

A Guide to the 2017
International Standards
of Care for SMA





CONTENTS

Chapter 1	5
Introduction	
Chapter 2	11
Genetics and diagnosis	
Chapter 3	18
Physiotherapy and Rehabilitation	
Chapter 4	24
Orthopaedic Management	
Chapter 5	29
Nutrition, Growth and Bone Health	
Chapter 6	33
Breathing (Respiratory and Pulmonary Care)	
Chapter 7	37
Other Organs and Systems	
Chapter 8	38
Medication	
Chapter 9	39
Emergency Care	
Chapter 10	41
Anaesthetics	
Chapter 11	42
Administration of new treatments for SMA	
Chapter 12	43
Ethics and Choices	
Useful Resources	44
Appendix	45
Reference List	47
Glossary	48



If you are a young person reading this guide **it might be helpful to speak to someone** who is familiar with the condition, such as your parent, carer or medical expert.

01

CHAPTER 1

INTRODUCTION

This guide is about the standards of care (SoC) for the most common form of spinal muscular atrophy (SMA), called 5q SMA (see Chapter 2, Genetics and Diagnosis). It is for both adults and young people who have 5q SMA and for parents and caregivers of children who have 5q SMA. Its aim is to give information about what care they may expect to receive, so that they can have active discussions with their medical team about how to best manage the condition, including possible options and choices.

The information and advice given is not intended to replace the services of your healthcare provider. If you are an adult who has SMA you should consult your healthcare provider about all matters relating to your health. Similarly, if you are a parent/carer reading this, you should consult your child's healthcare provider about all matters relating to their health, involving your child in discussions if age appropriate.

It may be helpful to have a copy of this guide to hand if at any time you need support from, or are having discussions with medical professionals who are not familiar with SMA. If you are a young person reading this guide it might be helpful to read it with someone who is familiar with the condition, such as your parent, carer or medical expert.

What is SMA?

Spinal Muscular Atrophy (SMA) is a rare, genetically inherited neuromuscular condition. It causes progressive muscle weakness and loss of movement due to muscle wasting (**atrophy**). This may affect crawling and walking ability, breathing and swallowing, and arm, hand, head and neck movement. There are different forms of SMA and a wide spectrum of how severely children, young people and adults are affected. The more common forms of SMA are broadly known as '5q SMA' and are often further described as a 'type' of SMA (see 'How to use this guide').



The group were aware that countries have different levels of resources so made recommendations based on the minimal care and support that anyone with SMA should receive wherever they live.

WHAT ARE THE STANDARDS OF CARE FOR SMA?

A committee of international healthcare and patient experts made recommendations for the care and management of children, young people, and adults with SMA. These were published for families in 2007 as the 'International Standards of Care for SMA'¹. Since then, there has been increasing evidence that people with SMA and their families can expect a better quality of life than was possible in the past, largely due to improvements in medical care and management.

It became clear that these improvements and changes in care and management practices were possibly no longer accurately reflected in the original standards. As management of SMA can require the expertise of many specialists, 26 experts and patient representatives from nine countries met during 2016 to work to update them². During this time, the first treatment for SMA, called Spinraza® (sometimes referred to by its

generic name, nusinersen), was approved in the USA. Though a significant achievement, such treatments are not a cure and must go hand in hand with best supportive care and management. Therefore, the need to update these guidelines became even more important.

Whether or not someone is receiving drug treatment, getting good supportive care right – including symptom management, mental and social well-being - is key to achieving the best possible quality of life.

The experts were divided into working groups according to their speciality area. Within their areas of expertise, they were tasked with looking at both the latest evidence and the views of specialists from around the world as to what care and management is best. They reviewed scientific publications and sought the opinions of many other international experts.

The group acknowledged there were limited studies that related to adults with SMA but that many of the discussions and recommendations applied to best supportive care for both children and adults. The key to the most appropriate intervention and care depended critically on the child's, young person's or adult's 'functional ability' – whether they could sit, stand or walk; whether their breathing was affected by their SMA; what other daily living activities they could manage. These SoC are therefore for all ages. However, it was agreed there needs to be more work focusing on understanding the impact of SMA over a person's lifetime and the implications of this for adult supportive care. There are already initiatives underway or being planned in many countries to help with this which will lead to the evolution of future SoC.

The group were aware that countries have different levels of resources so made recommendations based on the minimal care and support that anyone with SMA should receive, wherever they live.

In November 2017, following these meetings and discussions, two scientific articles were published with the updated guidance^{3,4}. These were written for medical professionals and contained a lot of complex medical terms and detail for them to refer to in their day-to-day care for people with SMA.



The 2017 Scientific Articles

- **Diagnosis and management of spinal muscular atrophy: Part 1:** Recommendations for diagnosis, rehabilitation, orthopaedic and nutritional care
- **Diagnosis and management of spinal muscular atrophy: Part 2:** Pulmonary and acute care; medications, supplements and immunisations; other organ systems; and ethics

WHAT IS IN THIS GUIDE?

To make the updated standards of care more accessible, TREAT-NMD worked with a number of international patient advocacy and support groups to develop this guide.

Advocacy websites

- ◆ **Spinal Muscular Atrophy UK**
www.smauk.org.uk
- ◆ **Cure SMA**
www.curesma.org
- ◆ **SMA Europe**
www.sma-europe.eu
- ◆ **Muscular Dystrophy UK**
www.musculardystrophyuk.org
- ◆ **TREAT-NMD Alliance**
www.treat-nmd.org

We have tried our best to explain medical terms in the text as clearly as possible. Where the words appear in **this colour**, the explanation can be found in the glossary. The guide has been checked for accuracy by medical specialists who were the authors of the November 2017 scientific articles.

The guide has been **checked for accuracy by medical specialists** who were the authors of the November 2017 scientific articles.



HOW TO USE THE GUIDE

The guide is divided into chapters; each chapter focuses on a specific aspect of SMA management, how and when this should be assessed, and the options for intervention. You will see within each chapter there are often different care and management guidelines and options based on physical milestones or type of SMA, as described below. As SMA affects each person differently, not all options may be appropriate for every individual.

The most common form of SMA is broadly known as ‘5q SMA’ and is often further described or classified as a type of SMA according to the age of onset of symptoms and the physical milestones reached:

Table 1. Clinical classification for SMA (Table adapted from RS Finkel et al, 2017, p.597)

SMA type	Usual age of symptoms onset	Impact of muscle weakness on sitting / walking
Type 1	Younger than 6 months	Unable to sit or roll independently
Type 2	7 months – 18 months	Able to sit but not walk independently
Type 3a	18 months – 36 months	Able to walk, though may lose this ability over time
Type 3b	3 years – 18 years	Able to walk, though may lose this ability over time
Type 4	Over 18 years	Mild walking (motor) difficulties

It is important to remember, however, that there are no distinct lines that distinguish the childhood onset types of SMA from each other and that the impact of 5q SMA varies greatly between individuals, just as it does in the adult onset form. Additionally, now that some individuals are receiving drug treatments, there may be even greater variation in the impact. It has therefore become important when discussing care and management, to look not only at the clinical classification of the person’s SMA, but also at what physical milestones they have reached. These may or may not be the same as in the above table.

It's important to always remember that the guidance is general, and every child, young person and adult is different. What is an appropriate intervention for one may not be appropriate for another.



HOW TO USE THE GUIDE

In this guide, for simplicity you will find the following summary words used to show which care and management guideline applies to which groups of children and adults:

non-sitters	those who are unable to sit
sitters	those who are able to sit but not walk
walkers	those who are able to walk

Guidance may also refer to the type of SMA as in table 1 or refer to 'early onset' SMA. This is when symptoms start before six months of age; typically those with 'early onset' are non-sitters. 'Later onset' SMA refers to symptom onset after six months of age; typically those with later onset include both sitters and walkers.

When you are discussing the management of SMA with healthcare professionals, it may be helpful to ask them what chapter you need to refer to in the family guide.

02

CHAPTER 2 GENETICS AND DIAGNOSIS

◆ THE *SMN1* GENE

Most people have two copies of the **survival motor neuron 1 (*SMN1*) gene** - one inherited from each parent. These genes contain the information needed to make the SMN protein that keeps the lower **motor neurons** in the spinal cord healthy. People with 5q SMA have a fault or **mutation** in both copies of their *SMN1* gene which means they are unable to produce the SMN protein they need. Without this, the lower **motor neurons** deteriorate which restricts their ability to carry electrical signals from the brain to move the muscles that are affected in SMA. This causes muscle weakness which can affect movement, breathing and swallowing.

The *SMN1* gene is on the fifth **chromosome** in the region labelled as 'q' which is why the main types of SMA are often referred to as 5q SMA.

◆ THE *SMN2* GENE

Another **gene** also has a role in producing SMN protein. This is the **survival motor neuron 2 (*SMN2*) gene**, sometimes referred to as the SMA "back-up **gene**". However, most of the SMN protein produced by *SMN2* lacks a key building block that is usually produced by *SMN1*. This means that while *SMN2* can make some functional SMN protein, it cannot fully make up for the faulty *SMN1* gene in people with SMA. The number of copies of *SMN2* can vary from one person to the next and can range from zero to eight. Having more *SMN2* copies is generally associated with less severe SMA symptoms. Table 2 shows the **generally expected** number of *SMN2* copies associated with each type of SMA. However, accurate predictions cannot be made about the severity of SMA based on the *SMN2* copy number alone. This is likely to be due to other genetic factors that affect how much SMN protein is produced by the *SMN2* gene(s).

Table 2. The number of *SMN2* copies generally associated with SMA type.

SMA type	Number of <i>SMN2</i> copies carried by the majority of people with SMA
1	2
2	3
3a	3
3b	4
4	4-6

The *SMN1* gene is on the fifth **chromosome** in the region labelled as 'q' which is why the main types of SMA are often referred to as 5q SMA.

If you would like to read more information about how a person may inherit SMA please go to “Appendix 1”.

You may also like to visit the “Useful Resources” section which lists the patient organisations available in various countries.

