What is 5q Spinal Muscular Atrophy?

You can also read this guide on our website at smauk.org.uk/g9nt where you can follow all the links we give to further information.

Spinal Muscular Atrophy (SMA) is a rare, neuromuscular condition. It causes progressive muscle wasting (atrophy) and weakness. It may affect crawling and walking ability, arm, hand, head and neck movement, breathing and swallowing. There are several forms of SMA that have different genetic causes, and a wide spectrum of how severely children and adults are affected. The most common form is known as '5q SMA', which includes SMA Types 1, 2, 3 and 4. The term '5q' refers to its genetic cause.

This information sheet tells you more about:

- What causes 5q SMA.
- Types of 5q SMA.
- How it is diagnosed.
- Drug treatments, care and support.
- How it is inherited.
- How many people are affected.

For information about some of the rarer forms of SMA that have different genetic causes (non-5q SMA), see: **Rarer Forms of SMA >** .

1. What Causes 5q SMA?

- ## The *SMN1* gene[1]

5q SMA affects the nerve cells called lower motor neurons.

Lower motor neurons are found within the spinal cord. They receive electrical signals from the brain and transfer these signals to the muscles This leads to movement – such as crawling and walking.

In the same way, the lower motor neurons also carry signals to the muscles we use for breathing and swallowing.

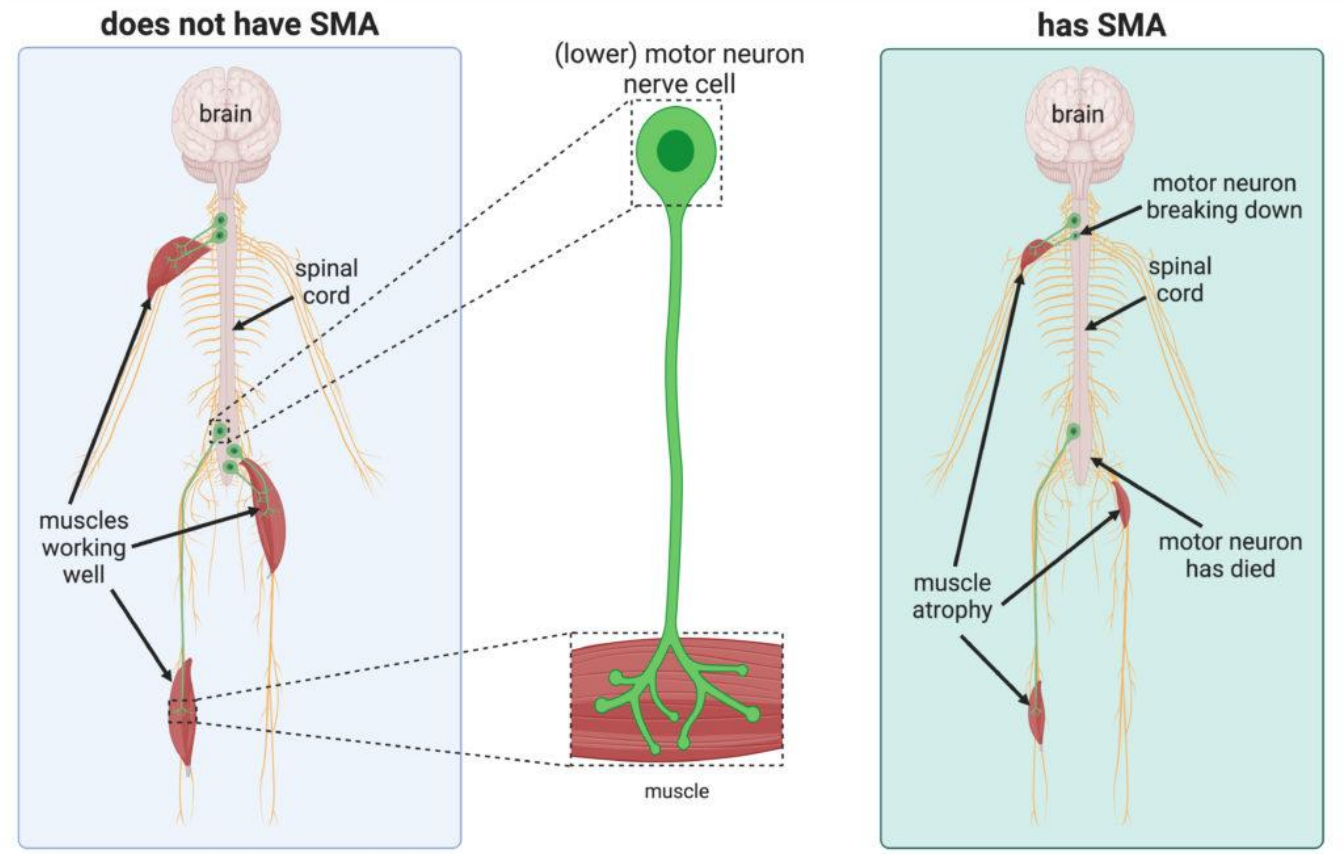
For these nerve cells to be healthy, our *Survival Motor Neuron 1* (*SMN1*) genes[1] must make enough Survival Motor Neuron (SMN) protein.

