Limb-Girdle Muscular Dystrophy Guide

for Families, Caregivers & HCPs

TREAT-NMD®
Neuromuscular Network

This Guide for Families and Caregivers was realised thanks to the contribution of:

Nicholas Johnson, MD, MS-CI

Kiera Berggren, PhD, CCC-SLP

Richard D. Shell, MD

Peter B. Kang, MD

Jordi Diaz Manera, MD

Meredith James, PhD, PT

Giorgio Tasca, MD

Ariele Barreto Haagsma, MD, MSc

Conrad “Chris” Weihl, MD/PhD

Lone Knudsen, MSc Psych, PhD

Frank Raucci, MD/PhD

Michelle Lorentzos, PhD, FRACP, MBBS, BA

Kat Bryant Knudson (The Speak Foundation)

Carol Abraham (LGMD Awareness Foundation)

Jennifer Levy (Coalition to Cure Calpain 3)

Beatrice Vola (GFB ONLUS)

Laura Rufibach (Jain Foundation)

Daniel Ferguson Foundation

Rachel DeConti (LGMD2D Foundation)

Maria Overgaard Jakobsen, MD

Kelly Brazzo (CureLGMD2i Foundation)

Matthew Garrow (TREAT-NMD)

Ella Vickers (TREAT-NMD)

Katie Laubscher, PT, DPT, PCS

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Introduction

Limb Girdle Muscular Dystrophies (LGMDs) are a group of over 30 rare, genetic muscle conditions that cause progressive weakness, primarily in the shoulder and hip areas. First described in the 1950s, LGMDs are now better understood thanks to advances in genetic research, helping to identify distinct subtypes and potential treatment approaches.

To support individuals and families affected by LGMD, TREAT-NMD* has developed a plain-language LGMD Family Guide. It is designed for patients, families, and non-specialist clinicians, with contributions from 9 international clinician teams - each including a key opinion leader (KOL) and a patient advocacy representative. The guide focuses initially on general LGMD information and 7 specific subtypes (1D/D, 2A/R1, 2B/R2, 2C/R5, 2D/R3, 2E/ R4, 2I/R9, and 2L/R12), with the long-term goal of expanding to cover all subtypes and translating into as many languages as possible.

This guide aims to be globally accessible and relevant, with chapters addressing a broad range of topics - from swallowing and psychosocial support to emerging treatments - offering practical information for navigating life with LGMD. It is important to note, however, that there may be differences between countries on how care is managed and assistive support delivered.

* *In partnership with Sarepta Therapeutics*

How to Use This Document

This guide is designed to empower patients and caregivers with **clear, actionable steps** for proactive healthcare management. By using it effectively, you can:

- **Ensure Informed Care**
  Share the guide with healthcare providers, especially those unfamiliar with the condition, to improve communication and treatment.

- **Navigate Emergencies**
  Keep the guide accessible during urgent medical situations, making use of its emergency resources when needed.

- **Educate & Share**
  Distribute it within online communities and among specialists to enhance understanding and awareness.

- **Strengthen Partnerships**
  Collaborate with your healthcare team to set shared goals, leading to better patient outcomes.

- **Connect with Others**
  Engage with patient communities to exchange experiences, advocate for better access to care, and build support networks.

- **Stay Informed**
  Learn about expected care standards, essential medical tests, therapies, and referrals to make informed decisions.

To aid understanding, an up to date LGMD specific glossary is maintained by the LGMD Awareness Foundation which can be found here:

www.lgmd-info.org/knowledge-base/all-about-lgmd/glossary/

02

Disease Stages and Overview of Limb Girdle Muscular Dystrophy (LGMD)

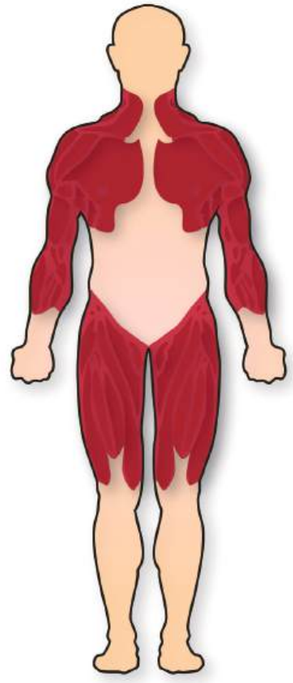
Overview of Limb Girdle Muscular Dystrophies

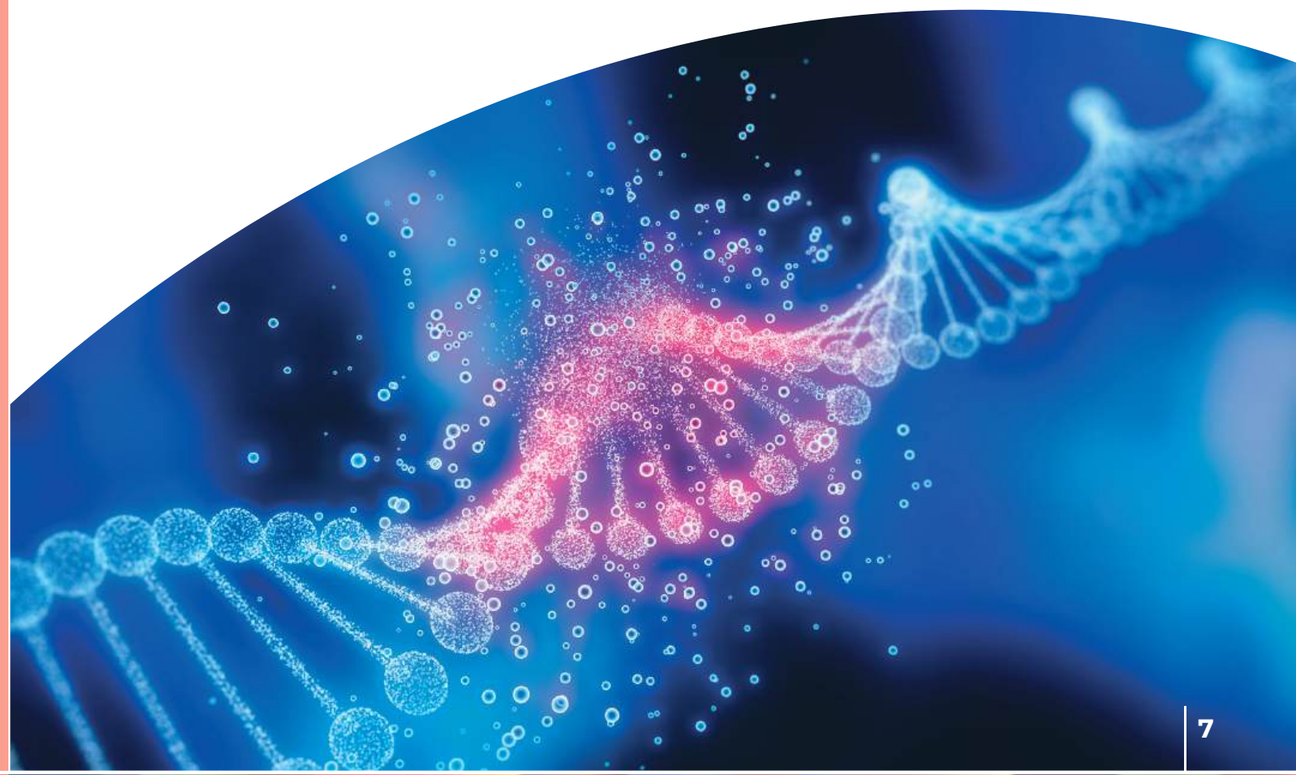
Limb Girdle Muscular Dystrophies represent a group of over 30 different diseases that share some common features. Originally described in the 1950s by Drs. Walton and Natrass as individuals with slowly progressive weakness of their shoulders and hips, more recent genetic discoveries have allowed a better understanding of the similarities and differences between the LGMDs as well as the development of potential therapies that may address the underlying disease mechanism of each LGMD subtype.

Here, we will provide an overview of the LGMDs. More in-depth information is provided in subsequent chapters throughout this guide.

What makes LGMD, LGMD?