HOW 5q SMA IS INHERITED

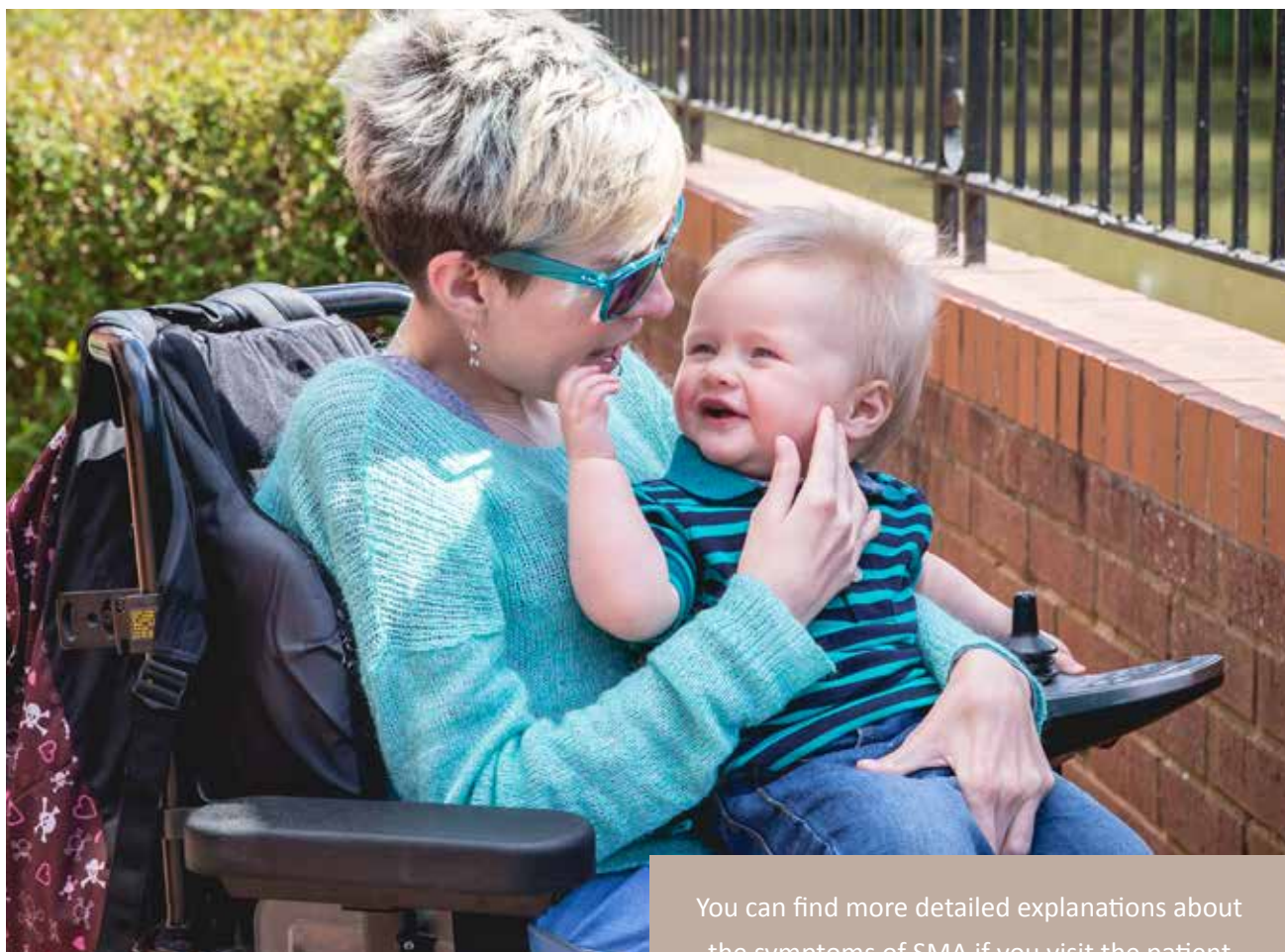
5q SMA is passed from parents to their children through faulty *SMN1* **genes**. It usually follows an **autosomal recessive** pattern of inheritance which means it is passed from parents to their children through faulty *SMN1* **genes**. This means that:

- ◆ People who inherit two faulty copies of the *SMN1* **gene** (one from each parent) have SMA.
- ◆ People who inherit one faulty copy and one healthy copy of the *SMN1* **gene** (one from each parent) are **carriers** of SMA. Around 1 in 40 people are **carriers** of SMA; **carriers** do not have SMA or any symptoms of SMA.
- ◆ People who inherit two healthy copies of the *SMN1* **gene** (one from each parent) do not have SMA and are not **Carriers**.

Though most inherit SMA from both parents, for around 2% of people the **mutation** is new, most likely due to an error in the **DNA** of the egg or sperm cell from which they were conceived. This is called a **de novo mutation**.

It is important that family members understand the results of the genetic testing that has led to the diagnosis of SMA. Genetic counselling should take place with a healthcare professional who has expert training in genetics. They will answer any questions families may have about the genetic aspects of the diagnosis and provide information on the possible options for future pregnancies.

If you would like to read more information about genetics and how a person may inherit SMA, please go to the inheritance page we have provided in addition to this chapter (see “Appendix 1”). You may also like to visit the “Useful Resources” section which lists patient organisations available in various countries.



You can find more detailed explanations about the symptoms of SMA if you visit the patient organisation website(s) listed in the “Useful Resources” section at the end of this guide.

SYMPTOMS

The journey to a diagnosis for a child is usually triggered by a parent or healthcare professional.

In the more severe early onset form, SMA type 1 (non-sitters), parents and carers usually become worried about their infant’s floppiness (low muscle tone) and difficulty achieving physical milestones. Low muscle tone affects their child’s leg muscles more than their arms. It is also common for an infant to have feeding difficulties due to their weak swallowing muscles. Similarly, they often have breathing problems due to their weak breathing muscles.

Children with SMA type 2 (sitters), though not as severely affected as those with SMA type 1, also show signs of having muscle weakness in their legs more than their arms. Their swallowing and breathing muscles may or may not show signs of being affected.

Children with SMA type 3 (walkers) also show symptoms of leg rather than arm weakness. As their swallowing and breathing muscles are not usually affected, they do not tend to have swallowing and breathing symptoms.

Adults with adult onset SMA type 4 (walkers) usually experience first symptoms of muscle discomfort and/or pain. As their swallowing and breathing muscles are not usually affected, they do not usually have swallowing and breathing symptoms.

You can find more detailed explanations about the symptoms of SMA if you visit the patient organisation website(s) listed in the “Useful Resources” section at the end of this guide.



CONFIRMING A DIAGNOSIS

If a doctor thinks a child or adult has symptoms that suggest they may have SMA, they will arrange for a blood sample to be taken and sent for the **SMN1 gene deletion test**. If the test shows that both copies of the **SMN1 gene** have the deletion fault, a diagnosis of 5q SMA will be given. It is now recommended that the number of **SMN2** copies is also counted as this can be a helpful indicator of how the condition will affect them in the future (their prognosis), which will in turn guide best care and management. This is also helpful as clinical trials of new treatments often have entry criteria that specify the number of **SMN2** copies someone must have to take part.

If the test comes back and only one copy of the **SMN1 gene** appears to have a fault but the

symptoms still suggest SMA, further in-depth genetic testing is recommended via a process called **SMN1 gene sequencing**. This looks for single, subtle mutations in the **gene** which if found, confirm a diagnosis of 5q SMA. If both copies of **SMN1** are present and not faulty it is very unlikely that SMA is causing the symptoms. Other tests will be needed to make a diagnosis.

Other tests, such as surgically taking a small sample of muscle (**muscle biopsy**) and tests of nerve function, are **not** needed to diagnose 5q SMA. However, further tests may be needed for those with later onset SMA as symptoms may be subtler and more difficult to diagnose. For example, a blood test which looks at muscle **enzyme (creatine kinase or CK)** may be done.

RECEIVING THE DIAGNOSIS

A diagnosis of SMA should be given sensitively, in person, by a geneticist or neurologist. During this first meeting the discussion should include:

- ◆ What has caused the condition
- ◆ How the condition usually progresses
- ◆ How it is likely to affect your child with SMA or you as an adult with SMA and the impact this may have on the family
- ◆ What, if any, treatment options are available
- ◆ Discussion about appropriate symptom management options

It is especially important that psychological and emotional support is provided at this time as well as in the future.

The doctor giving the diagnosis should also inform the family doctor and local medical team about the diagnosis and advise them about the correct management of SMA.

It's especially important that psychological and emotional support is provided at this time, as well as in the future.



SETTING UP CARE AND SUPPORT

SMA is a complex condition which affects people differently. Best management requires input from many different health specialists (Fig.1). Anyone diagnosed with SMA should be referred to a specialist neuromuscular clinic, and other relevant specialties. These may include specialists in:

- ◆ Breathing (respiratory care)
- ◆ Nutrition (gastroenterology and dietetics)
- ◆ Bones and muscles (orthopaedic care)
- ◆ Rehabilitation (physiotherapists (PT) and occupational therapists (OT))

Families and adults affected by SMA should also be provided with genetic counselling.



Figure 1.

The multidisciplinary expertise and type of care someone with SMA might receive (adapted from E. Mercuri et al, 2018, p.106.)

Specialists should work together as a multidisciplinary team who will not only consider your or your child's medical needs but also take into account and be respectful of any social, cultural and spiritual needs you may have. The team may also include specialists in **palliative care** who have expertise in the control of complex symptoms. **Palliative care** is often only associated with end of life care when in practice it has a much broader focus to help a person achieve good quality of life.

Palliative care teams are there to help ensure a person's life goals match treatment choices and to provide help to overcome challenges, it should be seen as a complementary service to other forms of medical support.

Soon after diagnosis you should discuss care options in open consultation with your multi-disciplinary medical team. This should be an ongoing basis. Choices for or against interventional care should be revisited with changing circumstances if you or the medical team think it appropriate.

It is recommended that all care assessments and visits should be co-ordinated by one of the medical team who is knowledgeable about the possible progression and potential challenges of SMA, this is generally the neurologist, paediatric neurologist or in some centres a 'care-coordinator'.