The *SMN1* gene is on chromosome 5 in the region labelled 'q'. This is why this form of SMA is called '**5q SMA'.**

For more information, see: The Genetics of 5q SMA >.

Most people have two copies of the *SMN1* gene. People with 5q SMA have two altered copies of the *SMN1* gene. They are unable to produce enough working (functional) SMN protein to have healthy lower motor neurons[2].

As a result, the lower motor neurons in the spinal cord deteriorate:

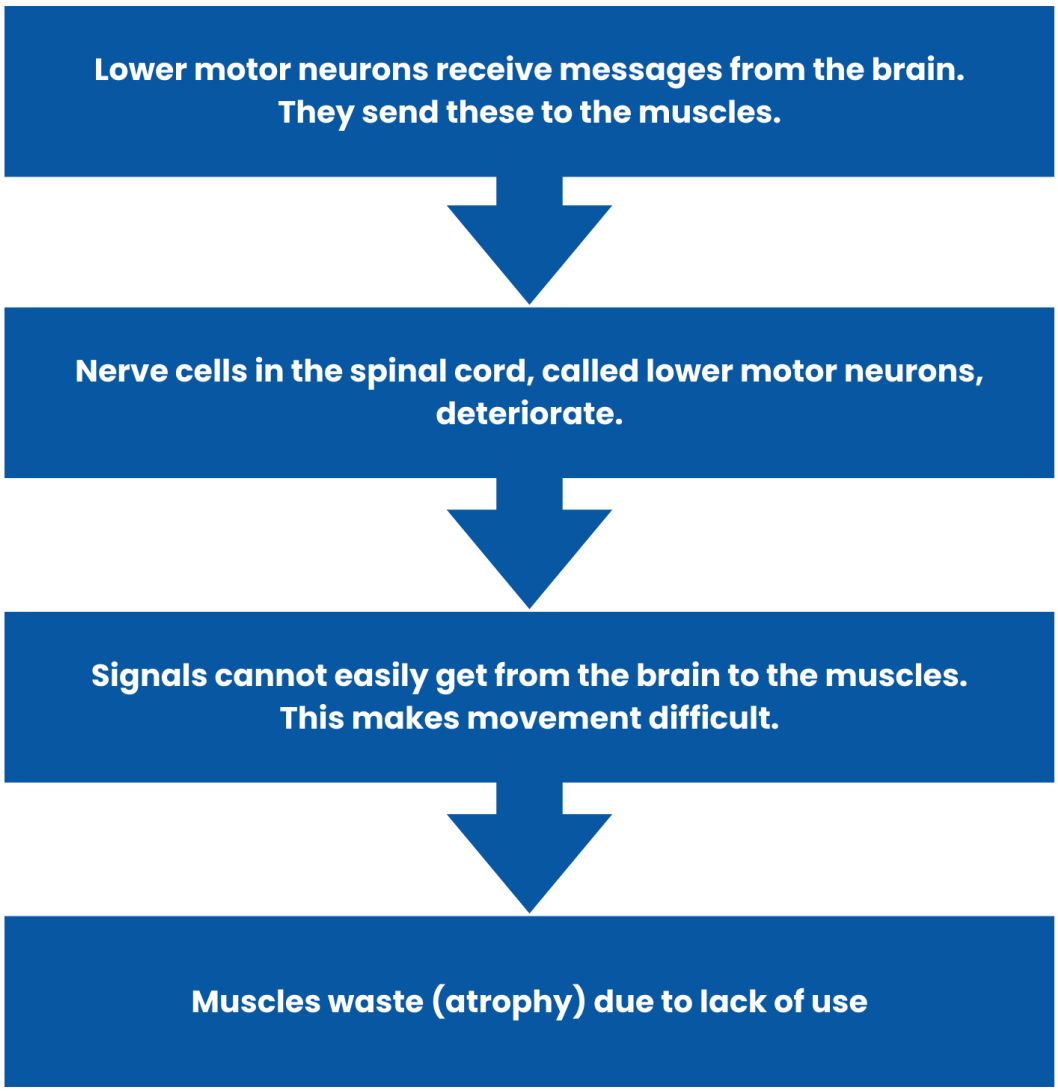


Adapted from Sleigh et al. (2023). Figure adapted with permission from Reference 3 under the CC BY 4.0 licence.

This means that signals are not effectively carried from the brain to the muscles. This makes movement difficult.

The muscles then waste due to a lack of use — this is known as muscular atrophy.

In summary:



- ## The *SMN2* gene[1]

A second gene is also able to make SMN protein. This is the *Survival Motor Neuron 2* gene (*SMN2*). It is sometimes called the SMA 'back-up' gene.

However, researchers have shown that only about 1 in 10 (10%) of the SMN protein made from *SMN2* works properly. The remaining 9 out of 10 (90%) of the protein made from *SMN2* is missing an essential part called Exon 7— so, it does not work[4].

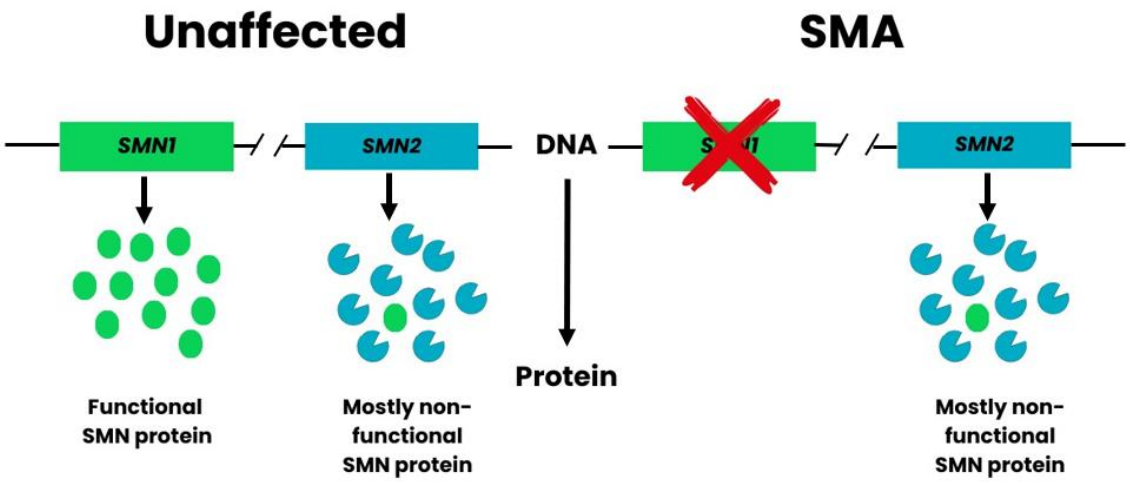


Figure adapted from Burghes, A.H. and Beattie, C.E[5]

However, researchers have shown that only about 1 in 10 (10%) of the SMN protein made from *SMN2* works properly. The remaining 9 out of 10 (90%) of the protein made from *SMN2* is missing an essential part — so, it does not work[3].

So, although *SMN2* can make some functional SMN protein, it cannot produce enough to fully make up for the altered *SMN1* gene in people with 5q SMA.

Unlike most genes, the number of copies of *SMN2* on each chromosome can vary from one person to the next[4]. There can be between 0 and 8 copies.

Looking across all people with 5q SMA, the severity of SMA is linked to SMN protein levels[4,5]. There is a general relationship between the number of *SMN2* copies and the likely severity of SMA symptoms.

Having more *SMN2* copies is generally associated with less severe SMA symptoms. However, a person's '*SMN2* copy number' does not fully predict their SMA type or severity[6,7]. This is likely to be because other genetic, and possibly environmental, factors have an influence on the condition.

Bearing this in mind, the following table gives a summary of:

- how many *SMN2* copies the majority of people with each Type of SMA may have (see 'usual number' column), *and*
- the possible range of copy numbers that people with each Type of SMA can have (see 'range' column).