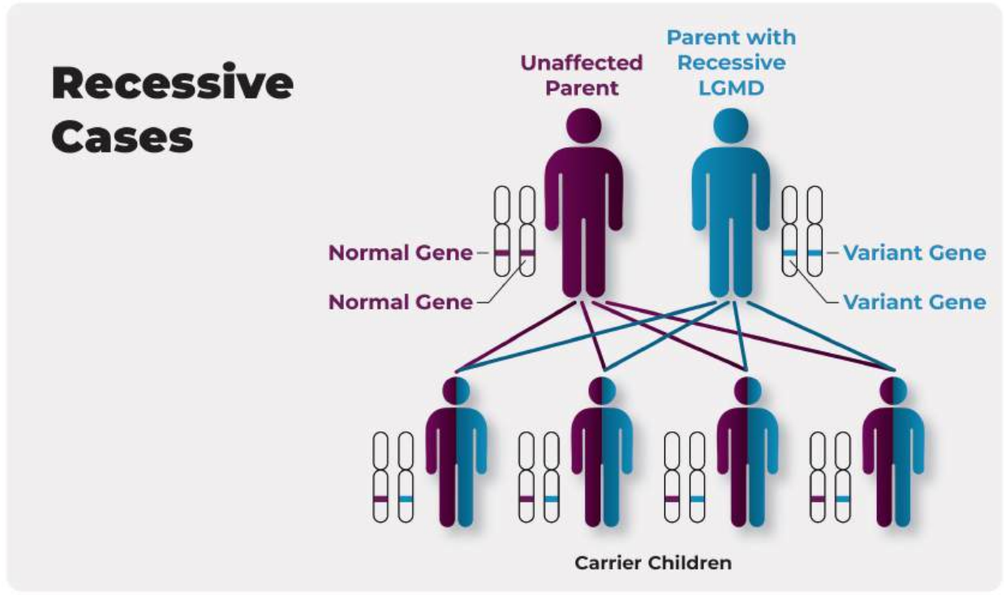
The term limb girdle muscular dystrophy is used to describe a progressive, genetic muscle disorder where the weakness begins in the shoulder and hip girdle. LGMDs have an “autosomal” inheritance, which means that they occur in both males and females equally and can be inherited from either mothers or fathers in the case of dominant inheritance or from both parents in the case of recessive inheritance. These points differentiate the LGMDs from muscular dystrophies like Duchenne and Becker muscular dystrophy, which are X-linked diseases that predominantly occur in males and are inherited from the mother. As discussed in the genetics chapter, since the advent of more comprehensive genetic testing, we now know that all these rules have exceptions.

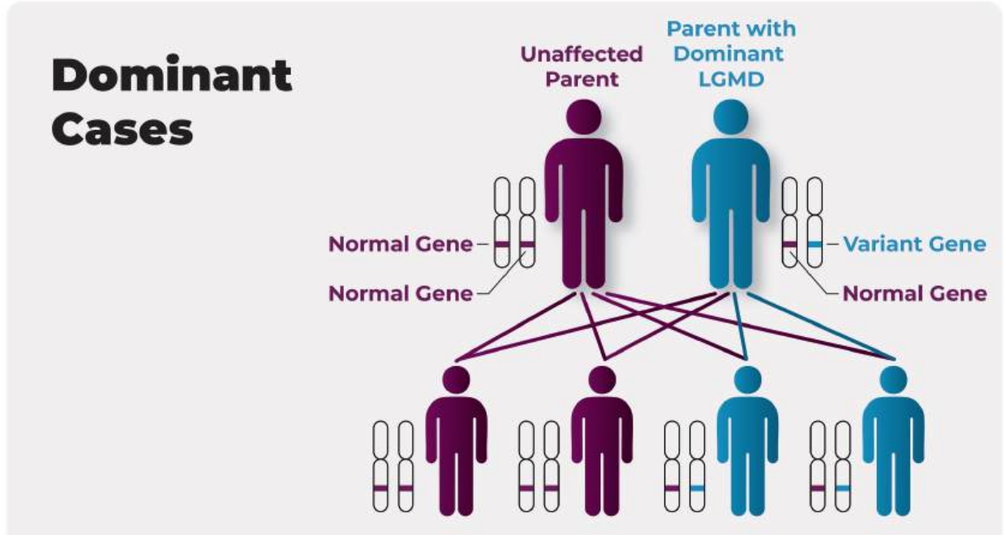




The Naming System for LGMDs

Each gene that causes a form of LGMD is classified as a specific subtype. The way we name the various subtypes of LGMDs is complicated. It is first important to remember that some LGMDs are autosomal dominant, meaning you only need to inherit the altered gene from one parent to have the disease. On the other hand, some are autosomal recessive, which means that you need both copies of the gene to carry a pathogenic variation, one from your mother and the other from your father.





Historically, autosomal dominant LGMDs were called LGMD 1 and autosomal recessive LGMDs were called LGMD2. After assigning the number based on the inheritance patter, the particular gene in which variants were identified was indicated by a letter of the alphabet, in the order in which the genes were discovered. So, for example, a person with 2 variants in the dysferlin gene would have LGMD2B since dysferlin was the second gene discovered to be associated with autosomal recessive LGMD, or someone with one pathogenic variant in DNAJB6 would have LGMD1D because DNAJB6 was the fourth gene to be associated with autosomal dominant LGMD. However, when over 26 different autosomal recessive LGMDs had been identified and we ran out of letters of the alphabet, the naming system needed to be changed.

The naming system for the LGMDs has now been changed so that autosomal dominant forms are now called LGMD D, and autosomal recessive forms are called LGMD R. In addition, a number is now used to denote the gene involved. Additionally, the number corresponds with the order in which the disease-causing variant was discovered which helps further our understanding.

Using the same examples as above, LGMD2B is now called LGMDR2, and LGMD1D is now called LGMDD1. It is a complicated system, so when in doubt the most important thing to tell your doctor is what gene you have a pathogenic variation in (also known as pathogenic variation). For example, you have variants in dysferlin if you have LGMD2B or LGMDR2. The gene itself is the most important feature.

Please see the tables on the following pages which help you understand more regarding the classification system and which gene is associate with which LGMD subtype.

Old name	Gene	New name	Reason why it is no longer considered a LGMD or if it has been added as a New LGMD subtype
Autosomal Dominant LGMD			
LGMD 1A	Myot	Myofibrillar myopathy	Not LGMD: Mainly weakness of the lower legs
LGMD 1B	LMNA	Emery-Dreifuss muscular dystrophy	Not LGMD: High risk on heart rhythm disorders, muscle weakness not according to the LGMD pattern
LGMD 1C	CAV3	Rippling muscle disease	Not LGMD: Most important symptoms are rippling muscles and muscle pain
LGMD 1D	DNAJB6	LGMD D1 DNAJB6-related	N/A
LGMD 1E	DES	Myofibrillar myopathy	Not LGMD: Mainly weakness of the lower legs and cardiomyopathy
LGMD 1F	TNP03	LGMD D2 TNP03-related	N/A
LGMD 1G	HNRNPDL	LGMD D3 HNRNPDL-related	N/A
LGMD 1H	Gene not known	N/A	Not LGMD: Is described in one family only
LGMD 1I	CAPN3	LGMD D4 Calpain3-related	New
Bethlem myopathy dominant	Collagen-6	LGMD D5 Collagen 6-related	New

Old name	Gene	New name	Reason why it is no longer considered a LGMD or if it has been added as a New LGMD subtype
Autosomal Recessive LGMD			
LGMD 2A	CAPN3	LGMD R1 Calpain3-related	N/A
LGMD 2B	DYSF	LGMD R2 Dysferlin-related	N/A
LGMD 2C	SGCG	LGMD R5 Gamma-sarcoglycan-related	The order of these LGMD diseases has changed for logical reasons: alpha, bèta, gamma, delta now have consecutive numbers
LGMD 2D	SGCA	LGMD R3 Alpha-sarcoglcan-related	N/A
LGMD 2E	SGCB	LGMD R4 Bèta-sarcoglycan-related	N/A
LGMD 2F	SGCD	LGMD R6 Delta-sarcoglycan-related	N/A
LGMD 2G	TCAP	LGMD R7 Telethonin-related	N/A
LGMD 2H	TRIM32	LGMD R8 Tripartite motif containing protein 32-related	N/A
LGMD 2I	FKRP	LGMD R9 Dystroglycan-related	N/A
LGMD 2J	TTN	LGMD R10 Titin-related	N/A
LGMD 2K	POMT1	LGMD R11 Dystroglycan-related	N/A
LGMD 2L	ANO5	LGMD R12 Anoctamin5-related	N/A
LGMD 2M	FKTN	LGMD R13 Dystroglycan-related	N/A
LGMD 2N	POMT2	LGMD R14 Dystroglycan-related	N/A
LGMD 2O	POMGnT1	LGMD R15 Dystroglycan-related	N/A

Old name	Gene	New name	Reason why it is no longer considered a LGMD or if it has been added as a New LGMD subtype
Autosomal Recessive LGMD			
LGMD 2P	DAG1	LGMD R16 Dystroglycan-related	N/A
LGMD 2Q	PLEC	LGMD R17 Plectin-related	N/A
LGMD 2R	DES	Myofibrillar myopathy	Not LGMD: Weakness of the distal limb muscles (lower leg, forearm)
LGMD 2S	TRAPPC11	LGMD R18 TRAPPC11-related	N/A
LGMD 2T	GMPPB	LGMD R19 GDP-mannose pyrophosphorylase-related	N/A
LGMD 2U	ISPD	LGMD R20 2-C-methyl-Derythritol 4-phosphate cytidylyltranferase-like protein-related	N/A
LGMD 2V	GAA	Pompe disease	Not LGMD: metabolic disease
LGMD 2W	PINCH2	PINCH-2 related myopathy	Not LGMD: Is described in one family
LGMD 2X	BVES	BVES-related myopathy	Not LGMD: Is described in one family only
LGMD 2Y	TOR1AIP1	TOR1AIP1-related myopathy	Not LGMD: Is described in one family only
LGMD 2Z	POGLUT1	LGMD R21 POGLUT1-related	N/A
Bethlem myopathy recessive	Collagen-6	LGMD R22 Collagen 6-related	New
Laminin α2-related muscular dystrophy	LAMA2	LGMD R23 Laminin α2-related	New
POMGNT2-related muscular dystrophy	POMNGT2	LGMD R24 POMNGT2-related	New

Shared Features

All subtypes of LGMD are caused by a cycle of degeneration and regeneration in your muscles. Because important proteins that form or protect the skeletal muscle are missing or damaged, the muscle is more sensitive to damage. As the muscle is damaged, the body tries to clean up the dead fibers and replace them. This cycle, when it occurs too quickly or too often, eventually leads to loss of muscle, scar tissue and fat replacing the muscle. This cycle is the definition of muscular dystrophy.