You should also be given information so that you have the option of:

- ◆ Contacting SMA-related support and advocacy groups
- ◆ Accessing trusted online resources for more information about management and care
- ◆ Discussing any clinical trials that may be appropriate





CHAPTER 3

03 PHYSIOTHERAPY AND REHABILITATION

This section looks at ways physiotherapy can be used to assist a person achieve or maintain their functional ability so they can have a good quality of life. The term functional ability can be used to explain someone's ability to perform daily activities and tasks like sitting up, using the toilet, getting dressed, eating, or climbing the stairs.

Tightening of joints (**contractures**) is commonly seen in people who have SMA and it can lead to pain and difficulty moving. Areas of the body usually affected are the shoulders, elbows, wrists, fingers, hips, knees, ankles and feet. **Contractures** and other effects of SMA can be alleviated by having regular access to physiotherapy sessions. Whatever the impact of their SMA, children, young people and adults should be given support, advice and equipment

so that they can do as much as possible for themselves. You can generally expect a physiotherapist (PT) and occupational therapist (OT) to design and demonstrate appropriate individualised exercises. They will also advise or provide equipment and adaptations to make mobility activities and daily living easier. Families and adults are usually shown how to assist with stretches and exercises and use equipment so that regular physiotherapy can be fitted into daily routines.

Throughout this section as we outline the SoC recommendations, we also include the SoC's prescriptive information about how long orthoses should be worn and how often stretches should be carried out. Always remember a PT or specialist will be able to provide you with an individualised plan.

NON-SITTERS

Physiotherapy and rehabilitation for non-sitters aims to reduce the impact of tight joints, optimise function, and help people tolerate different positions such as being on their back, side or sitting with assistance. When a PT or OT provides recommendations, they should give guidance and provide training where appropriate.

◆ Positioning

Different supports such as rolls, wedges, beanbags and pillows will help support non-sitters when lying on their back, side or in a sitting position.

Custom-made seats and sleep systems are recommended together with power chairs or strollers that allow a reclined or tilting position.



◆ Stretching

It is important that everyone with SMA has as much flexibility in their joints as possible to achieve or maintain independence. Stretching muscles that are usually tight is recommended.

Not all of these options are appropriate for everyone, but possibilities include:

Assisted stretches – when someone helps with the movement. The recommended minimum number of times per week is three to five sessions.

Splints - which support or immobilise a limb or the spine. Arm splints can assist with movement but still allow joint flexibility. To be effective at improving flexibility, splints should be applied for more than 60 minutes or overnight.

Serial casting - which puts the limb into a series of plaster casts over a period of time, slowly correcting the position with each re-casting.

Braces - which are similar to splints and are used to support part of the body to help stabilise and promote movement. For these to be effective, they have to be used at least five times per week.

Neck collars - can be helpful for head support and a good neck position that can assist with breathing.

Standing frames - are an assistive aid used to support people safely in an upright 'standing' position. They can be used to help maintain or improve posture, bone health (**bone mineral density, BMD**) and digestion. These aids are not suitable for everyone and should only be used if advised by a PT.

Exercise and physical movement can be a challenge for some non-sitters - **activities in water can be helpful, if the head is supported and there is appropriate supervision.** Your PT or OT can advise on this.

◆ Mobility and Exercise

Equipment and technology may be used to help with movement. Exercise and physical movement can be a challenge for some non-sitters - activities in water can be helpful, if the head is supported and there is appropriate supervision. A PT or OT can advise on this.

Regular use of different techniques and devices to maximise breathing ability and remove secretions is very important. Chest physiotherapy is especially important during illness or before surgery (see Chapter 6, Breathing (Respiratory and Pulmonary Care)).

◆ Communication

A good example of technology that can be used to aid communication and increase independence is an 'eye tracking device'. This enables a person to use their eye gaze as a way of giving instructions via a computer screen.



SITTERS

For sitters, the main objectives are to reduce the impact of tight joints keeping them flexible and to prevent curving of the spine (**scoliosis**), as well as maintaining a range of movement, which will help increase independence when carrying out day-to-day activities. A PT or OT should give guidance and training on how to achieve these aims using the following techniques:

◆ Positioning

Orthoses are external devices which support the arms, legs or spine to prevent or assist movement to achieve activities such as standing and supported walking. They include:

Braces - which are recommended to support and stabilise the spine and braces to help with arm movement. For these to be effective, they have to be used for a minimum of five times per week

Splints and braces - which can be used to keep joints in certain positions. To be effective, they should be worn for 60 minutes or, if appropriate, overnight.

Neck support - which may be helpful when travelling.

Supported standing - which stretches the legs, promotes a better posture, increases

bone density, blood circulation and eases constipation. This should be for up to 60 minutes for a minimum of three to five times a week but five to seven times a week is best and recommended.

◆ Stretching

Exercises aimed at muscles that are 'tight' can be done with assistance and may be helped by using splints, standing frames and orthoses that help with position.

It's important to be consistent in stretching. Combining effective stretches with splints and standing exercise is crucial. The routine should be adapted individually by a PT or OT. To be effective, stretching is recommended more than five to seven times per week.

◆ Mobility and exercise

All sitters should have a powered wheelchair with custom seating systems that meet their individual needs. Children usually have the cognitive and physical capabilities to use a powered wheelchair before they reach two years old so it is beneficial to carry out an assessment before the age of two.

Those who are stronger may prefer a lightweight manual wheelchair or perhaps one with power-assisted wheels which could enable greater independence.

Exercise should be encouraged for its many benefits such as maintaining and improving strength, flexibility, endurance and balance. It may also improve participation in school, college, work, leisure and social activities. Exercises should be performed in different ways; this can include exercise which involves lifting increasing weight (resistance training), swimming, physiotherapy that involves horse riding (**hippotherapy**), and wheelchair sports which are all enjoyable ways to exercise. A PT can advise on these.

As with non-sitters, different techniques and aids can be used to help maintain breathing and reduce secretions (see Chapter 6, Breathing (Respiratory and Pulmonary Care)). This is particularly important during any episodes of illness and before surgery.



The main aims for sitters are to reduce the impact of tight joints keeping them flexible, prevent curving of the spine (scoliosis), as well as maintaining a range of movement, which will help increase independence when carrying out day-to-day activities.

WALKERS

For walkers, the aim is to maintain and promote maximum mobility, overall range of movement, and as much independence as possible with day-to-day activities. To achieve this, it is important to work on flexibility, strength, endurance and balance. A PT or OT should discuss this, give guidance and provide appropriate training. They may advise the following ways to achieve these aims:

◆ Stretching

Stretches should be part of the exercise programme to preserve flexibility of joints, especially ankles and knees. These can be done with assistance or independently. Splints can also be used to prolong stretches and help with this. The minimum frequency for stretches is two to three times a week with the best option being three to five times a week.

◆ Positioning

Lower limb **orthoses** (splints) can be used to maintain flexibility, posture and function at the ankle and knee. Braces worn around the chest and spine can be used to promote posture when sitting but use is not recommended when walking.

◆ Mobility and exercise

Lightweight manual wheelchairs or ones with power-assisted wheels may be useful due to the tiring effort it takes to walk. Powered wheelchairs or scooters may be helpful for longer distances.

Exercise programmes that focus on strength, endurance, flexibility and balance will be beneficial. The SoC recommend aerobic exercise, swimming, walking, cycling, yoga, rowing, elliptical/cross trainers, and a type of physiotherapy that involves horse riding (**hippotherapy**), as good ways to take exercise.

A PT should advise you about how often and how long to exercise.



SMA commonly causes people to have bone and muscle (orthopaedic) problems. These can include problems with the spine, hips, joints and bones.

04 CHAPTER 4 ORTHOPAEDIC MANAGEMENT

SMA commonly causes people to have bone and muscle (orthopaedic) problems. These can include problems with the spine, hips, joints and bones. Irrespective of drug or other treatments, all with SMA (sitters, non-sitters and walkers), should have regular assessments and reviews by trained team members such as an orthopaedic consultant, physiotherapist (PT) or occupational therapist (OT). This should allow for any issues to be managed in a way that will help with achieving or maintaining movement and well-being.

IMPACT ON THE SPINE

SMA can weaken the muscles that support the spine and without this support, the spine can be pulled by gravity and curve. It is estimated that as they grow, 60-90% of non-sitters and sitters develop a spinal curvature, as do 50% of walkers.

When the spine curves sideways into a “C” or “S” shape it is called a **scoliosis**. When the spine bends forward it is called a **kyphosis**. At the same time as the spine curves, there are changes to the chest wall and rib cage which reduce the space available for the lungs to grow and for breathing. Therefore, it is important to monitor everyone who has childhood onset SMA for the possibility of **scoliosis**. Spinal

curvature is best monitored by an **x-ray** of the individual’s whole spine so the curve can be measured. The measurement used is called the **Cobb angle**. For those who can sit or walk, the **x-ray** is taken in the most upright sitting or standing position they can manage. Those who are non-sitters should have their **x-ray** while they are lying flat. Non-sitters and sitters with a **Cobb angle** greater than 20° should be rechecked every six months until their bones are no longer growing, which is when they reach what is known as **skeletal maturity**. After that they should be checked every year, as spinal curvature can still progress into adulthood.

MANAGING SCOLIOSIS

Non-sitters

To try to prevent **scoliosis** and to assist with sitting or being in a more upright position, children who are non-sitters may find it helpful and will generally be more comfortable if they wear a spinal brace during the day. The brace should be custom-made and fitted by a specialist (an **orthotist**) so that it goes around the back and chest and fits comfortably.

Sitters

Anyone with a **scoliosis** over 20° may be provided with a spinal brace or body jacket, also called a TLSO (**thoraco-lumbar sacral orthosis**) to provide corrective support when in an upright sitting position; wearing this will not stop the further possible development of spinal curvature. Spinal braces are recommended for children who still have lots of growing to do; a soft or semi-rigid spinal **orthosis** is recommended. A brace helps to relieve pain, provide stability and may slow curve progression.

There may come a point when spinal surgery to straighten the spine is advised. This is to help with balance when sitting as well as allowing the lungs to expand more fully and so improve breathing. If this is being considered, there should be plenty of time to talk with the multidisciplinary medical team about the options and what is involved.

A recommendation to have spinal surgery is based on a number of factors. Most importantly

these are when the spinal curve **Cobb angle** has progressed to 50° or more and when the curve is increasing by 10° or more each year.