SMA Type	Usual Age of Symptoms	SMN2 Copies	
		Usual number	Range
Type 1	Younger than 6 months	2	1 - 3
Type 2	6-18 months	3	2 - 4
Type 3a	Under 3 years	3	3 - 5
Type 3b	Over 3 years	4	
Type 4	Over 18 years	4 - 5	

Table adapted from Tillman et al 2018[9]

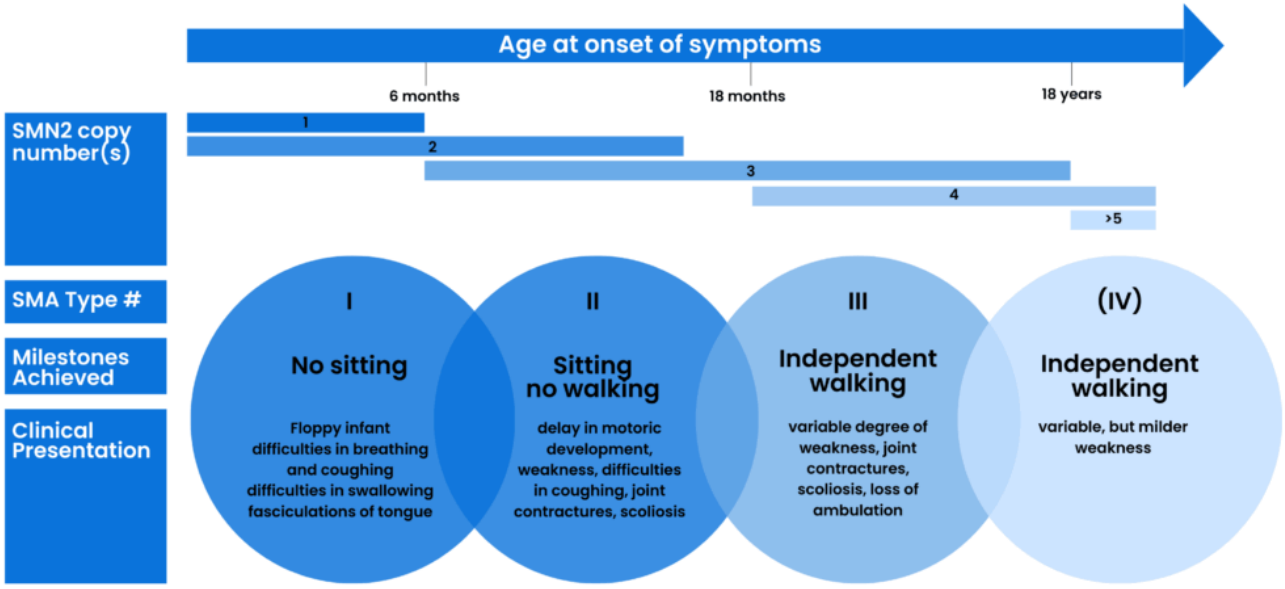
2. ‘Types’ of 5q SMA

Before the new drugs for 5q SMA were developed, clinicians studied the effects of SMA on people. This is called the **‘natural history**’ of the condition.

This led to 5q SMA being divided into four main Types of SMA: Types 1, 2, 3, and 4. Sometimes a baby is affected before birth; this is called Type 0.

These ‘Types’ of SMA are based on the age that symptoms begin, and what physical milestones (e.g. sitting, standing, walking) are achieved.

How severe and what impact SMA has varies from person to person, both within and between ‘Types’. Each child and adult is affected differently.



Clinical classification of SMA subtypes according to onset, milestones achieved, and clinical presentation. Typically associated *SMN2* copy numbers are shown. Figure taken with permission from Reference 10 under the CC BY-NC 4.0 licence .

This clinical classification system is still used in the UK for adults, teenagers and children living with SMA. For many, though, care and treatment are changing the outcome of their SMA.

3. How 5q SMA is Diagnosed

- ## Due to symptoms of SMA

SMA is confirmed via a test for the *SMN1* gene. The classification system of 'Type' is used when a baby, child, young person or adult shows symptoms.

Parents / carers will often have been concerned about symptoms of weakness in their child. Symptoms may have been noticed by doctors, the health visitor or community nurse.

Adults who are diagnosed with SMA Type 4 may have had concerns about their muscle weakness or fatigue.

