened for.

RCS is highly accurate for the genetic conditions that it screens for; however the accuracy is not 100%. If no variant is found, there is still a small chance that you are a genetic carrier of a variant that was not detected or for another condition that was not tested for. In some rare cases, additional testing may be needed to provide more information about what the results mean.

WHAT IF RCS SHOWS THAT I HAVE A HIGHER CHANCE OF HAVING A BABY WITH A GENETIC CONDITION?

If you receive an increased chance result, how you use this information is completely up to you. You should discuss your options with your healthcare provider. Some of the options couples in this situation may consider include:

- Falling pregnant naturally (or continuing if you are already pregnant) and having no extra testing for the genetic condition in the pregnancy.
- Falling pregnant naturally and having specific prenatal testing to see if the pregnancy has inherited the genetic condition. If the pregnancy has the condition you would have the option to end the pregnancy (termination).
- Falling pregnant using Pre-Implantation Genetic Diagnosis (PGD) and In Vitro Fertilization (IVF) to reduce the chance of having a child with the genetic condition. Some of the costs associated with PGD may be covered by Medicare.
- Falling pregnant using IVF and using a sperm or egg donor to reduce the chance of having a child with the genetic condition.

DO I NEED TO HAVE RCS EVERY TIME I HAVE A BABY?

RCS is optional. If you choose to have RCS, you only need to have this test once in your lifetime. If you are not a genetic carrier, you remain at a very low chance of having a child with the genetic condition(s) tested for. If you have had RCS but have a new partner, your new partner may need to be tested (and you may need to be retested).

IF THE TEST SHOWS THAT I AM A GENETIC CARRIER, DO I NEED TO TELL MY FAMILY?

If you are found to be a genetic carrier, it is very likely that one of your parents is also a genetic carrier. This means that your siblings and extended relatives may also be genetic carriers

and unaware of this. You may wish to share this information with adult family members. This is usually only relevant for family planning. Family members can discuss their chance of being a genetic carrier with their healthcare provider or a local genetic service.

OTHER THINGS TO KNOW

No test can guarantee that a baby will be healthy at birth. **RCS does not replace other genetic screening tests available in pregnancy**, such as Thalassemia Screening, Non-Invasive Prenatal screening (NIPT) or Combined First Trimester Screening. It is recommended you discuss these tests with your healthcare provider.

If you discover you are pregnant prior to your RCS results being available, it is recommended you let your healthcare provider know as soon as possible.

Finding out that one or both parents are genetic carriers will usually be unexpected, because in most cases there is no family history of the condition. It may lead to a range of emotional responses.

Further information and support should be given to you by your healthcare provider or by referral to a specialist service.