When discussing the possibility of surgery, other factors that will be assessed and considered include:

- ◆ Age in years and months (chronological age) and whether bones and skeleton are fully grown (**skeletal maturity**). Since skeletal age and actual age often don't match, **skeletal maturity** can be estimated by taking an **X-ray** of the bones in the left wrist
- ◆ How much breathing ability has decreased
- ◆ If the chest wall shape has changed or ribs are collapsing
- ◆ If the curve is causing problems with day-to-day activities
- ◆ If there is persistent back and hip pain
- ◆ If hips and pelvis are positioned unevenly, making sitting in a balanced way difficult

There are two types of spinal surgery:

Spinal fusion involves straightening the spine by attaching two metal rods, one on each side of the spine, to many bones of the spine (**vertebrae**) and ribs along the spinal curve. This is to correct the curve and support the spine against gravity. In addition, the **vertebrae** are fused together to provide additional support.

‘Growth friendly’ spinal surgery is recommended for children less than 10 years old who have significant spine and rib cage growth remaining. The spinal rods are only anchored to the spine or ribs at the top and bottom of the curve, leaving the spine segments and ribs in-between untouched to allow for continued growth. The spinal curve is straightened as much as possible when the rods are placed, then every two to six months the rods supporting the spine are gradually lengthened. This procedure allows for continued spine and chest growth. New technologies are becoming available for growth-friendly spinal surgery, for example magnetically controlled growing rods may be available which allow for lengthening without the need of repeated surgery.

Before any operation, the multidisciplinary medical team should carry out a full evaluation of health and well-being. This includes any weight or dietary challenges, bone health and breathing ability, and any need for support with breathing during surgery. So that decision making is shared, the team should have an in-depth discussion about the risks and benefits of the procedure. The medical team that will be involved should have a plan for how breathing will be managed after the operation.

Recommended age of spinal interventions:

The SoC recommendations to medical teams vary depending on age and are as follows:

- **Under 4 years:** in general, spinal surgery should be delayed until after four years of age.
- **Age 4 – 10 years:** As children are skeletally immature, growth-friendly spinal surgery is recommended.
- **Age 10 – 12 years:** At this age children are transitioning to **skeletal maturity**. If surgery is needed, the type will depend on the child’s **skeletal maturity** and how much more their spine is likely to grow.
- **Age over 12 years:** This is when children are **skeletally mature**. If surgery is needed, spinal fusion surgery is recommended.

Experts advise that any future spinal surgery should leave an unfused area in the middle of the lower back (mid-lumbar) to allow for the administration of therapies, such as Spinraza®, that are injected via a needle directly into the spinal canal (intrathecally) (see Chapter 11, Administration of New Treatments for SMA).

New technologies are becoming available for growth friendly spine surgery, for example magnetically controlled growing rods may be available; these allow for lengthening without the need of repeated surgery



Impact on the hips

It is common for non-sitters and sitters to have unstable hips which may affect one hip or both. If someone can stand, manage assisted transfers and/or walk, and their hip instability is interfering with these activities or causing pain, surgical hip reconstruction to stabilise a dislocated or partly dislocated hip is recommended. Surgical stabilisation is also recommended for non-walkers if they have persistent pain or their limited hip mobility makes managing any activities such as eating, going to the toilet, dressing or sitting, difficult.

Impact on the joints

Tightening of joints (**contractures**) is a common problem which can lead to pain and difficulty moving. Physiotherapy and splints are recommended to help manage this (see Chapter 3, Physiotherapy and Rehabilitation). Surgical intervention should only be considered when **contractures** cause pain or limit the ability to move and use the joint.

Impact on the bones

Non-sitters and sitters are at higher risk of bone fracture due to osteoporosis from not standing (bearing weight) and not using the bones and muscles. It is important to make sure that children and adults with SMA have enough dietary calcium and vitamin D3 (see Chapter 5, Nutrition, Growth and Bone Health).

If a bone is fractured, the SoC advise medical teams:

For sitters and non-sitters	For walkers
<ul style="list-style-type: none">• Avoid using a plaster cast which restricts movement for longer than four weeks.• Avoid surgery whenever possible and perhaps instead use a cast.	<ul style="list-style-type: none">• Consider surgery if someone is usually able to walk and has fractured their leg bone.• Consider surgery using rods or plates if someone can't usually walk and has fractured their hip. This can speed up healing of the fracture and gives the greatest chance of maintaining movement.

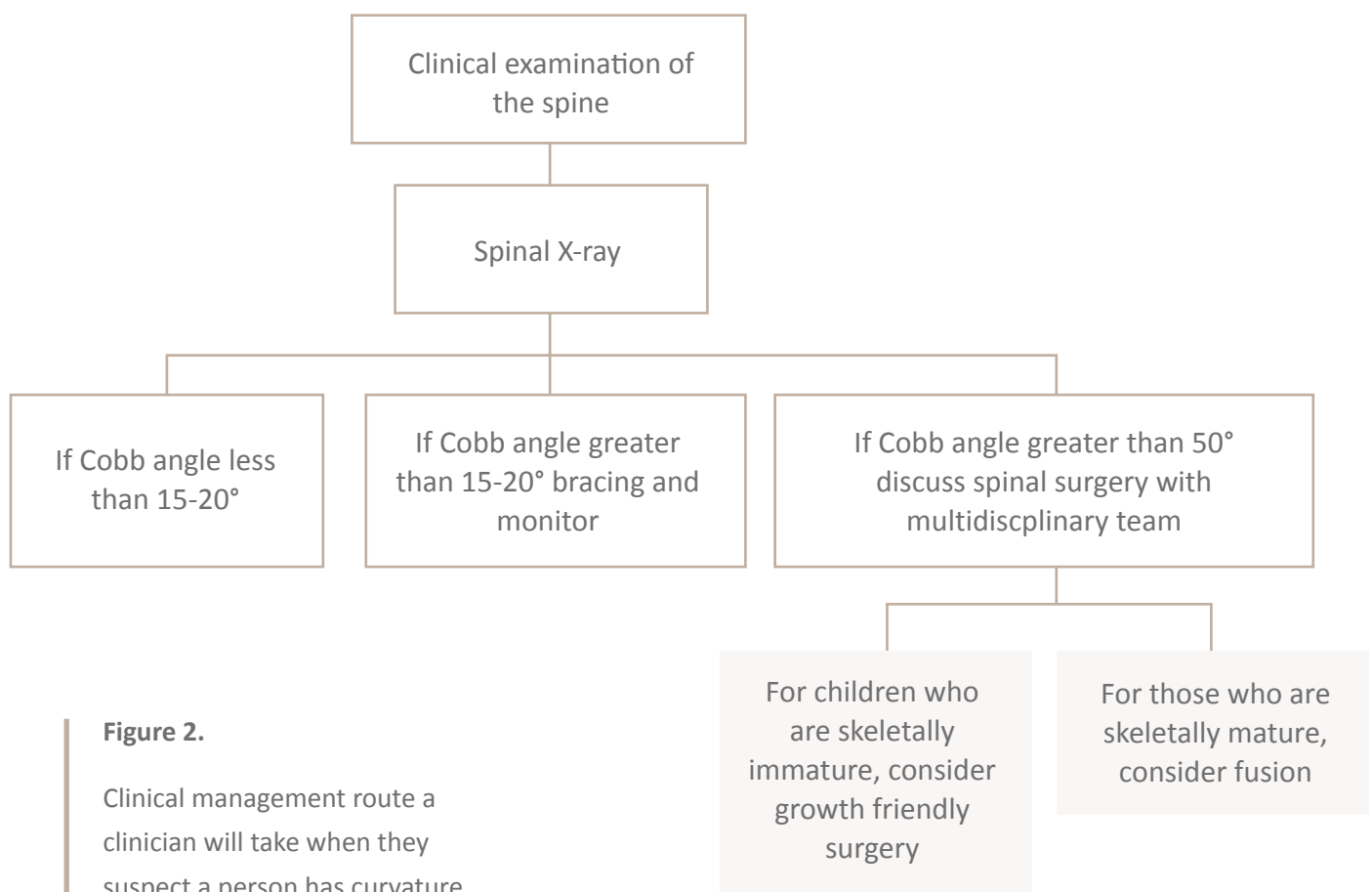


Figure 2.

Clinical management route a clinician will take when they suspect a person has curvature of the spine (figure adapted from E Mercuri et al. 2018, p.109)

Anyone with SMA should have their growth, weight and diet assessed regularly by a dietitian with the aim of working on achieving an appropriate weight, diet and fluid intake.

CHAPTER 5

05 NUTRITION, GROWTH AND BONE HEALTH

The main nutrition-related problems associated with SMA are:

- Difficulty swallowing
- Weight management
- Movement of food through the digestive system



Anyone with SMA should have their growth, weight and diet assessed regularly by a dietitian with the aim of working on achieving an appropriate weight, diet and fluid intake. There are no specific growth charts for children with SMA, but a dietitian may refer to standard World Health Organisation (WHO) growth charts. It is recommended a measure of weight and height is recorded at hospital appointments and that **Body Mass Index** (BMI) is calculated. BMI is a measure that uses height and weight to work out if a person's weight is within a low, healthy or high range. Anyone with SMA who has a BMI over the 25th percentile should be evaluated for possible obesity and/or excess fat. Body composition should also be measured to make sure the proportion of bone, fat and muscle present in the body is healthy.

Everyone is different but important **gastrointestinal** (GI) symptoms that medical teams will monitor and treat include: reflux, delayed stomach emptying, vomiting and constipation. People with SMA may also have problems with their ability to break down foods to produce energy (their metabolism). This can result in the blood becoming more acidic - called 'metabolic acidosis' or **ketoacidosis**. They may also have high or low blood sugar and problems with breaking down fat.