A GP may have met few, or even no children or adults who have SMA. They should make an immediate referral to a **Regional (Specialist) Neuromuscular Centre >.**

A paediatrician or neurologist will then examine any child or adult with suspected SMA. They will also ask about their medical history and any concerns.

A blood sample is then taken for DNA (genetic) testing. This looks for a 'deletion mutation' in the *Survival Motor Neuron 1* (*SMN1*) gene on chromosome 5.

The result of the *SMN1* deletion test is usually available within 2 weeks though sometimes it can take longer.

At the same time, the number of copies of the *SMN2* gene (the back-up gene for *SMN1*) is also tested. Having more copies of the *SMN2* gene is generally associated with less severe symptoms of SMA.

- ## Due to newborn screening:

The UK screens for 9 rare conditions at birth. SMA is not currently one of them.

A newborn bloodspot screening test looks for the *SMN1* gene deletion and the number of copies of the *SMN2* gene. The number of *SMN2* copies indicates what symptoms and effects the baby's SMA would be likely to cause if they do not receive drug treatment and appropriate care. The baby may or may not be showing symptoms at this stage.

You can read more about the symptoms & effects or 'natural history' of the different Types of 5q SMA >.

The UK National Screening Committee (NSC) is responsible for assessing the evidence for national screening programmes and recommending which conditions should be screened for.

The NSC is developing an In-Service Evaluation (ISE) of newborn screening for SMA in the UK >

Some babies in the UK may be screened for SMA if:

- Their siblings have SMA
- They are part of the **Generation Research Study >**

4. Drug Treatments, Care and Support

There is no cure for SMA and until late 2019 there were no NHS-approved drug treatments specifically for SMA in the UK.

There are now three NHS-funded, disease-modifying drug treatments:

- **Spinraza™ / Nusinersen >**
- **Zolgensma™ / Onasemnogene Abeparvovec >**
- **Evrysdi™/ Risdiplam >**

These treatments are not suitable for everyone who has 5q SMA, but most people in the UK who have SMA Type 1, 2 or 3 can receive one of them. There have been no clinical trials of any of the treatments with people who have SMA Type 4.

These drugs can change what motor milestones babies and children may be able to achieve and improve their general health.

The treatments work best if started before there is any muscle weakness, or when this is minimal. It is therefore important for treatment to be started as soon as possible[10].

This is why clinicians and patient groups are calling for the earliest possible introduction of newborn screening for SMA in the UK. You can read about progress towards this on our page on **Newborn Screening for SMA >.**

For adults living with SMA, drug treatment that can stabilise the condition later in life may also make a positive difference – for example, helping with fatigue or preventing the loss of the ability to use a finger to control a powerchair or laptop.

For summaries about these NHS-funded drug treatments, see:

- **Drug Treatments for Children who have 5q SMA >**
- **Drug Treatments for Adults who have 5q SMA Type 1, 2 or 3 >**

Whatever the outcome, any of these drug treatments must be combined with the best supportive care and management of symptoms.

The **International Standards of Care for SMA' (SoC)[7,11] >** were agreed in 2017. They were summarised the following year in the **Family Guide >.** The recommended standards of care for children, young people and adults varied and were based on:

- whether they could sit, stand or walk
- whether their breathing was affected by their SMA
- what other daily living activities they could manage.

Though they are still important, these standards were written before the new disease-modifying drug treatments became more widely available.

This is why a 3-year project is now underway to update these standards for the UK. Clinicians and patient reps are reviewing all aspects of care and management.