In the LGMDs, the muscle loss and subsequent weakness generally starts in the shoulder or hip girdle. The weakness is progressive and eventually includes muscle further down the arms or legs. The trunk and core muscles may also be affected. In many cases (and depending on the subtype), severe weakness may eventually lead to difficulty breathing. In general, the LGMDs will not affect the facial muscles. In some, but not all, subtypes the heart muscle is likely to be affected leading to cardiomyopathy and rhythm disorders. There is further information on respiratory and cardiac issues in later chapters.

Because each LGMD subtype can have unique features and risks, it is important to get genetic testing to understand what specific LGMD subtype you have.

Epidemiology

The LGMDs represent a collection of over 30 different disorders, each of which would qualify as a rare disorder. It is very likely that, worldwide, LGMD2A/R1 is the most common subtype. That said, there is significant regional variation due to founder pathogenic variations in certain genes. For example, LGMD2I/R9 is more prevalent in individuals with a northern European ancestry. LGMD 2C/R5 is common in Tunisia where there is a founder pathogenic variation. Taken together the LGMDs have a prevalence estimate of 0.8-6.9 cases per 100,000 persons. This yields a conservative estimate of between 2,800-24,150 affected individuals in the United States. Limits to prevalence estimates include the challenges of getting genetic testing prior to 2014 when free testing programs became available, and the lack of any central registry for tracking LGMD. It is important for families to participate in patient or academic registries to improve our ability to obtain an accurate count of the number of individuals with LGMD worldwide.

Diagnostic Process

The approach to diagnosing someone suspected of having LGMD will be discussed in future chapters. The development of rapid genetic sequencing and the increasing accessibility of gene testing panels has altered the approach to diagnosing individuals suspected of having LGMD. If available, the diagnostic gold standard is genetic sequencing of genes associated with LGMD.

Other testing might include muscle MRI (a magnetic resonance image that measures how much muscle or fat is present in an individual muscle) which can be helpful for assessing the degree to which muscles are affected. It may also identify specific patterns of muscle involvement associated with specific LGMD subtypes. A biopsy of the skeletal muscle may also be necessary to reveal the cycle of degeneration and regeneration and allows for the evaluation of whether there is an issue with the expression of the various LGMD proteins, which can aid in the diagnosis, especially if the genetic testing is unclear or negative. A common measurement of muscle damage, creatine kinase (CK), may be checked as the degree of elevation may be helpful in differentiating between different subtypes.

LGMD Across the Lifespan

Childhood

Many LGMDs, particularly the autosomal recessive ones, develop in late childhood. Some common LGMDs that develop in childhood include the sarcoglycanopathies (LGMD R3-6) and the dystroglycanopathies (LGMD R9, R13-15, R21, R24). In some instances, the diagnosis may be suspected when a child has motor delays, though this is uncommon with the LGMDs except for the most severely affected. More commonly, the child notices that he or she has difficulty keeping up with peers when playing games or may be extra tired after physical activity. Some forms of LGMD are associated with a “pseudometabolic” syndrome such that they may have a condition called rhabdomyolysis after exercise or illnesses. Rhabdomyolysis results in dark coloured urine and general muscle aches or cramping and often recovers after rest and significant hydration. In general, the weakness in this age group is mostly in the hip or shoulder girdle. It is important in this age group that parents find ways to help a child balance physical activity with exertion.

Adolescence

This is a common decade for individuals to develop the symptoms associated with LGMD and seek medical care. This is the most common age of onset across all LGMDs and is the least likely to be subtype specific. This is likely due to several reasons. First, in this age group individuals often exercise more intensely, and it may be easier to see differences from peers. Secondly, rapid growth spurts may exacerbate weakness. This is biomechanical, in that if the thighs are weak but there is more weight that they must carry, it becomes more difficult. Third, there are likely both protective and detrimental effects from the increased estrogen and testosterone in adolescence. The association between sex hormones and disease progression is not well studied across the LGMDs so there are not specific recommendations associated with this, but in general physicians often see boys develop symptoms earlier than girls. This may be in part related to these hormone changes. In this age group, it is important that planning begin to occur for educational and future career considerations to minimize physically exertive occupations.

Adulthood

The progression of LGMD is typically very slow and measured in years. Some subtypes of LGMD such as LGMDD1-D4, R1, R2, and R12 are more likely to have onset in adulthood, though almost all subtypes have a wide range of age of onset. However, LGMDs are progressive. As individuals progress through adulthood it is quite common to require a motorized wheelchair to move around. Individuals may need a caregiver to help prepare food, bathe, or accomplish other activities of daily living.

Pain may develop, particularly in muscles that do not get as much movement as previously. In many instances it is important to keep track of symptoms that may suggest that the individual has obstructive sleep apnea, like morning headaches or more daytime fatigue.

Cardiac management is dependent on the individual subtype. It is important that pulmonary function tests and echocardiograms (assessments of the heart) be given yearly in suspected cases starting early on. For subtypes where we know there are issues, monitoring should begin much earlier than adulthood to establish baselines. Unfortunately, the natural history, or long-term outcome of these different LGMD subtypes is not known. In some instances, breathing difficulties or cardiac problems may shorten the lifespan. However, there are many individuals with LGMD subtypes who also live a normal lifespan.

Pregnancy

The role of LGMD during pregnancy is twofold. First, women with LGMD should speak with their physician or genetic counsellor prior to pregnancy to assess the potential risk of passing the LGMD subtype to the fetus. In autosomal dominant LGMD, the risk of the child having the disorder is 50/50. In autosomal recessive LGMDs, the child of an individual with recessive LGMD would have a 50% chance of being affected should the non-LGMD parent also have one variant in the same LGMD gene, but the child would only be a non-affected carrier if the non-LGMD parent has no variant in the same LGMD gene.

In the case of family planning for autosomal recessive form of LGMD, the chance that the non-LGMD parent also has a pathogenic variation in the same gene is quite low as long as the parents are not related or from a very isolated community.

Regardless, a discussion with a trained clinician, such as a genetic counsellor, of the risk of passing LGMD to the child is recommended. If needed, use of preimplantation genetic testing with in vitro fertilization is an option that could be used to ensure the condition is not passed to the child.

Second, pregnancy may be more difficult for some women with LGMD. Anecdotally, some women report that the weakness progresses with pregnancy. Also, particularly for women with weak pelvic muscles, labor and delivery may be more difficult. For these reasons it is recommended to discuss any potential pregnancy with your neuromuscular physician and consider care for the pregnancy with a high-risk obstetrician.

Summary of the Common Clinical Elements

- Variable onset across all stages of life (early childhood/adolescence/adulthood)
- Delay in the acquisition of normal motor milestones or progressive loss of autonomy
- Gait disorders with frequent falls
- Possible tendon retractions
- Progressive weakness of the proximal muscles, difficulty climbing stairs or running, lifting arms or weights
- Gowers' sign (climbing maneuver when moving from a supine to an upright position)
- Lumbar hyperlordosis (weakness of core muscles)
- Early fatigue during walking, shortness of breath on exertion
- Due to progressive muscle loss, will likely require assistive devices to help with ambulation with possible loss of ambulation at various ages

Selected Subtypes

Common Subtypes: Dominant

The dominant forms of LGMD are less common than the recessive forms with only five subtypes identified based on the new naming system. Given their rarity only the first and most common dominant LGMD is described below.

LGMD D1 (1D)

LGMD D1, formerly LGMD1D, is caused by pathogenic variations in the gene DNAJB6. As with other dominant forms of LGMD, the typical age of onset is in the 30s or 40s, though there can be considerable variation, including childhood onset. The pattern of weakness is typical for LGMDs. Need for a wheelchair may occur late in the disease. The CK is typically mildly elevated. Involvement of the cardiac or pulmonary systems is not typical.

Common Subtypes: Recessive

The recessive subtypes of LGMD are more common than the dominant ones with 24 recessive LGMDs identified so far. Only the most common 8 recessive subtypes are described below. While the remaining recessive subtypes are ultra rare and not described, they can be identified based on genetic testing.

LGMD R1 (2A)

LGMD R1 is due to pathogenic variations in the CAPN3 gene. As with many of the autosomal recessive conditions, age of onset is during childhood, often in the teens. While some individuals may present with the characteristic weakness of the shoulder and hip girdles, several other patterns of weakness have been identified, including early scapular winging (when shoulder blades protrude from the back) and weakness in the calves. The thigh muscles are often spared. Muscular presentation can be asymmetric, and it may be mistaken for facioscapulohumeral muscular dystrophy (FSHD) in these instances. Contractures, particularly in the ankles, may develop early in the disease course with the child walking on tip toes. Loss of ambulation is common in LGMDR1. Respiratory involvement is rare and typically follows pelvic girdle weakness, once individuals require a wheelchair. Cardiac involvement is not typically reported. Creatine kinase (CK) levels may be very elevated in LGMDR1. There are known founder pathogenic variations in LGMD R1 in the Amish and Basque populations.