It is important to see a dietitian to advise on an appropriate individualised diet

NON-SITTERS

The most important assessment for an infant is how well they can swallow. Difficulties with this are known as **dysphagia** which brings a risk of inhaling food or drink (**aspiration**), which can cause a chest infection. Shortly after diagnosis, children should have a swallow test (**video fluoroscopic swallow study**). If the test shows there are problems swallowing safely, there are two temporary ways of providing food through the nose: a **nasogastric (NG)** tube which then goes into the stomach, or a **nasojejunal (NJ)** tube which goes through the small intestine. A longer-term option that is recommended is a **gastrostomy** tube or **PEG endoscopy** which is when a tube is surgically put through the skin and into the stomach. Some experts recommend an additional surgical procedure to reduce reflux. Another issue can be if jaw muscles start to stiffen which can make it difficult to chew and swallow. If a child or adult is experiencing difficulties with any of these things mentioned above please talk to the medical team for advice.

In addition to weak swallowing muscles and **dysphagia** contributing to poor calorie intake, non-sitters use a lot of energy to breathe

and fight chest infections. This means they are at risk of undernutrition and may have difficulty gaining weight. Many types of diet are possible and each person needs one that is individualised, ensuring adequate fluids. Live bacteria and yeasts (**probiotics**) these are especially beneficial for the digestive system. Non-sitters may also need medication to help with constipation and their reduced ability to empty their stomach as food may move more slowly through the digestive system.

In the event of illness, it is important to consult the medical team about care and management as it is essential extra fluids are given early and that salts in the blood are monitored. Having SMA means that metabolising fat normally can be difficult and can sometimes lead to an excessive build-up of **ketones** and other byproducts. To avoid this, a steady diet with sugars and protein to limit the breakdown of fats to make energy is recommended. This is especially important during illness, and it is recommended that nutrition with sugars and protein is given within six hours of becoming ill and continued. Fasting should be avoided.



SITTERS

Sitters often have difficulties with chewing and may get tired when eating. It is important they see a dietitian to advise on an appropriate individualised diet. Sitters who are children should have their nutrition status assessed every three to six months after their diagnosis and then annually.

If they have had choking or coughing episodes when they have been feeding or eating, sitters should have a swallow test (**video fluoroscopic swallow study**). Their diet, chewing and swallowing abilities should also be reviewed by a speech and language therapist who will recommend how food should be prepared in terms of its consistency (e.g. pureed or semi solid or thicker liquids such as milkshakes). The speech and language therapist will also advise on feeding modifications if necessary.

If an individual is showing signs that they are not growing well, a feeding tube should be considered so that they get the extra nutrition they need. If they can still swallow safely, they should also be encouraged to have some food by mouth.

As their ability to move around is reduced and their body composition is altered, sitters are at risk of becoming overweight. If they are showing signs of this, it is recommended that they should have blood tests to check how they are managing to process sugars (glucose metabolism).

If regular constipation is an issue, fluid and fibre consumption should be increased; talk to the medical team for advice. Medication to assist with bowel movement may also be helpful.

In the event of illness, it is important to consult the medical team about care and management as it is essential extra fluids are given early and that salts in the blood are monitored. Having SMA means that metabolising fat normally can be difficult and can sometimes lead to an excessive build-up of **ketones** and other byproducts. To avoid this, a steady diet with sugars and protein to limit the breakdown of fats to make energy is recommended. This is especially important during illness, and it is recommended that nutrition with sugars and protein is given within six hours of becoming ill and continued. Fasting should be avoided.

WALKERS

It is rare for walkers to have swallowing and feeding difficulties. They should see a dietitian if they do have weight-related issues, in particular weight gain and obesity, as this can contribute to reduced mobility and increase the risk of other health problems, such as **high blood pressure** and **diabetes**. If a person is showing signs of becoming overweight, it is recommended that they have blood tests to check how they are processing sugars (glucose metabolism).

BONE HEALTH FOR ALL WITH SMA

Anyone with SMA is at risk of thinning of the bones (**osteopenia**) and fractures. Annual scans or **bone mineral density** studies are recommended to monitor bone density. Vitamin D blood levels should also be monitored annually and supplements should be taken if this is low or if someone has **osteopenia**. Calcium supplementation may also be advised. If someone is having frequent fractures, they may be given medications (**bisphosphonates**) to increase their bone density.

Annual scans or **Bone Mineral Density** studies are recommended to monitor bone density



06

CHAPTER 6 BREATHING (RESPIRATORY AND PULMONARY CARE)

The muscle weakness caused by SMA can affect the muscles for breathing (respiratory muscles). Breathing problems can be common for non-sitters and sitters but they are rare for walkers. However, it is recommended that **everyone with SMA** has both the annual influenza (flu) vaccination and the pneumococcal vaccine. All other routine vaccinations should be given as for standard healthcare recommendations unless the healthcare team advises otherwise.

There are different ways of helping to manage breathing problems. These vary depending on the impact of the SMA.

NON-SITTERS

Respiratory issues are a leading cause of severe health problems in those with the earlier onset form of SMA. The main issues are:

- Due to a weak cough, it may not be possible to clear mucus from the lungs, which may lead to chest infections
- Muscle weakness may mean someone is not able to take a big enough breath to exchange carbon dioxide for oxygen (**hypoventilation**) which can cause low oxygen levels in the blood (**oxygen desaturation**). **Hypoventilation** and low oxygen first occur during sleep when the muscles for breathing are most relaxed and gradually the difficulty exchanging carbon dioxide for oxygen extends to when the person is awake also.

no symptoms (this is called ‘proactive’ treatment). A specialist respiratory doctor should be involved as soon as possible after diagnosis.

All infants with SMA who are unable to sit should be seen at least once every three months in clinic when they should have a physical examination. If they are not breathing effectively (hypoventilating), carbon dioxide can build up. It is important therefore that they have their carbon dioxide levels checked at the end of a breath out. They should also have regular **sleep studies** so that their overnight breathing can be tested for **hypoventilation** and low oxygen saturation. These tests will help joint decision making around whether to begin using a machine to help with breathing (**non-invasive ventilation** or NIV – see over) during sleep.

As breathing problems are common and more likely to be severe, breathing management should be started early and take place regularly, even if there are

Management:

Colds can lead to chest infections which are common and are made worse when someone is unable to cough up mucus and other secretions well enough. Chest physiotherapy combined with machines that make it easier to cough (e.g. Cough Assist®, Vital Cough®) should be available to all non-sitters. Anyone with an ineffective cough and swallow should also be provided with a machine to suck out (suction) oral secretions. Parents and carers should be given training and support so that they can follow through with medical advice and use machines effectively.

Non-invasive ventilation (NIV) is the recommended way to improve low oxygen saturations and high carbon dioxide levels during sleep (**hypoventilation**). NIV is also called 'bi-level positive airway pressure' (**BiPAP**) which is delivered by a machine which gives two levels of air pressure via an individually fitted mask for the nose or the nose and mouth. A higher pressure is given while inhaling to give a bigger breath than the person can take on their own during sleep. The machine pressure then drops to a lower pressure while exhaling. NIV is designed to synchronise with normal breathing. The settings should be set to give a big enough breath so that oxygen is not needed.

Other breathing supports such as 'continuous positive airway pressure' (**CPAP**), with rare exceptions, are not recommended because they do not facilitate carbon dioxide exchange for oxygen.

Following a detailed discussion between clinicians and the family, invasive ventilation is an option that may be considered for

those for whom NIV does not work. This is surgery that creates an opening in the windpipe that allows breathing through a tube called a **tracheostomy** tube rather than through the nose and mouth. This is generally long-term. The options for breathing support should be discussed with the medical team at a time of good health. Any decision should focus on what is best for the person with SMA.

Medications used to open the airways (**nebulised bronchodilators**) should be available if there is high suspicion of asthma or if a clear improvement in breathing is seen after it has been given. Medications to reduce salivary secretions (such as **glycopyrrolate**) should be used carefully and, with medical guidance, the dose changed as needed. This is to avoid the possibility of the secretions drying out too much, which makes them harder to remove. Long-term daily use of medications to break down secretions (Pulmozyme® or hypertonic saline) is not recommended. Antibiotic use during illness should be discussed on an individual basis with the medical team.

In addition to the annual influenza vaccine and pneumococcal vaccinations and other recommended routine vaccinations, it is recommended that infants up to the age of 2 years are vaccinated with Palivizumab which acts against a common virus – respiratory syncytial virus (RSV) that can cause breathing problems. As discussed in Chapter 5, Nutrition, Growth and Bone Health, there can be other factors which exacerbate breathing problems and should also be treated, such as reflux.

SITTERS

Breathing problems are less frequent in sitters, but it is still recommended that they have a physical examination at least once every six months. At this appointment, if they are able, they should have breathing tests (**spirometry**) to measure lung size and breathing muscle strength. **Sleep studies** to check on breathing during sleep should be completed for all who have any symptoms, or suspicion of 'insufficient breathing'. Examples of symptoms are poor sleep quality, morning headaches, and daytime sleepiness.

Management:

If a sitter has a weak cough they should be given chest physiotherapy. Parents and carers should be shown techniques and a cough assist device (e.g. Cough Assist®, Vital Cough®) should be provided with a demonstration and clear instructions as to how and when to use it. **Non-invasive ventilation** (NIV) should be used for everyone who shows symptoms that suggest they are not breathing well enough during sleep (poor sleep quality, headaches, and daytime sleepiness).

Sleep studies should be used to confirm if breathing issues are causing the problems, and to determine optimal settings for the NIV. NIV should be set to give a big enough breath so that oxygen is not needed. (Read more about the NIV and how it works in the non-sitters/management section or in the glossary).

Other breathing supports such as 'continuous positive airway pressure' (**CPAP**), with rare exceptions, are not recommended because they do not facilitate carbon dioxide exchange for oxygen.

Colds can lead to chest infections which are common and are made worse when



someone is unable to cough up mucus and other secretions well enough. Chest physiotherapy combined with a cough assist machine should be available to all sitters. Those with an ineffective cough and swallow should also be provided with a machine to suck out (suction) their oral secretions. Parents and carers should be given training and support so that they can follow through with advice and use machines effectively.

Medications used to open the airways (**nebulised bronchodilators**) should be available if there is high suspicion of asthma or if a clear improvement in breathing is seen after it has been given. Medications to reduce salivary secretions (such as **glycopyrrolate**) should be used carefully and, with medical guidance, the dose changed as needed. This is to avoid the possibility of the secretions drying out too much, which makes them harder to remove. Long term daily use of medications to break down secretions (Pulmozyme® or hypertonic saline) is not recommended. Antibiotic use during illness should be discussed on an individual basis with the medical team.