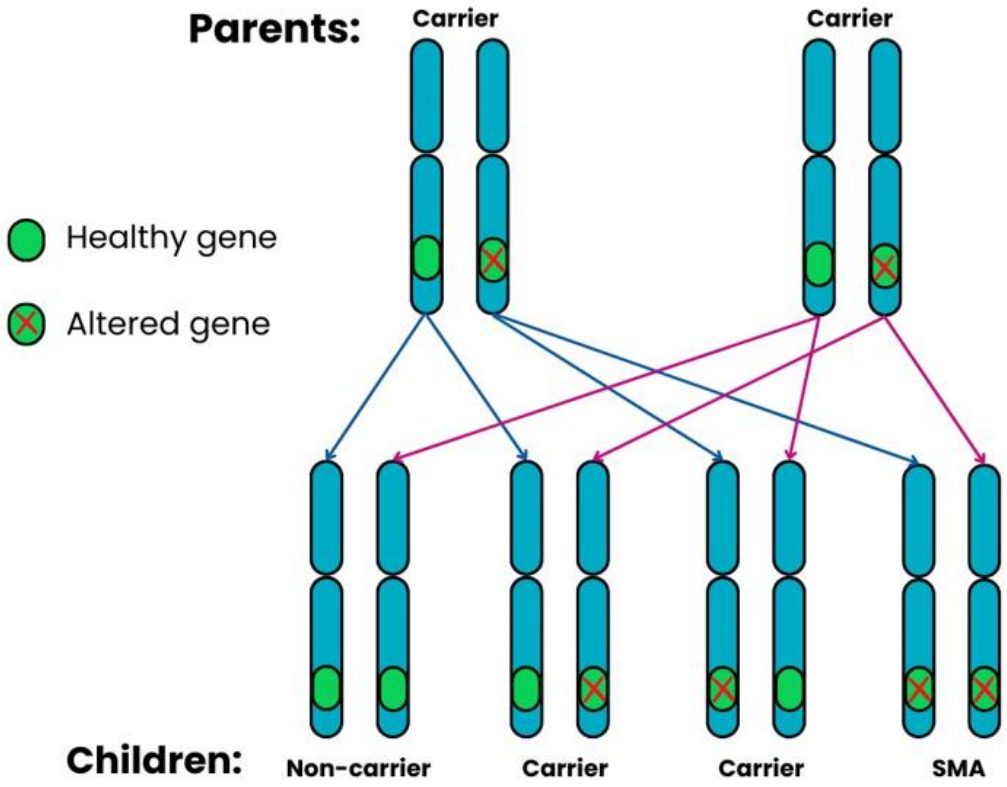
You can find out more and keep up to date with recommendations at SMA Care UK >.

5. How People Inherit 5q SMA

5q SMA is passed from parents to their children through altered *SMN1* genes. This usually follows an **autosomal, recessive pattern of inheritance**. It means that:

When two SMA **carriers** have a child together, for **each** pregnancy there is a:

- 1 in 4 (25%) chance that the child will inherit both altered copies of the *SMN1* gene and will have SMA.
- 2 in 4 (50%) chance that the child will inherit one altered copy and one healthy copy of the *SMN1* gene and will be a carrier.
- 1 in 4 (25%) chance that the child will inherit two healthy copies of the *SMN1* gene and will not be a carrier or have SMA.



A very small number of people develop 5q SMA despite standard carrier tests showing that one or both parents are not carriers. For example, for around 2 in every 100 (2%) people who have 5q SMA, the 'alteration' (when part of the DNA changes or is missing) has occurred for the first time.

It is important that all parents have genetic counselling, including anyone who is a 'non-carrier'. Genetic counselling explores each person's specific circumstances.

For more detailed information, please see: The Genetics of 5q SMA >.

5. How Many People are Affected by SMA?

- **Every month in the UK, 4 babies are born with 5q SMA.**

This is the **incidence** of SMA – the number of new people diagnosed with SMA at any one time.

Pooling all published newborn screening data has shown that **one in every 14,000 babies worldwide are born with a Type of 5q-linked SMA**[14,15].

In the UK in mid-2023, there were 664,400 live births [13]. This suggests that:

- approximately 47 babies were born who will develop a **Type of 5q SMA**
- approximately 28 of these babies (60%) would have the more severe SMA Type 1.

This would mean that every month in the UK, on average 4 babies are born with SMA.

Between 1st January 2019 and 1st November 2024, 507 children in the UK were registered in the SMA Research and Clinical Hub (REACH) UK database[17]. Of these

- **213 [42%] were diagnosed with SMA type 1**
- **188 [37%] were diagnosed with SMA type 2**
- **106 [21%] were diagnosed with SMA type 3[17].**

This suggests that approximately 85 babies with a type of 5q-linked SMA are born each year in the UK. This is approximately one baby born every 4 days.

Further UK population research will allow a more accurate measure of SMA incidence in the UK.

- **Global studies suggest that worldwide, between 1 and 2 people in every 100,000 have a Type of 5q SMA[12].**

This is the **prevalence** – how many people are living with SMA in a population at any one time.

In mid-2023, the UK population was approximately 68.3 million[13]. The global studies therefore suggest that:

- between 683 and 1,366 people have SMA in the UK at any one time.

There is no central information source, so the exact number is unknown.

However, these global studies were published before drug treatments became available. These treatments have had a life-saving impact for many children who have SMA Type 1 and have led to life-changing, healthier lives for many others.