LGMDR2 (2B)

LGMDR2 is caused by loss of function variations in the dysferlin gene and has a distinctive pattern of weakness that is somewhat different than most of the other LGMDs. Aside from progressive shoulder and hip girdle weakness, muscles of the lower limbs can also have weakness. In fact, studies have shown that the muscle that allows standing on tip toes is one of the first muscles affected in LGMDR2 and during later stages of the disease weakness in the hand or finger muscles can be detected. The detection of lower limb weakness in some individuals with variants in the dysferlin gene has led to an alternative disease name, Miyoshi Myopathy type 1 (MM1). However, extensive study of LGMDR2 and MM1 have shown that they are the same disease. The cardiac muscles are not typically affected but it is possible to develop mild respiratory symptoms as the disease progresses. Most individuals with LGMDR2 lose ambulation over a prolonged disease course. Like LGMDR1, CK can be very high in LGMDR2.

LGMDR3-6 (2D-2F)

As a group, LGMDR3, R4, R5, and R6 are called the sarcoglycanopathies because they affect 4 different sarcoglycan genes. Loss of alpha-sarcoglycan results in LGMDR3(2D), loss of beta-sarcoglycan results in LGMDR4(2E), loss of gamma-sarcoglycan causes LGMDR5 (2C), and loss of delta-sarcoglycan causes LGMDR6(2F). LGMDR3 is the most common and LGMDR6 is the least common. The 4 sarcoglycan molecules form a complex at the muscle membrane. Pathogenic variations in any of the sarcoglycan genes result in a severe form of LGMD.

LGMDR4 has a founder population in the Amish population and LGMDR5 has a founder pathogenic variation in Tunisia and North Africa. In many instances, all individuals with LGMD R3-6 have a more severe disease course and may present early in childhood. Given the age of onset and high CK, boys with sarcoglycanopathies may be mistaken for the more common Duchenne muscular dystrophy (DMD). The weakness seen in DMD is in a characteristic LGMD pattern and calf and tongue hypertrophy are common together with other features. Loss of ambulation may occur during teenage years. Respiratory failure is a common feature of late disease. Cardiac function is typically affected with a cardiomyopathy and associated arrhythmias. The CK is often very high in LGMDR3-6.

LGMDR9 (2I)

LGMDR9 (2I) is caused by loss of function variants in the FKRP gene. It is more commonly found in Scandinavia and parts of England, often with a common homozygous variant (L276I) (meaning the same variant is present on both gene copies). In general, homozygous L276I variants have a less severe course than those with compound heterozygous variants (meaning have a different variant on each copy of FKRP). Weakness often develops in adolescence, though this is variable and somewhat related to the variation present. Shoulder and hip girdle weakness is common. In this subtype, patients have better arm strength than other subtypes early on. In the majority of individuals, enlarged calves may be present. Exercise has been reported to induce symptoms and there are multiple instances where the initial symptoms may be of rhabdomyolysis or myoglobinuria (where the muscle leaks into the urine to make it look tea-colored). Compared to other forms of LGMD, individuals will often report exercise induced pain. Loss of ambulation typically occurs in the 20s-30s, particularly with compound heterozygote pathogenic variations. Respiratory function is affected earlier in the disease course compared to many other subtypes. Individuals may also develop mild cardiomyopathy. The CK is high, but less so than LGMDR1-6.

LGMDR12

LGMDR12 (2L) is due to loss of function variants in the ANO5 gene. LGMDR12 is common in Northern Europe. In contrast to other recessive forms of LGMD, LGMDR12 has a later age of onset and possibly a slower rate of progression. Similar to LGMDR9, individuals may have pain with exercise and may present with rhabdomyolysis. Like LGMDR2, LGMDR12 can also be associated with weakness in the lower limbs and has also been given the alternative clinical diagnosis of Miyoshi Myopathy type 3 (MM3). With a later age of onset and slower progression, it is uncommon for patients to lose ambulation. Respiratory and cardiac function is usually not affected. Creatine kinase is highly variable and may be normal or highly elevated.

General Approach to Care

Individuals living with LGMD often benefit from a multidisciplinary care approach. It is recommended that this care approach include an LGMD physician specialist, genetic counselor, physical therapist, respiratory therapist, speech therapist, dietician, psychologist, and a nurse navigator. Other important members of the care team that may be scheduled outside of the clinic include a cardiologist as well as a pulmonologist. This comprehensive care approach promotes the management techniques discussed throughout the following chapters, which provide more detail about individual care and management. Importantly, care is best provided in centers with access to a multidisciplinary clinic.

03

Diagnosis

History

Limb Girdle Muscular Dystrophy (LGMD) was first recognized as a disease category separate from Duchenne muscular dystrophy (DMD) and other categories of muscular dystrophy in the 1950s. In light of inheritance patterns including multiple affected individuals within families, it was long believed that LGMD had genetic origins. Due to the significant variability of symptom onset, rate of progression, and complications among patients with LGMD, physicians, scientists, and families also suspected that there were multiple genetic causes of LGMD. These suspicions were confirmed beginning in the 1990s, when the first LGMD genes were discovered. A flood of genetic discoveries followed, to the point where today over 30 different genetic subtypes of LGMD are recognized. As research progresses, we expect new subtypes to be identified.

Diagnostic Principles

Due to the rapid advances in genetic diagnostic technologies in recent decades, genetic testing is now central to the complete diagnosis of LGMD. However, there are many cases in which genetic testing is inaccessible, genetic test results are non-diagnostic, or genetic test results do not provide a definitive answer. For these reasons, it is important to remember that for clinical care purposes, a diagnosis of LGMD does not require genetic confirmation. We will thus review classic and modern clinical methods of diagnosing LGMD and then discuss genetic diagnosis.

Clinical Diagnosis: History and Physical Examination

Primary care physicians are often the first line of assessment for children and adults who develop symptoms of LGMD. Primary care physicians may do some basic testing, but in most cases will rapidly refer a patient with suspected LGMD to a specialist for more definitive diagnostic evaluations. These specialists may include paediatric and adult neurologists, as well as geneticists and genetic counsellors.

The fundamental clinical feature of LGMD is muscle weakness, typically starting in the hip muscles and then spreading outwards to other muscles. In the upper extremities, the shoulder and upper arm muscles are typically affected first. Some of the genes associated with LGMD are also associated with what are called distal myopathies (DD), also known as distal muscular dystrophies, in which weakness is most prominent in the hands and/or feet, with symptoms spreading inwards. There is some controversy about whether DD is a separate category of muscular dystrophy than LGMD.

The age of symptom onset varies widely, not only between different genetic subtypes of LGMD but even within subtypes. Symptoms may begin anytime from early childhood to adulthood. The age of symptom onset has classically distinguished LGMD from congenital muscular dystrophy (CMD), with CMD having onset before 2 years of age and LGMD having onset after 2 years of age. However, more recently some physicians have proposed using motor milestones as a means of distinguishing the two categories, with CMD defined as a muscular dystrophy in which a patient never walks independently, and LGMD defined as a muscular dystrophy in which a patient is able to walk independently for at least part of their lives.

Inheritance patterns also help distinguish LGMD from other types of muscular dystrophy, particularly X-linked forms such as Duchenne muscular dystrophy (DMD). These patterns are discussed in more detail in the Genetic Diagnosis section.

Clinical Diagnosis: Basic Laboratory Studies

Blood tests that could detect the possibility of muscular dystrophy began to be discovered in the mid-20th century. The most famous of these blood tests is the creatine kinase (CK) level, also known as the creatine phosphokinase (CPK) level. LGMD R2, R3, R4, and R5 are always very high (>100 times the normal value) while in many other subtypes the CK is 3-5 times above normal. The value tends to decrease over time with muscle loss. Aldolase is another blood test that is often abnormal in the setting of muscular dystrophy. What is less well known is that 3 other blood tests that are usually associated with liver function may also be slightly abnormal in muscular dystrophy: alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate dehydrogenase (LDH). Some patients with muscular dystrophy first come to medical attention due to mild elevations in ALT, AST, and/or LDH, and if the possibility of muscular dystrophy does not come to mind immediately, these patients may end up having a significant evaluation for liver disease before the diagnosis of muscular dystrophy is eventually pursued.

Clinical Diagnosis: Muscle Biopsy

Muscle biopsies have been performed since the 19th century to assist with the diagnostic evaluation of suspected muscular dystrophy. Muscle specimens are frozen and then cut into very thin slices that are stained in various ways to help illuminate various structures inside and outside the muscle fibers. The oldest stains for muscle biopsy specimens are based on dyes and chemicals. In recent decades, since the discovery of specific genes and proteins associated with muscular dystrophy, antibody-based stains detect the presence or absence of specific proteins in the muscle slices. In some cases, evidence for specific genetic subtypes of muscular dystrophy can be detected on muscle biopsy, but in many other cases, such specificity is not attainable, and the conclusion of the biopsy may simply be muscular dystrophy, without a definite clue regarding the genetic subtype.