For most walkers breathing is normal, though one study has suggested that there may be a small reduction of breathing ability over time

WALKERS

For most walkers breathing is normal, though one study has suggested that there may be a small reduction of breathing ability over time. If chest infections do occur then there should be a careful assessment in clinic of a person's ability to cough effectively and an exploration of whether they have any symptoms of 'insufficient breathing' (poor sleep quality, headaches, and daytime sleepiness). Regular breathing tests (**spirometry**) should be considered for those that are showing signs of difficulties. However, proactive management of breathing problems is not needed unless the adult or family raises concerns.

Medications used to open the airways (**nebulised bronchodilators**) should be available if there is high suspicion of asthma or if a clear improvement in breathing is seen after it has been given. Medications to reduce salivary secretions (such as **glycopyrrolate**) should be used carefully and, with medical guidance, the dose changed as needed. This is to avoid the possibility of the secretions drying out too much, which makes them harder to remove. Long term daily use of medications to breakdown secretions (Pulmozyme® or hypertonic saline) is not recommended. Antibiotic use during illness should be discussed on an individual basis with the medical team.

07

CHAPTER 7 OTHER ORGANS AND SYSTEMS

SMN protein is not just found in the spinal cord, it is also present in all cells as soon as an egg is first fertilised. This means that other organs and parts of the body may be affected by a lack of the protein. Scientists investigating animal models of SMA have suggested that reduced SMN protein may have an impact on the brain, nerves, heart and pancreas. However, only a minority of people with SMA have clearly had challenges with other organs and in those who have, it has not been demonstrated that the cause is the SMA.



HEART

Changes to the structure of the heart have been reported for the most severely affected infants (usually those who have problems breathing from birth) and some may experience a slower than usual heart rate, which may require treatment. It is therefore recommended that infants severely affected by SMA are monitored for heart problems. Heart problems are rare in sitters and walkers and they do not require regular heart checks unless symptoms develop that suggest a heart problem.

OTHER SYSTEMS

There are early studies (cell, animal and human) that indicate the following may be **slightly** more common in people with SMA:

- ◆ Problems of the pancreas (which can include diabetes)
- ◆ High levels of **leptin** (a **hormone** which regulates appetite and body weight by reducing feelings of hunger)
- ◆ Problems with muscle mitochondria (parts of a cell which produce energy)

It is recommended that everyone with SMA should have the levels of sugar in their blood checked, particularly when unwell.

08

CHAPTER 8 MEDICATION

At the time of producing this guide, Spinraza® is an approved drug treatment which has shown positive results in the treatment of SMA. Some information about how it is delivered can be found in Chapter 11, Administration of New Treatments for SMA.

Albuterol (also known as salbutamol), which is usually associated with asthma treatment, has been trialled by mouth in tablet or liquid form with some positive results in terms of muscle strength. However, it has not yet been proved whether it definitely has a beneficial effect. Despite this, it is sometimes prescribed for sitters and walkers. For further information about how this medication works, please visit the useful resources section.

Medications may be recommended that aim to treat symptoms or effects of living with SMA. These include, among others:

- ◆ Vitamin D (Chapter 5, Nutrition, Growth and Bone Health)
- ◆ Calcium (Chapter 5, Nutrition, Growth and Bone Health)
- ◆ **Bisphosphonates** (Chapter 5, Nutrition, Growth and Bone Health)
- ◆ Anti-reflux medications (Chapter 5, Nutrition, Growth and Bone Health)
- ◆ Antibiotics (Chapter 6, Breathing (Respiratory and Pulmonary Care))

It is likely that Spinraza® will become more widely available and that other potential treatments will also emerge. Talk to your medical team about latest research, clinical trials and availability of drug treatments in your country.

09

CHAPTER 9

EMERGENCY CARE

Chest infections and breathing issues are the most frequent problems that require urgent treatment. Anyone with SMA who becomes unwell, should have a plan of action that any medical team can follow. This plan should be agreed between the doctor and adult while they are well, or between the doctor and parent while their child is well. Children should be involved in the discussions if they have an appropriate level of understanding. There should be a written record of this in the form of an ‘**Emergency Healthcare Plan**’. The aim is to empower adults and families to state their wishes and improve communication between them, urgent care teams and long-term care specialists.

The **Emergency Healthcare Plan** (EHP) or ‘Illness Plan’ should be written with the medical team. It should cover information about:

- ◆ What the warning signs or indications would be that would mean the person with SMA should be taken to hospital.
- ◆ Which healthcare providers should be contacted in case of an emergency.
- ◆ Preferences around breathing management including your views on different ways of supporting breathing. Respiratory support may be delivered non-invasively using a mask (NIV), or in the short-term ventilation may be delivered via a flexible plastic tube into the windpipe (intubation). Longer term an opening can be created at the front of the neck so that a tube can be inserted into the windpipe to help with breathing (a **tracheostomy**).
- ◆ Any neck and jaw mobility problems and limits.
- ◆ Techniques used for clearing secretions, including how often.
- ◆ Nutritional and fluid needs during illness.
- ◆ When and which antibiotics should be used.
- ◆ What action has been agreed and will be taken if resuscitation is required.

Where possible, local emergency medical services should be contacted in advance to discuss any specific needs and what equipment is used at home. In an emergency, you should go to the closest hospital. Wherever possible, the equipment used at home should also be used, even if this is in an ambulance that is well equipped. Sometimes non-sitters and sitters may need to be transferred between hospitals as they should be cared for at a specialist (tertiary) centre that is equipped to look after them. The clinical team responsible for their long-term care should always be notified about the illness.

An '**Emergency Healthcare Plan**' aims to empower adults and families to state their wishes and improve communication between them, urgent care teams and long-term care specialists.

Breathing assessment and support is the most important issue during an emergency. To address this and other key emergency care practices, the authors of the SoC advise medical teams to consider the following:

- ◆ Management should include early use of NIV and clearing of secretions before giving oxygen.
- ◆ Oxygen alone should **not** replace NIV and should only be added if oxygen levels in the blood remain low while NIV is being used and secretions are being cleared as described in the EHP. Only then may oxygen be added at the lowest flow required to optimise oxygenation, and then slowly stopped during recovery from the illness.
- ◆ Carbon dioxide levels should be monitored by either a blood test or **transcutaneous skin probe** during the time oxygen is being given.
- ◆ If it looks like **intubation** is required take into account the views of the patient or if the patient is a child consult with their parent/legal guardian.
- ◆ If **intubation** is no longer needed and the tube is going to be taken out, the lungs should be fully inflated and oxygenation optimised beforehand. NIV should be used as transitional support following extubation.
- ◆ Children, young people and adults should only be given antibiotics if there is a specific cause of the illness such as sepsis or a chest infection.
- ◆ Urgent care teams should review symptoms on admission, predisposing factors such as recent surgery, and non-respiratory causes of sepsis e.g. urinary tract infection, skin infection etc.
- ◆ If there is a need for an anaesthetic, guidance in Chapter 10, Anaesthetics should be followed

It is essential that emergency care includes giving fluids early and that hydration, levels of salts and minerals, kidney function and glucose levels in the blood are monitored. Nutrition with protein should be given within six hours of becoming ill and there should not be long periods without food. Special attention should be paid to swallowing during an illness due to the risks of inhalation of food or liquids into the lungs (**aspiration**) (See Chapter 5, Nutrition. Growth and Bone Health).

Shortly after admission, discussions should start with the team as to what goals need to be achieved and what plans need to be put in place to make it safe and manageable to go home. Discharge planning should set goals with you, the hospital team, and the primary healthcare team. Physical and occupational therapy, speech therapy, psychosocial and **palliative care** services can all help with recovery from illness and efforts to maintain abilities.

10

CHAPTER 10 ANAESTHETICS



Anaesthetics may be used for planned surgery as well as for other reasons, such as administering new drug treatments.

Recommendations to the medical team in charge are:

- ◆ A review of the heart by a cardiologist only if there is known to be a pre-existing problem.
- ◆ A full assessment before any anaesthetics are used. This may include a sleep study and involvement of a dietitian.
- ◆ Assessment of difficulties in intubating that may be caused by:
 - Tightening of the jaw
 - Limited neck mobility
 - Difficulties in positioning
- ◆ Considerations of local anaesthesia or regional analgesia; as a general rule anaesthesia does bring challenges.
- ◆ Monitoring blood carbon dioxide and oxygen at all times, whatever anaesthetic method is used.
- ◆ Anticipating any other possible needs such as use of NIV and other breathing interventions
- ◆ Medication for pain management may be needed after an operation

Anaesthetics may be used for planned surgery as well as for other reasons, such as administering new drug treatments.

At the time the scientific articles were written, Spinraza® was the first, and only, potentially available disease-modifying drug treatment for SMA.

11

CHAPTER 11

ADMINISTRATION OF NEW TREATMENTS FOR SMA

At the time the scientific articles were written, Spinraza® was the first, and only, potentially available disease-modifying drug treatment for SMA.

Spinraza® is delivered directly into the **Cerebro Spinal Fluid (CSF)** which circulates around the spine and brain; this is how Spinraza® directly reaches the part of the central nervous system that is affected by SMA. Doctors access the CSF using a lumbar puncture which is when a needle is inserted in the lower back through the skin into the space between the back bones of the spine (**vertebrae**). Doctors may use an **x-ray** to locate the best place for the insertion and they will usually use a local anaesthetic such as a **numbing cream**, although occasionally a general anaesthetic may be considered necessary. A small amount of CSF is drawn off and then Spinraza® is injected over one to three minutes.

If Spinraza® is an available and appropriate treatment that is agreed between the medical team and the person or the person's legal guardian, the medical team need to plan carefully how to administer the drug, so that the intervention and care is safe and appropriate to the physical development of the individual.

