# PGT-M Eligibility - Spinal Muscular Atrophy (SMA) Edition

Preimplantation genetic testing for monogenic conditions (PGT-M) is not always indicated or feasible for every family. There are specific requirements that need to be met in order to undergo PGT-M. One requirement is confirming there is a risk for a particular condition.

This handout will focus on a situation that comes up periodically in which someone's carrier screening report identifies they may be at an increased risk to being a carrier of spinal muscular atrophy, but the carrier screening test does not know for certain if the person is a carrier. This handout will discuss spinal muscular atrophy, genes, inheritance, the meaning of a 2+0 carrier, and how this complicates the indication for PGT-M.

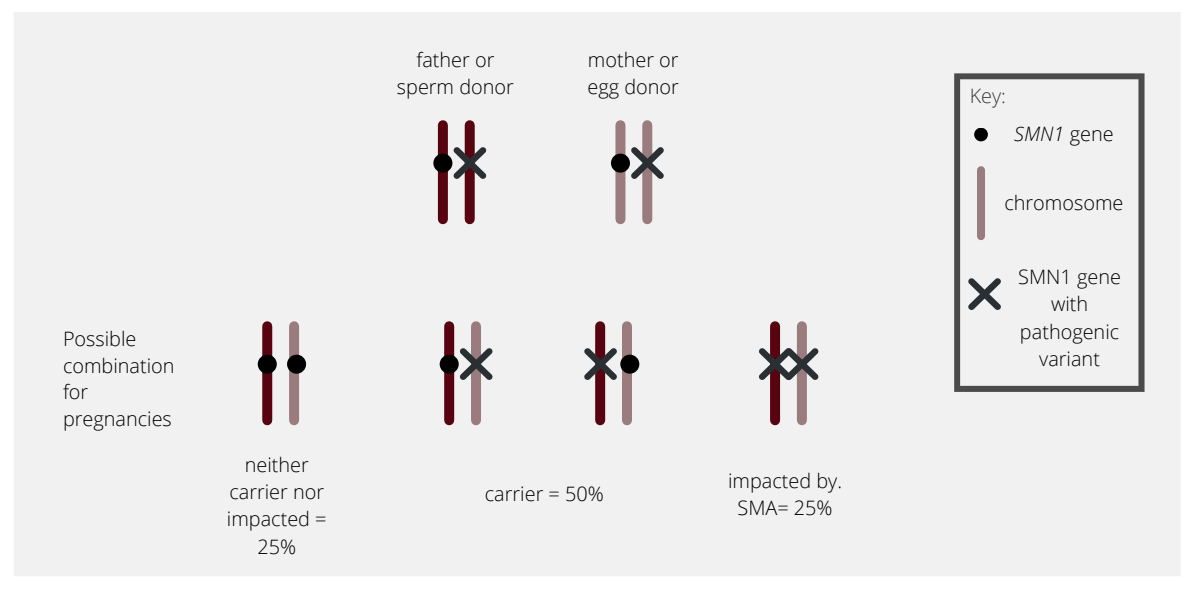
## What is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is a genetic condition that impacts the nerves that control our muscles, so someone with SMA can have difficulty with breathing, eating, crawling, and walking. SMA is a lifelong condition with some treatment options available. For more details of the features of SMA, please visit: MedLine Plus and CureSMA.

## Genes and Inheritance:

Our genes carry instructions that determine our traits and can influence the risk of certain conditions. Spinal muscular atrophy (SMA) is caused by changes in both copies of the SMN1 gene. Inheritance of genes follows different patterns, like autosomal recessive inheritance, which is the case for SMA.

Autosomal recessive inheritance means that both gene copies have a variant that causes the gene not to work in the way it is expected. People can inherit SMA from their parents, who are carriers. A carrier has one gene copy with the variant but usually doesn't have symptoms. However, if their partner or sperm/egg donor is also a carrier, there's a 25% chance that any pregnancy between them will have SMA. The image below shows how autosomal recessive inheritance works. The possible outcomes for a pregnancy are: 25% chance of having SMA, 50% chance of being a carrier, and 25% chance of not being a carrier or impacted by the condition.



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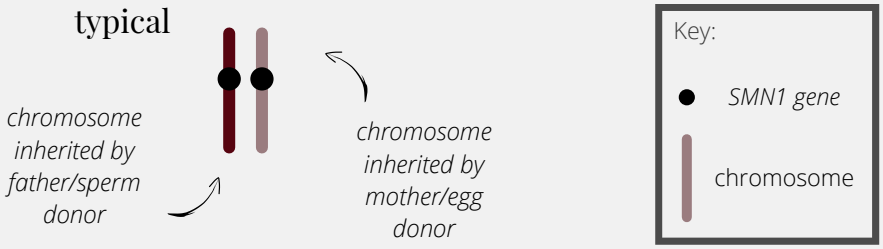
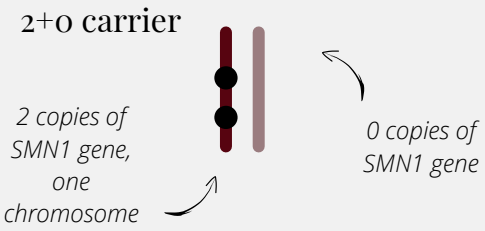
**Carrier Screening and Uncertainty:**
Carrier screening is a genetic test that helps identify individuals who carry a single copy of a gene variant associated with a specific condition. However, carrier screening reports may indicate an increased risk of being a carrier without providing certainty. This situation often arises when the screening identifies a person as a 2+0 carrier.