Clinical Diagnosis: Muscle Ultrasound and Muscle MRI

It has become increasingly apparent that imaging technologies such as ultrasound and MRI can be helpful in the diagnostic evaluation of potential muscular dystrophy. Certain patterns on these tests can suggest the diagnosis of muscular dystrophy. In some cases, patterns of muscle involvement, particularly on MRI, can even suggest specific genetic subtypes of muscular dystrophy.

Diseases that can mimic LGMD

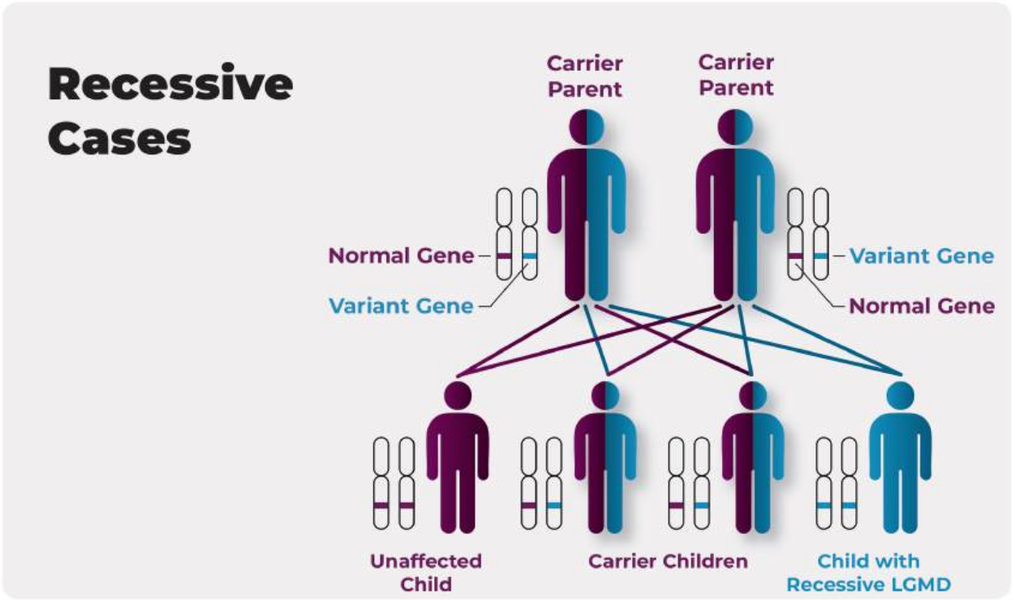
Other muscular dystrophies can mimic LGMD. These include Duchenne muscular dystrophy (DMD), Becker muscular dystrophy (BMD) and facioscapulohumeral muscular dystrophy (FSHD). It is important to note that the most common form of FSHD is not always detected on next generation sequencing panels and often requires a specific genetic test in order to rule it in or out. Aside from other forms of muscular dystrophy, several other types of neuromuscular disorders are known to mimic LGMD. Some of the disorders that most often mimic LGMD include spinal muscular atrophy type III (which can even be accompanied by mild to moderate elevations in serum CK levels), late onset Pompe disease (which is typically associated with elevated CK levels), and some forms of congenital myasthenic syndrome. Many next generation genetic sequencing panels that include LGMD also include testing for these other disorders. Lastly, there are rare occasions when a non-genetic disorder can mimic LGMD, particularly some autoimmune muscle diseases such as anti-HMGCR myopathy. Genetic testing will not detect autoimmune disorders so different diagnostic tests will be needed if these disorders are under consideration.

Genetic Diagnosis

The double helix structure of DNA was discovered in the mid-20th century. This knowledge helped scientists and physicians understand how genetic traits could be inherited from one generation to the next, showing symptoms in some individuals but not others. In the decades that followed, scientists developed techniques to link specific regions of DNA with specific diseases. Methods to read DNA sequences were also developed. These advances laid the foundation for the seminal genetic discovery in the muscular dystrophy field, the identification of the gene linked to Duchenne muscular dystrophy in 1986. In the 1990s, the first genes for LGMD were discovered, followed by many more, leading to a current total of over 30 genes associated with LGMD.

All genes linked to LGMD are autosomal, meaning that each one is located on one of the 22 regular paired chromosomes, not on the X or Y sex chromosomes. Each gene on these 22 paired chromosomes thus has two copies, one on each chromosome. Some of the genes linked to LGMD are autosomal dominant, meaning that only one affected copy of the gene is needed to cause disease. If one parent is affected by autosomal dominant LGMD, then there is a 50% chance that their child will also have LGMD and a 50% chance that the child will have two normal genes (unaffected and not a carrier). Other LGMD genes are autosomal recessive, meaning that both copies of the gene must be affected to cause disease. Individuals with only one copy of the affected gene are not affected but are carriers and can pass the abnormal gene to their children. If both parents are carriers for LGMD and neither are affected, there is a 25% chance their child will have LGMD, a 50% chance the child will be a carrier for the disease, and a 25% chance the child will have two normal genes (unaffected and not a carrier)

In some cases, the disease-causing genetic change is not inherited from either parent but arises spontaneously in the affected individual during embryonic development. It is also important to note that sometimes the genetic change has what we call variable penetrance, which means, 2 people can have the same genetic change, but it will affect them differently, causing symptoms of LGMD in one person but not the other.



For years after the first genes for LGMD were discovered, individual segments of genes had to be sequenced to pursue genetic diagnoses. This approach, called Sanger sequencing, was laborious and difficult to scale up as more and more LGMD genes were discovered. Over the past decade or so, newer genetic sequencing techniques were developed, especially targeted sequence panels and whole exome sequencing, collectively known as next generation sequencing approaches.

Whole genome sequencing has also become increasingly available on a clinical basis, though not as widely as whole exome sequencing. These techniques can seek DNA changes in many genes simultaneously and have now been fully absorbed into clinical genetic diagnostic laboratories and have become routinely available in many countries. These technologies enable us to confirm genetic diagnoses in up to half of the individuals with LGMD.

It is important to pursue a genetic test whenever possible. An accurate genetic subtype diagnosis will guide disease management because certain subtypes are more likely to be associated with complications affecting the heart or lungs. An individual's genetic test results could also help them make family planning decisions and can help identify other family members who may be affected by LGMD. Since most drugs in development are designed to treat specific subtypes, a genetic diagnosis is often a requirement to participate in clinical trials. It will also likely be necessary for access to many future targeted treatments.

For some individuals with LGMD, a situation arises where genetic testing does not yield any relevant pathogenic variants. This is sometimes due to a total lack of genetic findings and sometimes due to incomplete results, often involving indeterminate findings called "variants of unknown significance", abbreviated as VUS or sometimes VOUS. These situations are frustrating for patients, their families, and the health care professionals involved with their care.

It is important for patients to continue follow-up care even when a genetic diagnosis is not initially forthcoming, as variant interpretations may change over time, newer genetic test technologies may become available, and new genes associated with LGMD may be discovered. Some research laboratories use genetic techniques that are not widely available in clinical diagnostic laboratories, including long read whole genome sequencing (an advanced form of whole genome sequencing) and transcriptome sequencing (RNAseq) to find genetic variants that are not easily detected by more widely used techniques. Following patterns seen with older technologies, we anticipate that these research-based techniques will eventually find their way into many clinical diagnostic laboratories, increasing the diagnostic capabilities of clinical genetic testing even further.

04

Neuromuscular Management

After being diagnosed with LGMD, a neuromuscular specialist will take the lead in your care. This doctor has specialized training in treating conditions that affect the muscles and nerves, like LGMD. They will be there to guide you and your family throughout the course of the disease, helping to manage symptoms, recommend treatments, and address any concerns that arise over time. Neuromuscular specialists are experts in understanding the complex nature of muscle diseases, and they work closely with other healthcare providers to make sure you get the most comprehensive care.

If you're unsure how to find a neuromuscular specialist, you can start by asking your primary care doctor for a referral. You can also reach out to organizations like the Muscular Dystrophy Association (MDA), TREAT-NMD or the World Muscle Society, which can help connect you to specialists in your area. Finding the right expert is an important step in ensuring you get the best possible care and support for living with LGMD.

Websites

www.mda.org
www.treat-nmd.org
www.worldmusclesociety.org

Communicating the Diagnosis

When you are diagnosed with LGMD, it's important that the news is shared with you in a visit that is focused entirely on explaining the disease, answering your questions, and giving you all the information you need to understand your diagnosis. The appointment should be at least one hour long to ensure there's enough time to talk through your diagnosis, discuss what the future might look like, create a care plan, and provide genetic counselling.

Your diagnosis should be communicated in a calm and private setting, away from interruptions. It's recommended that you bring at least one family member with you for support. Both you and your family should feel encouraged to ask any questions during the visit.

The diagnosis should only be given once it is fully confirmed to avoid any confusion. If the diagnosis is not yet clear—like if there are uncertain genetic results or only one variant is identified—the doctor should clearly explain the next steps and what will be done to confirm the diagnosis.

During this visit, your doctor will discuss what to expect in terms of the progression of the disease. However, it's important to note that it's better to focus on the facts and avoid being overly pessimistic, especially in the beginning. The goal is to provide clear information and help you understand that while there is currently no cure that can reverse the progression of the disease, there are ways to manage it. Many patients prefer to not hear about the long-term consequences right away, as this can often be discussed more fully in follow-up appointments when you're ready.