The SoC **advice to the medical team** discussing delivery of this treatment with the person or their family includes recommendations that they consider:

- ◆ What sedation method or procedure to use
- ◆ What radiology (e.g. X-ray) support is needed
- ◆ What possible problems there could be due to spinal surgery or **scoliosis** (See Chapter 4, Orthopaedic Management)

12

CHAPTER 12

ETHICS AND CHOICES



As discussed throughout this guide, every person with SMA is different, as is every family and their circumstances. There are often different options for care and treatment which will be individualised. It is therefore very important that the medical team discuss all aspects of care openly starting from the point of diagnosis onwards. This discussion should explore all the possible options for care and treatment, what could be appropriate and any potential benefits and risks. Discussion should be with you as an adult with SMA, or with you as the parent / carer of a child with SMA and, if age appropriate, with your child. You should feel free to initiate a discussion at any time and to ask questions about any aspects of care. You should know that any decisions can be revisited at any time, especially if there are any changes with the condition. Some of these discussions will be initiated by the

clinical team and include quite difficult topics including what would be the appropriate response to any potential life-threatening emergency such as breathing complications.

Though research into the treatment of SMA is ongoing and new treatments may arise that offer significant benefit, it remains a priority for everyone with SMA to maintain a good quality of life and be supported to manage symptoms as effectively as possible.

We hope that this guide has given you helpful information that you can discuss with the medical team.

Always remember that there are neuromuscular centres and teams, and patient support and advocacy groups, as well as your families and friends who are able to support you.

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USEFUL RESOURCES



ORGANISATIONS WHO DEVELOPED THIS GUIDE

- ◆ **Spinal Muscular Atrophy UK**
www.smauk.org.uk
- ◆ **Cure SMA**
www.curesma.org
- ◆ **SMA Europe**
www.sma-europe.eu
- ◆ **Muscular Dystrophy UK**
www.musculardystrophyuk.org
- ◆ **TREAT-NMD Alliance**
www.treat-nmd.org

COUNTRY SPECIFIC ORGANISATIONS - UK

- ◆ **Spinal Muscular Atrophy UK**
<https://smauk.org.uk/>
- ◆ **Muscular Dystrophy UK**
<https://www.musculardystrophyuk.org/>
- ◆ **NHS**
<https://www.nhs.uk/conditions/spinal-muscular-atrophy-sma/>

APPENDIX 1

The following diagrams explain the chances, **for each pregnancy**, of a child inheriting SMA in different families. Please note the chances of inheriting SMA are the same for males and females; the sex shown for children and parents in the diagrams is purely illustrative.

FAMILY 1.

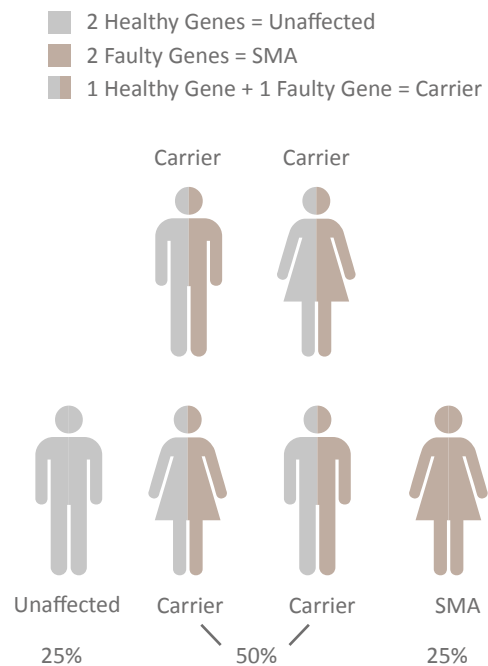
Both parents are carriers.

For each pregnancy, the chances are:

25% (1 in 4) child has both faulty copies of the *SMN1* gene and **will have SMA**

50% (1 in 2) child has one faulty copy and one healthy copy of the *SMN1* gene and **will be a carrier**

25% (1 in 4) child has two healthy copies of the *SMN1* gene and **will not be a carrier or have SMA**



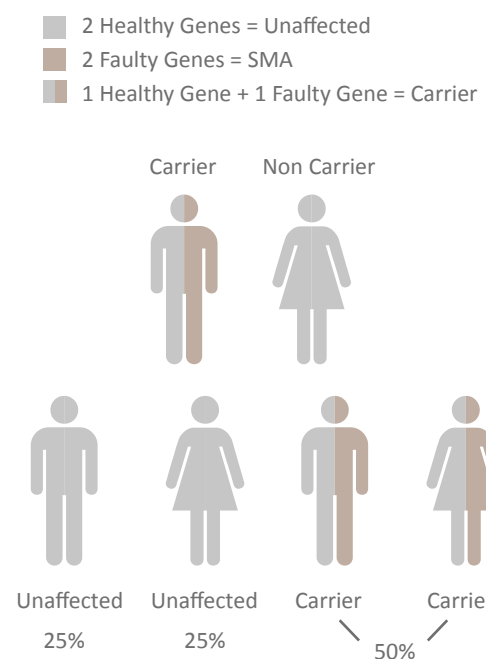
FAMILY 2.

One parent is a carrier, the other parent does not have SMA and is not a carrier.

For each pregnancy, the chances are:

50% (1 in 2) child has two healthy copies of the *SMN1* gene and will not have SMA and **will not be a carrier**

50% (1 in 2) child has one faulty copy and one healthy copy of the *SMN1* gene and **will be a carrier**



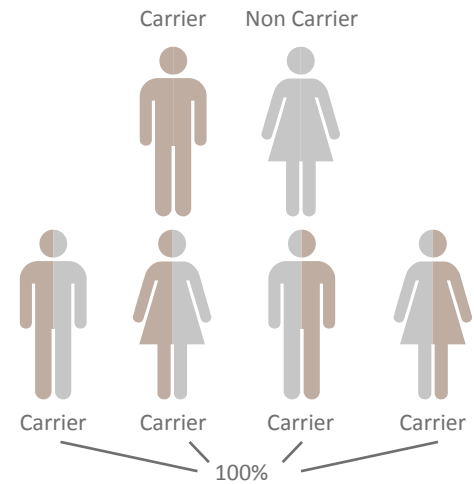
- 2 Healthy Genes = Unaffected
- 2 Faulty Genes = SMA
- 1 Healthy Gene + 1 Faulty Gene = Carrier

FAMILY 3.

One parent has SMA; the other does not have SMA and is not a carrier.

For each pregnancy, the chances are:

100% (4 in 4) child has one faulty copy and one healthy copy of the *SMN1* gene and **will be a carrier**



FAMILY 4.

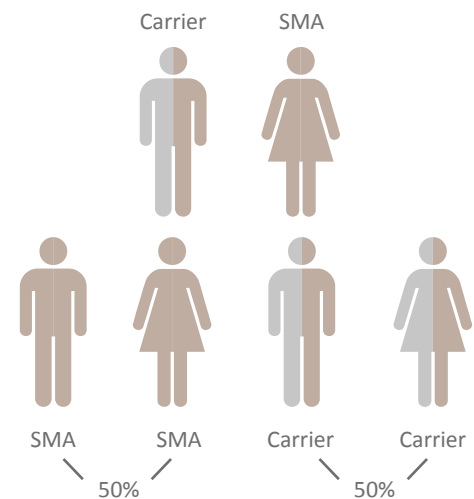
One parent has SMA; the other is a carrier.

For each pregnancy, the chances are:

50% (1 in 2) child has two faulty copies of the *SMN1* gene and **will have SMA**

50% (1 in 2) child has one faulty copy and one healthy copy of the *SMN1* gene and **will be a carrier**

- 2 Healthy Genes = Unaffected
- 2 Faulty Genes = SMA
- 1 Healthy Gene + 1 Faulty Gene = Carrier



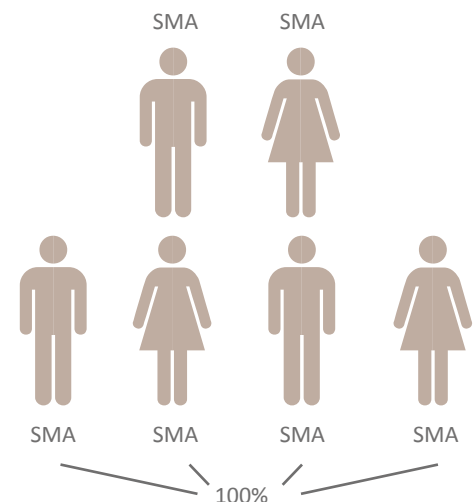
- 2 Healthy Genes = Unaffected
- 2 Faulty Genes = SMA
- 1 Healthy Gene + 1 Faulty Gene = Carrier

FAMILY 5.

Both parents have SMA.

For each pregnancy, the chances are:

100% (4 in 4) child has two faulty copies of the *SMN1* gene and **will have SMA**



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GLOSSARY

Aspiration occurs when food, saliva, liquids or vomit is breathed into the airways leading to the lungs, instead of moving through the swallowing tube that connects the mouth (**oesophagus**) to the stomach.

Atrophy Muscle atrophy is the wasting or loss of muscle tissue. In SMA this is due to degeneration of nerve cells called **motor neurons**.

Autosomal recessive is the pattern of inheritance where someone who has the condition inherits two faulty copies of a **gene**, one from each parent. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated **gene**, but they typically do not show signs and symptoms of the condition. The parents are known as '**Carriers**'.

BiPAP (Bi-level Positive Airway Pressure) refers to a breathing support device that delivers 2 levels of air through a mask over the nose or nose and mouth, to support breathing. While breathing in, the BiPAP device delivers a higher pressure to give a bigger breath in followed by dropping the pressure to a lower pressure to help with breathing out.

Bisphosphonates are a group of drugs usually prescribed to slow the loss of bone density, by slowing down cells (osteoclasts) that are responsible for the breakdown of bone.

Body Mass Index (BMI) is the relationship between weight and height used to estimate the amount of body fat according to a mathematical formula: weight, in kg, divided by the square of the person's height, in metres ($BMI = kg/m^2$).

Bone Mineral Density (BMD) is the amount of mineral (calcium and phosphorous) content per unit volume of bone. It indicates the strength of bones.

Carriers refer to people affected by either an autosomal recessively inherited or X-linked recessively inherited condition who both have a faulty copy and a healthy copy of the affected **gene**. Carriers usually have no symptoms due to the healthy copy of the **gene**, but they may pass on the condition to their children.

Cerebrospinal Fluid (CSF) is a clear fluid that surrounds the spinal cord and brain. The fluid acts as a liquid cushion for the spine. It also transports waste and chemical products and antibodies away from the brain and spinal-cord tissue into the bloodstream.