**What Does Being a 2+0 Carrier Mean?**
Being a 2+0 carrier means that a person has both copies of the SMN1 gene on one chromosome, instead of having one copy on each chromosome like most people. Our chromosomes are packages of genes, which are the instructions for our bodies. Typically, we inherit one copy of a gene on one chromosome from our father or sperm donor and the other copy of the gene on the another chromosome from our mother or egg donor.




Having two copies of the genes on one chromosome generally does not cause any health risks for the person themselves. However, if they decide to have children, there is a possibility that they could pass on the chromosome with zero copies of the SMN1 gene. If their partner is a carrier of spinal muscular atrophy (SMA), there would be a 25% chance of having a child with SMA.

Carrier screening tests may not always accurately determine if someone is truly a 2+0 carrier due to limitations in technology. However, these tests can look for a specific change in the DNA sequence called g.27134T>G. This change is usually harmless and does not cause any health concerns. The presence of this change may influence the likelihood of being a 2+0 carrier, which can vary depending on a person's ancestry.

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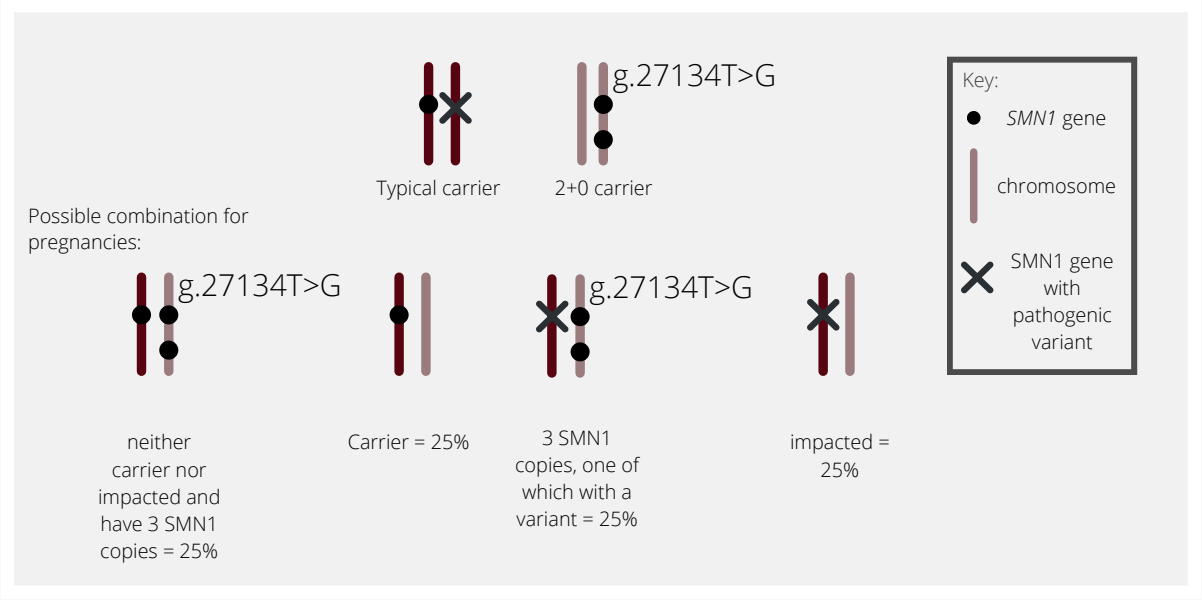
For a 2+0 carrier (someone with two copies of the SMN1 gene on one chromosome), and a typical carrier (someone with one normal copy of the gene and one copy with a variant), the possible pregnancy outcomes are shown below. A person can only pass on one chromosome to each pregnancy.




**Complications for PGT-M Indication:**
The uncertainty of carrier status poses challenges when considering preimplantation genetic testing for monogenic conditions (PGT-M). PGT-M is typically indicated when there is a confirmed risk of passing on a specific condition. However, in cases of 2+0 carriers, where carrier status is not definitively established, the indication for PGT-M becomes more complex.

In order to determine if someone is a 2+0 carrier, they could have their parents or children tested in order to figure out their status. If that testing shows they are 2+0 carriers, then PGT-M would likely be indicated, if they had a partner that is also a known carrier.

**Considerations and Consultation:**
If you have received a carrier screening report indicating a 2+0 carrier status for SMA, it is crucial to consult with a healthcare professional or genetic counselor. They can provide personalized guidance, explain the implications of your carrier status, and help navigate the decision-making process regarding PGT-M.

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