You and your family will also work with your doctor to create a care plan. This plan will include how often you should come for check-ups and make sure you have a team of doctors, including a neuromuscular specialist, who can help manage not just the muscle-related issues but also any other health problems that might arise, like heart, lung, or digestive issues. It's important to also involve physiotherapists and other specialists like speech or occupational therapists as soon as possible to help you manage the disease more effectively.

Once your diagnosis is confirmed, genetic counselling will be an important part of your care. If there are specialized genetic counsellors in your area, your doctor may suggest scheduling a session with them to discuss testing for family members—whether they are affected or not. They will help you understand what genetic testing means for you and your loved ones, and it's important that you feel comfortable asking questions to make sure everything is clear.

In addition to verbal information, your doctor will give you written resources - these will explain the diagnosis in simple terms and outline your next steps. It's also important to discuss any potential treatments, including approved therapies or ongoing clinical trials. Your doctor may also mention other research opportunities that could be available to you, either in your local area or at specialized centers.

You may feel isolated after your diagnosis but remember that there are support groups and patient advocacy organizations that can connect you with others who are living with LGMD. It's highly recommended to reach out to these groups for support and information and many URLs are included in this guide.

Lastly, after the diagnosis, you might still have questions or concerns. It's always helpful to schedule another appointment soon after the initial visit, or if needed, you can contact the medical team directly with any questions you may have in the meantime.

Assessments

Periodic assessments are crucial for managing LGMD. We generally recommend having at least one appointment per year to monitor your health and ensure the best care. During these visits, your healthcare team will discuss your motor function, looking at any changes you've noticed and new challenges you may face in daily activities. This conversation helps your doctors identify any risks and figure out ways to support you. It's also important to discuss symptoms that go beyond just muscle weakness, such as breathing difficulties, trouble sleeping, heart problems, swallowing issues, gastrointestinal problems, or muscle pain. If any of these are affecting you, your doctors will refer you to the right specialists for further care.

You may also find it helpful to keep a symptom diary, noting any changes or challenges you experience, along with any questions you have. This will be useful during your appointments and ensure nothing is overlooked.

Consistent and thorough clinical assessments are key to managing LGMD. Your healthcare providers will use a set of muscle function tests to track your progress and adjust your care plan. It's important that the same set of tests is used consistently, so your team can understand how your disease is progressing. Questionnaires about your daily activities and quality of life can also help track your needs and symptoms. The goal is to avoid unnecessary tests and ensure that everyone on your care team is working together efficiently.

Roles and Responsibilities of the Neuromuscular Specialist in Your Care
Your neuromuscular specialist plays a central role in your care. Here's how they'll support you and your family:

A. Assess your unique disease trajectory: The specialist will use proven tools to monitor your condition over time, helping to predict how the disease might progress and advising on potential complications. This will help them offer the best guidance for your future care.
B. Create a personalized treatment plan: Using the information gathered from assessments, your doctor will develop a customized plan to meet your needs and goals. This plan will focus on improving your quality of life and addressing any specific concerns you have.
C. Coordinate care with other specialists: Your neuromuscular specialist will involve other healthcare providers as needed, especially if you are part of a multidisciplinary LGMD clinic. This collaborative care approach ensures you receive comprehensive support from a team of experts.
D. Connect you with support services: From the moment you are diagnosed, your specialist will help connect you with community resources, patient organizations, and support services that can assist with your care needs. These organizations can provide you with reports and help with accessing support in your local area.
E. Guide you through treatment options: Your neuromuscular specialist will be your first point of contact when it comes to deciding on treatments. They will help you weigh the risks and benefits of different options, including:
   - Technological interventions for managing your breathing and heart health
   - Surgical and non-surgical options for things like spinal fusion or contracture management, as well as aids and appliances that might help
   - Pharmacological treatments and access to new therapies, including participation in clinical trials for investigational drugs
   - Your doctor will work with you to ensure the treatments you choose align with your goals and values.
F. Advocate for your care: Your specialist will advocate for the best possible LGMD care both at your healthcare facilities and in the community. They'll address concerns like the transition from pediatric to adult care providers, ensuring that your hospital care is tailored to your unique medical and physical needs.
G. Support in end-of-life care: While this is a difficult subject, your neuromuscular specialist will also help you and your family navigate end-of-life care if it becomes necessary. They will focus on maintaining comfort, dignity, and quality of life, ensuring your preferences are respected throughout this process.

05

Pulmonary Management and Swallowing

Some LGMD subtypes may develop problems with breathing over time. In general, subtypes that affect the ability to walk in adolescence or early adulthood are the most likely to have breathing problems develop during the course of the disease. Respiratory symptoms in some subtypes of LGMD may emerge gradually over time. While the lungs themselves are not directly affected by LGMD, the muscles that facilitate breathing can weaken, leading to progressive respiratory challenges. Weakness in these muscles, particularly in the chest and diaphragm, may reduce the ability to take full breaths or clear secretions effectively through coughing.

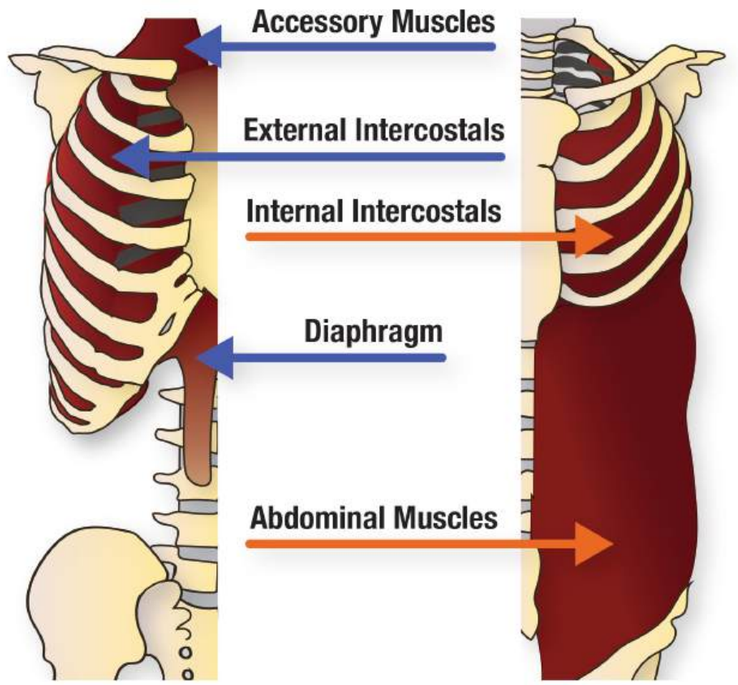
In individuals with LGMD, respiratory issues often begin to manifest during adolescence or early adulthood, particularly following the loss of ambulation or the development of scoliosis. Scoliosis — a curvature of the spine — can occur as postural muscles weaken and lose the ability to support the torso. Severe scoliosis can further compromise lung function by reducing thoracic volume and impairing the clearance of respiratory secretions.

It is important that any new or changing respiratory symptoms - including shortness of breath, weak cough, or frequent respiratory infections - be promptly discussed with your care team. Early identification of respiratory involvement enables timely intervention, which may reduce the risk of complications and preserve quality of life.

Thanks to advances in clinical care and research there are things that you can do to manage the respiratory effects of LGMD. Preventative measures and interventions can help you maintain your respiratory health and treat respiratory complications. Prevention and appropriate treatment of respiratory complications is critical to prevent hospital admissions, loss of independence or life-threatening conditions.

If your team does not include a pulmonologist or a doctor who specializes in breathing, it may be best to ask to see them when you have these concerns.

Muscles of Breathing



Symptoms of Respiratory Muscle Weakness

· Shortness of breath (sometimes referred to dyspnea)
· The feeling that you cannot take a deep breath
· Difficulty breathing with activities
· Weak cough or the inability to clear secretions (mucous)
· Recurrent respiratory infections or illness that takes a long time to recover
· Trouble swallowing

In clinic, your provider may order a pulmonary function test (PFTs) which is a measure of the amount and the force of the air you are able to inhale, exhale and cough. These measurements can help to diagnose respiratory muscle weakness and guide your provider to proper therapy. Measuring the strength of your cough is especially important as this is our body's best mechanism to get rid of the secretions in our lungs that do not need to be there. It is very important to get a baseline test in times of health, so your team has the ability to follow these results over time.

Losing the ability to cough may lead to worsening respiratory problems and infection. When and if your cough weakens your provider may, or should, talk to you about a device called a cough-assist. This device can help you take a deep breath and then work with your cough to remove the mucous that you may have trouble clearing on your own. If you have trouble swallowing or getting the mucous out of your mouth as well, you should also have a suction machine at home. The effective use of the cough-assist when needed can keep you healthy. PFTs will also alert your care team to when breathing muscles are getting weaker and this may trigger more questions about how you are doing when you are asleep.