It therefore seems reasonable to suggest that the SMA prevalent population will slowly increase year by year.

- **An estimated 1 in 40 people carry the SMN1 gene[12].**

  This means that although SMA is a rare condition, around 1.7 million people[13] in the UK are carriers of the altered *SMN1* gene.

6. Research and Further Developments

There is still a considerable amount of research into SMA taking place around the world, and there are more drugs being tested in clinical trials. This will continue to improve our understanding of SMA and the effects of, and responses people have to, the current treatments. It will also help with the further development of effective management and care.

To keep up to date with the latest developments in research and drug treatments, see **Treatments and Research >.**

7. References

1. Lefebvre S et al. (1995) Identification and characterization of a spinal muscular atrophy-determining gene. Cell 80: 155-165.

2. Lunn MR & Wang CH (2008) Spinal muscular atrophy. Lancet 371: 2120-2133.

3. Sleigh J et al. (2023) Spinal Muscular Atrophy: A Rare but Treatable Disease of the Nervous System. Frontiers for Young Minds 11:1023423 Under the CC BY 4.0 licence.

4. Ruggiu M et al. (2012) A role for SMN exon 7 splicing in the selective vulnerability of motor neurons in spinal muscular atrophy. Mol Cell Biol 32: 126-138.

5. Burghes, A.H. and Beattie, C.E. (2009) 'Spinal muscular atrophy: why do low levels of survival motor neuron protein make motor neurons sick?' *Nature Reviews Neuroscience*, 10, pp. 597-609.

6. Mailman MD et al. (2002). Molecular analysis of spinal muscular atrophy and modification of the phenotype by SMN2. Genet Med 4: 20-26.

7. Lefebvre S et al. (1997). Correlation between severity and SMN protein level in spinal muscular atrophy. Nat Genet 16: 265-269.

8. A Guide to the 2017 International Standards of Care for SMA >. (Last accessed: 21st October 2024).

9. Mercuri E et al. (2018) Diagnosis and management of spinal muscular atrophy: Part 1: recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. Neuromuscul Disord 28: 103-115.

10. Tillmann R et al. (2018) Spinal Muscular Atrophy (SMA) type 1, a changing phenotype: implications for motor function and physiotherapy management from the Nusinersen Expanded Access Program (EAP). APCP Journal 9: 4-12.

11. Schorling D *et al.* (2019) Advances in Treatment of Spinal Muscular Atrophy – New Phenotypes, New Challenges, New Implications for Care > *J Neuromuscul Dis* 7: 1-13, under the CC BY-NC 4.0 licence >.

12. Dangouloff T & Servais L (2019) Clinical evidence supporting early treatment of patients with spinal muscular atrophy: current perspectives. Ther Clin Risk Manag 15: 1153-1161.

13. Finkel RS et al. (2017) ENMC SMA Workshop Study Group. 218th ENMC International Workshop: Revisiting the consensus on standards of care in SMA Naarden, The Netherlands, 19-21 February 2016. Neuromuscul Disord 27: 596-605.

14. Finkel RS et al. (2018) Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics. Neuromuscul Disord 28: 197-207.

15. Verhaart IEC et al. (2017) Prevalence, incidence and carrier frequency of 5q–linked spinal muscular atrophy – a literature review. Orphanet J Rare Dis 12: 124.

16. Population estimates for the UK, England, Wales, Scotland and Northern Ireland: mid-2023 – published 8th October 2024 > (last accessed 21st October 2024)

17. Aragon-Gawinska et al. (2023) Spinal muscular atrophy treatment in patients identified by newborn screening—A systematic review. Genes 14: 1377.

18. Belter et al (2024) Newborn Screening and Birth Prevalence for Spinal Muscular Atrophy in the US" in JAMA Pediatrics on July 15, 2024.

19. Verhaart IEC, et al. (2017) A multi-source approach to determine SMA incidence and research ready population. J Neurol 264: 1465-1473.

20. Servais L et al. (2025) Spinal muscular atrophy in the UK: the human toll of slow decisions. Lancet (February 20, 2025.)

Version 15

Author: SMA UK Information Production Team

Last updated: June 2025

Next full review due: November 2027

Links last checked: November 2024

This publication, and its links, provides information. This is meant to support, not replace, clinical and professional care.

Find out more about how we produce our information .

If you have any feedback about this information, please do let us know at: information@smauk.org.uk .