Chromosome is an organised 'package' of **DNA** found in the nucleus of each cell. Humans have 46 chromosomes in each cell. They inherit 23 from their mother and 23 from their father.

Cobb angle is the measurement of the curvature of the spine. It is calculated in degrees by analysing an **x-ray** image. It helps the doctor decide what treatment is necessary. It is named after John Robert Cobb an America orthopaedic surgeon who was the first to use it.

Contractures are the shortening of the muscle or tendons around a joint leading to it becoming fixed in a particular position or having less than full range of motion at that joint.

CPAP (Continuous Positive Airway Pressure) is a type of ventilation, through a mask, that is driven by a specifically designed **non-invasive ventilation** machine called a **CPAP**. It provides a continuous flow of air to help with breathing.

Creatine Kinase (CK) is an **enzyme** needed to enable muscles to function. After skeletal muscle injury or other illness, CK levels can rise. A CK levels test measures the amount of CK in the blood and can be requested by a clinician to aid diagnosis.

DEXA (Dual energy **X-ray** absorptiometry) scan is a test that uses low dose **X-ray** to measure how much calcium and other minerals are present in an area of your bone. A DEXA machine is usually used where you lie on a bed and the scanner passes over your lower spine and hips. The results of a DEXA scan are given as a 'T score' which will indicate to the clinician whether or not a person has **osteopenia** or osteoporosis.

De novo mutation refers to a spontaneous mutation arising in a gene rather than an inherited mutation.

Diabetes Mellitus, commonly called 'diabetes', describes a group of conditions in which there are high blood sugar levels over a prolonged time. It occurs where the body does not produce sufficient insulin or where cells respond inadequately to the insulin available. Insulin is a **hormone** produced in the pancreas, which regulates the amount of glucose in the blood.

DNA Deoxyribonucleic acid is the molecule that contains the genetic instruction manual to build all known organisms. **DNA** is often compared to a set of blueprints, a recipe, or a code, since it contains instructions needed to construct other components of cells such as protein.

Dysphagia is difficulty or discomfort when swallowing liquids, foods, or saliva. This can sometimes make it difficult to take in enough calories and fluids.

Emergency Healthcare Plan (EHP) is a tool designed to make communication easier in the event of a healthcare emergency. It facilitates shared decision making between clinicians and patients allowing them to discuss and record actions that should be taken by medical professions should any foreseeable emergencies arise. Development may take several discussions and should include multidisciplinary input.

Enzyme is a protein that speeds up the rate of chemical reaction in a living organism.

Gastroesophageal reflux occurs when the muscle joining the **oesophagus** (swallowing tube from the mouth) to the stomach either opens on its own, or does not close properly which means that the stomach contents (food/ liquid) rise up into the **oesophagus**. It may also be called acid reflux or acid regurgitation, because digestive juices which are acidic, rise up with the food, causing a burning sensation.

Gastrointestinal Tract is the system of organs which include the mouth, **oesophagus**, stomach, small intestine, large intestine and rectum. It processes the food we eat to extract and absorb energy, nutrients, water and to extract waste as faeces.

Gastrostomy or Gastric tube or G tube is a surgical opening into the stomach, in this case to insert a flexible feeding tube through the abdominal wall and into the stomach to allow direct delivery of adequate nutrition. Sometimes referred to as a PEG (Percutaneous endoscopic gastrostomy).

Gene is the basic physical unit of inheritance. Genes are passed from parents to offspring and are made up of **DNA** which contains the information needed to determine specific characteristics of a person. Some genes act as instructions to 'code' for proteins. Every person has two copies of each gene, one inherited from each parent.

Glycopyrrolate comes in the form of an inhaler and is sometimes prescribed to treat excessive saliva production.

Hippotherapy means 'treatment with the help of the horse' it is a therapeutic and rehabilitative treatment as a means to improve coordination, balance and strength.

High Blood Pressure or Hypertension is considered to be 140/90mmHG or higher. The first number is systolic pressure - the force at which your heart pumps blood around your body. The second number is diastolic pressure the resistance to the blood flow in the blood vessels. They're both measured in millimetres of mercury (mmHg).

Hormone is a chemical produced in the body that controls and regulates the activity of specific cells and organs.

Hypoventilation is when someone is not able to take a big enough breath to exchange carbon dioxide for oxygen resulting in low blood levels of oxygen and an increase of carbon dioxide.

Intubation is the placement of a flexible plastic tube into the windpipe (trachea) to act as an airway and a possible route for some drugs.

Intrathecal Administration is a way to provide drug delivery via an injection into the spinal canal so that it reaches the **cerebrospinal fluid**.

Ketoacidosis or Diabetic Ketoacidosis affects people when their body starts breaking down fat at a rate that is too fast. The liver processes the fat into a fuel called **ketones**, which causes the blood to become acidic.

Ketones are substances that are produced in the liver when fat cells are broken down (metabolised).

Kyphosis is an outward curvature of the spine which, if excessive, can lead to 'hunching' of the back.

Leptin is a **hormone** that is produced by the adipose tissue (which stores energy in the form of fat, and also cushions and insulates the body) and has a role in regulating appetite. Typically, an increased amount of adipose tissue results in higher concentrations of **leptin** and a reduction in

appetite. However, some people are less sensitive to it and don't experience this reduction in appetite.

Motor Neurons are located in the spinal cord and the part of the brain that is connected to the spinal cord. **Motor neurons** transmit signals from the brain and spinal cord that tell the skeletal muscles to contract, which allows the body to move.

Muscle Biopsy is a minor surgical procedure that removes a small sample of muscle tissue for testing in a laboratory. It is usually carried out under local anaesthetic. The sample can be used to aid diagnosis.

Mutation is a permanent change in the **DNA** sequence of a gene that can be inherited by subsequent generations. Mutations can result from **DNA** copying mistakes made during cell division.

Nasogastric (NG) Intubation is the insertion of a tube through the nose, past the throat and down into the stomach to allow delivery of adequate nutrients (Fat, carbohydrate, protein, vitamin and minerals).

Nasojejunal (NJ) Intubation is the insertion of a tube through the nose, past the throat and stomach down into the small intestine, to allow delivery of adequate nutrients (fat, carbohydrate, protein, vitamin and minerals).

Nebulised Bronchodilators are a type of medication that are delivered as a mist that is inhaled into the lungs makes breathing easier by relaxing the muscles in the lungs and widening the airways (bronchi).

Non-Invasive Ventilation (NIV) uses airway support that is administered through a nose or face mask.

Numbing Cream is a type of local anaesthetic

used on healthy, unbroken skin to prevent pain before certain procedures such as inserting a needle. It works by temporarily numbing the skin and surrounding area.

Oesophagus is the swallowing tube that connects the mouth with the stomach

Orthotist is a medical doctor who is trained to prescribe, manufacture and manage orthoses.

Orthosis or Orthotic (Orthoses plural) is a manufactured device or aid that is fitted to limbs or the spine to prevent or assist movement. They can be splints, a spinal jacket, a spinal brace, ankle-foot orthoses (AFOs), Knee-foot orthoses (KAFOs).

Osteopenia is when bone mineral density (BMD) is lower than normal density but not low enough to be considered osteoporosis (a medical condition in which the bones become brittle and fragile from loss of tissue). A doctor will determine whether or not someone has **osteopenia** or osteoporosis by carrying out a **DEXA** scan.

Oxygen Desaturation means a reduction in blood oxygen levels.

Palliative Care is an interdisciplinary approach to specialised medical care that aims to reduce the severity of a disease or slows its progression but does not provide a cure. The goal is to improve quality of life for both the patient and family by providing relief from the symptoms and stress.

PEG Endoscopy is a surgical procedure where a tube is passed into a person's stomach through the abdominal wall. This is sometimes needed when intake by mouth is not adequate because of dysphagia or anaesthetic sedation.

Probiotics are live bacteria and yeasts that beneficially affect health by improving the balance or function of our gut bacteria. They can be found naturally in food or as a supplement (yoghurts,

tablets, capsules and sachets).

Scoliosis refers to the spine curving sideways.

Skeletal Maturity or 'bone age' refers to the age of a child's skeletal system, which is different to a child's chronological age. As a child grows the size and shape of their bones change; **skeletal maturity** is measured by taking an **X-ray** of the hand and wrist.

Sleep Studies are tests that record the body's activity during sleep; they can record heart rate, breathing and the oxygen level in your blood.

Survival Motor Neuron 1 (SMN1) gene provides instructions for making the survival motor neuron (SMN) protein. The SMN protein is concentrated in the spinal cord but found throughout the body. It is needed for the maintenance of specialised nerve cells called **motor neurons**.

Survival Motor Neuron 2 (SMN2) or 'back-up' gene provides instructions for making the survival motor neuron (SMN) protein. The SMN protein is concentrated in the spinal cord but found throughout the body. It is integral for the maintenance of specialised nerve cells called **motor neurons**. However, several different versions of the SMN protein are produced from the **SMN2** gene and only one version is full size and functional enough to maintain the specialised nerve cells.

Spirometry is a test used to assess how well a person's lungs work by measuring how much air they inhale.

Thoraco-lumbar sacral orthosis (TLSOs) is a firm inflexible brace that spans the full back (thoracic, lumbar and sacrum part of the spine). It is used to give the spine structural support

Tracheostomy is surgery to create an opening in the neck that goes into the windpipe so a tube can be inserted to help a person breathe more easily.

This can be permanent or temporary.

Transcutaneous Skin Srobe uses non-invasive electrochemical sensors that are applied directly to the skin surface, so clinicians can continuously monitor carbon dioxide (CO²) to make sure breathing is adequate.

Vertebrae refers to the 33 bones which form the backbone.

Video Fluoroscopic Swallow Study or Modified Barium Swallow is a real time **X-ray** that is carried out to look closely at the swallowing process to see if any interventions are required to make eating safe.

X-ray creates an image of the inside of a person's body using radiation called electromagnetic waves. Various tissues within the body absorb different amounts of radiation resulting in an image where bones look white and soft tissue, such as fat, looks grey. Lungs look black because of the air which absorbs the least radiation.

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