Hypercapnia

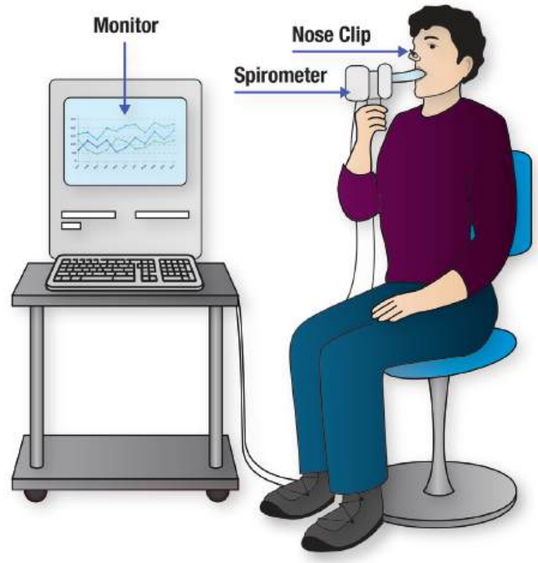
The danger of CO_2 retention (hypercapnia) in individuals with LGMD - or any condition that weakens respiratory muscles - can be serious if not managed properly. This may result in the retention of carbon dioxide (CO_2) in the blood, a condition known as hypercapnia.

Signs of CO_2 retention can include:

- Confusion, irritability, or difficulty concentrating
- Fatigue and daytime sleepiness
- Shortness of breath, especially lying down (orthopnea)
- Morning headaches
- Shortness of breath
- Restless sleep or frequent waking

Respiratory failure can be a result of CO_2 retention which is a life-threatening condition requiring urgent intervention.

People with LGMD often have trouble breathing while they are asleep, and these symptoms can be difficult to diagnose. Everyone's muscles naturally relax during sleep, but in people with a muscle disease, this can lead to hypoventilation, or shallow breathing. When breathing becomes shallower at night, carbon dioxide builds up in the body, which can cause headaches, trouble concentrating, and increased tiredness during the day. These are all signs of poor sleep quality. If you experience any of these symptoms, it is important to discuss them with your healthcare team.



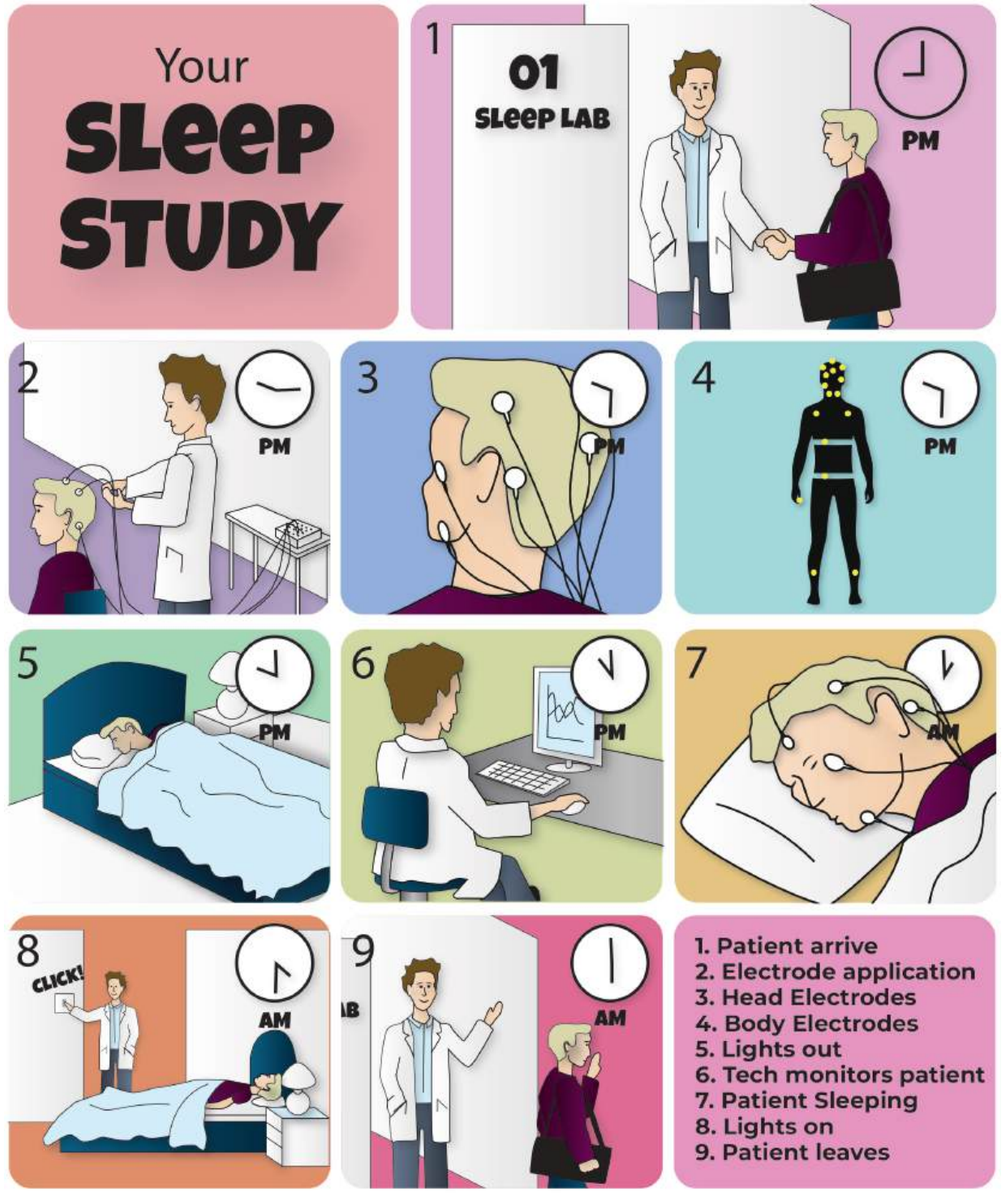
Symptoms of Sleep Disordered Breathing (Trouble sleeping)

- Morning headaches
- Trouble sleeping or waking up throughout the night
- Restless sleeping
- Difficulty lying flat in bed
- Waking up tired
- Feeling tired during the day
- Trouble concentrating at school or work

If you feel like you're having trouble breathing while you sleep, your provider may order a sleep study to better understand what's happening at night. This test is done overnight in a hospital and should be performed at a certified centre that specializes in neuromuscular diseases. This expertise is important because not all sleep centres measure carbon dioxide levels during the night, and that information is key to diagnosing hypoventilation, or shallow breathing.
A sleep study also looks at whether breathing stops or pauses during sleep, which is known as apnea. While helpful, the test isn't perfect—you're not in your usual sleeping environment, and you'll have monitors tracking your breathing, heart rate, and oxygen levels. Sensors on your head help identify sleep stages, which is important because people with muscle disease may have more difficulty during certain stages, like dreaming.

If a sleep lab isn't easily accessible, your provider might begin with a home device that measures oxygen levels and heart rate—this is called an oxygen saturation test. While not as detailed, it can provide helpful clues about what might be happening during the night.

Sleep Study



If you do have symptoms overnight and have an abnormal sleep evaluation your provider may talk to you about using respiratory support overnight.
This support, called non-invasive ventilation, has two forms:

1) CPAP or Continuous Positive Airway Pressure
2) BIPAP or Bi-level Positive Airway Pressure

Though we do not have the depth to go into the differences here in detail it is important to understand that in neuromuscular disease, BIPAP is the most appropriate choice of therapy to use in most situations. About 25% of patients with LGMD will require support at night and this risk can be even higher if there is scoliosis as well. BIPAP helps you to take a deep breath and helps keep your lungs open. The best analogy is that it moves your breathing muscles just like a wheelchair helps you with mobility when you have lost the ability to walk. Your provider should have a detailed discussion about using this therapy and you should never hesitate to ask questions when you have them.

BIPAP is the most appropriate and preferred choice of therapy for individuals with LGMD. CPAP is usually not recommended for patients with muscular dystrophy (MD) who have exhausted respiratory muscles.

It is particularly important to think about emergency care in LGMD, especially if you have respiratory problems already, as emergencies and illness can make them worse. We all get a little weaker when we get sick and when you start out with LGMD, symptoms and severity multiply.

We spoke about the cough-assist already, and when sick, you should be using it as much as you can tolerate to keep your lungs clear. If you use support overnight and you are feeling bad during the day, there is no reason you cannot use this support when needed but you should always update your provider if you are having trouble.

Though most patients will be able to manage their respiratory symptoms with a combination of the cough assist and non-invasive ventilation overnight, there may be some patients who have more difficulty as they get older and lose more muscle strength and there may be options for them to discuss with caregivers if they need to use the BIPAP more than just when asleep. Some patients may use BIPAP during the day to help rest or some may choose more permanent ventilation if that fits better with their quality of life.

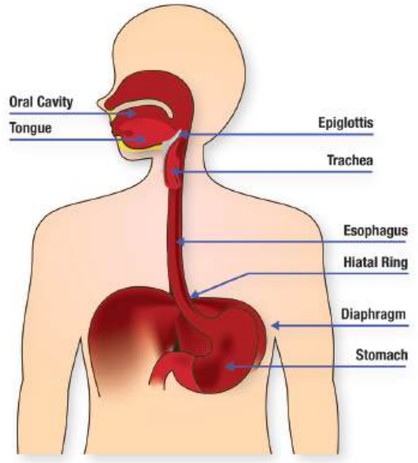
We also recommend that if you feel you need to go to the ER or urgent care it is best if you bring your equipment with you because it may not be available to you outside of a specialized center. It is also very important to always carry an emergency card with you, with guidelines to follow in case of an emergency. Hopefully, you will never have a respiratory emergency, but it is always better to be prepared and have a plan just in case.

AFM-Telethon have produced a medical emergency information sheet for LGMD, which can be found here:

https://lgmd.afm-telethon.fr/fiche-durgence-medicale-lgmd/

Difficulty Swallowing (Dysphagia) in LGMD

Eating safely is a complex task requiring coordination between breathing and moving the food safely from the mouth to the stomach. Swallowing difficulty, also known as dysphagia, can occur in some individuals with LGMD, especially in people with weakness of the diaphragm muscle. Though this is not a common symptom in LGMD, if there are signs of dysphagia these should be addressed to help lessen any potential impacts to overall health. Left untreated, dysphagia can result in aspiration pneumonia, especially in someone with breathing difficulties already, and this can make individuals very sick.



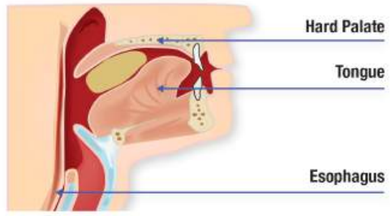
What does normal swallowing look like?

Swallowing requires finely tuned timing and coordination of ~50 pairs of muscles to safely eat and drink. Since the mouth and throat are used for both eating and breathing, it is very important for the body to protect the airway and avoid food or liquid getting into the windpipe (trachea). The timing of when the food moves through the mouth and throat and when the airway closes is of vital importance for lung (pulmonary) health.

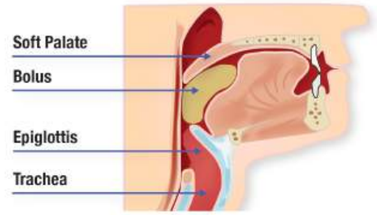
The act of eating and swallowing foods is divided into four phases:

Phases of swallow	Actions occurring
Oral preparatory	· taking food or liquid into the mouth · moving liquid/solids (a “bolus”) around in the oral cavity · chewing of solids · airway is open during this stage
Oral swallow	· movement of liquid/solids out of the mouth and into the throat (pharynx) · airway starts to close to protect itself
Pharyngeal swallow	· movement of liquid/solids through the throat into the esophagus · airway is closed throughout this phase and breath holding occurs
Esophageal swallow	· movement of liquid/solids through esophagus and into stomach · airway is open

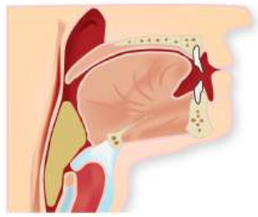
For the oral and pharyngeal phases, coordination of the movement of the food as a unit or “bolus” also must be timed relative to breathing to avoid food or liquid entering the windpipe (trachea) or deeper into the lungs.



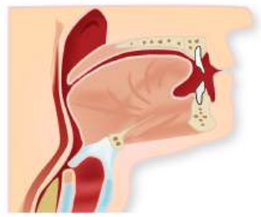
Oral Preparatory Phase



Oral Transport Phase



Pharyngeal Phase



Esophageal Phase

Signs of Difficulty Swallowing

Dysphagia symptoms can be different for everyone. They can occur when drinking or eating or both. Often symptoms start happening only occasionally and can be only with pills, with certain foods, or later in the day when someone may be more fatigued. Symptoms of dysphagia may include any or all the following:

- fatigue or difficulty chewing
- limiting or avoiding harder to eat foods
- limiting liquids if they are more challenging to drink in a way that feels safe
- difficulty starting to swallow
- feeling that foods get “stuck” when going down
- swallowing multiple times on a single bite or sip
- coughing or throat clearing during or right after meals
- a wet or “gurgly” sounding voice during or right after meals
- mealtimes taking longer
- unintentional weight loss

How to Assess dysphagia

If you are concerned about your swallowing for any reason, be sure to speak about it with the physician you see for your LGMD. They can refer you to a speech-language pathologist/therapist (SLP or SLT) who can work with you to assess your swallow and provide recommendations. If you are seen in a multidisciplinary care clinic you may have an SLP in clinic that you can see to discuss your concerns. For children, an occupational therapist may also be helpful for concerns with feeding.

- For any swallowing evaluation there is an initial, general assessment of anatomy and function of the muscles of the head and neck as well as overall oral hygiene

- For all assessment types your therapist will likely also try positional changes, swallowing strategies, or adaptive utensils to help improve function. These will be individualized to your specific needs and function.

Types of swallowing tests:

Clinical swallow evaluation
- this usually takes place in an office or can be done at bedside for individuals in the hospital
- evaluation involves an assessment of anatomy and physiology as it relates to eating
- trials of liquids and/or food are generally provided to observe swallowing

Videofluoroscopic swallow study/modified barium swallow study (VFSS/MBS)
- done in x-ray suite, often with radiologist present
- evaluation of swallow using x-ray video
- utilizes barium liquids and coated foods to observe swallowing

Fiberoptic endoscopic evaluation of swallowing (FEES)
- Done in outpatient office, an ear, nose, and throat doctor may also be present
- Evaluation of swallow using a scope with a camera to visualize the pharynx when eating
- Utilizes liquid and solid food trials that are often dyed with food coloring to help make them easier to see

Treatment options for dysphagia

Interventions for dysphagia focus on specific symptoms. A referral to an SLP/SLT should be consulted for development of an individualized treatment plan to address the unique needs of someone living with LGMD and dysphagia. Common options for supporting nutrition for someone with swallowing difficulty may include some of the following:

- Changing textures/consistencies of foods ingested
- Individualized positional changes or types of support to optimized safety when eating
- Being mindful of fatigue levels at mealtimes
- Use of adaptive utensils to help with ingestion of food and/or liquid
- Implementation of a consistent oral hygiene regimen
- Consultation with a dietitian to ensure proper nutrition and hydration

Care at the intersection of lung health and swallow function

The different systems of the body are often interconnected and overlap significantly. Some important considerations for individuals with LGMD that sit in the intersection of lung and swallow function include the following:

- Use of cough assist and/or suction as directed by your pulmonologist
- Consistent and good oral hygiene
    - Having a regular routine to brush and floss teeth is very important for dental health. Loss of teeth can impact intake of food and make it harder to support nutritional needs.
    - Brushing teeth is the best way to remove the bacteria that can stick to the teeth. These bacteria can also be present in our saliva and potentially be aspirated into the lungs where they may cause pneumonia.
    - The American Dental Association recommends
        - Brushing teeth 2 times a day for 2 minutes with a fluoride containing toothpaste
        - flossing at least once a day
        - limiting sugary snacks
        - regular dental checkups every 6 months

Be sure to talk with your dentist about any accommodations you may need for how you are positioned so you feel comfortable during your cleaning or any dental procedures. Many can accommodate patients remaining in their wheelchairs or being more upright – be sure to ask!

06

Rehab Management

Individuals living with LGMD may benefit from a collaborative approach with different specialists that focus on ways to optimize movement and function to participate in life activities.

The rehabilitation team may include some or all of the following providers:

1. Physical therapist: A healthcare provider who specializes in movement and working to improve physical function by managing chronic conditions, assisting with recovery from/preventing injury, and management of pain.

2. Occupational therapist: A healthcare provider who focuses on helping individuals perform life activities that are important to them including activities of daily living, work, recreation, social activities.

3. Physiatrist: A medical doctor who specializes in physical medicine and rehabilitation. They can diagnosis medical problems, prescribe treatment plans to improve an individual's ability to function. Treatments they prescribe may include injections, medications, and physical or occupational therapy.

4. Orthotist: A healthcare provider who specializes in designing, making and fitting orthotic devices that are intended to support or protect body areas. They may work in coordination with the Orthopedic Doctor, physical therapist and/or occupational therapist to do this. Some examples of orthotics may include ankle or leg braces (AFOs), hand splints, and back supports.

5. Speech and language therapist: A healthcare provider who specializes in supporting individuals to communicate effectively and to swallow safely. If muscle weakness affects muscles of the neck, mouth, or respiration, the ability to produce speech, chew or swallow may be impacted.

6. Wheelchair therapist: Some physical and occupational therapists specialize in evaluating and providing recommendations for wheelchairs and other mobility equipment. The physical or occupational therapist will work with individuals with movement difficulties and a mobility aids supplier to select and obtain the devices that are appropriate at different stages.

7. Psychologist or Counsellor: A healthcare provider who provides mental health support. Individuals with LGMD may benefit from talking to a professional given the evolving changes and uncertainty that accompanies living with LGMD.

8. Dietician: A healthcare provider who focuses on supporting individuals in optimizing health through a well-rounded diet as well as prevention or management of obesity and malnutrition. They are also the providers who help support nutrition for individuals with feeding tubes. They may provide food supplements or help manage PEG (Percutaneous Endoscopic Gastrostomy) feeding.

Physiotherapy and Occupational therapy

Physical and occupational therapy (PT and OT) focus on helping patients maintain or adapt to changes in their function and activities of daily living (ADLs) to promote independence and quality of life (QOL). The goal of rehabilitation is to maximise independence and manage decline with dignity. The impact of LGMD on daily function should be routinely monitored and proactively managed by a physiotherapist and occupational therapist to align with patient goals and to optimise independence in activities of daily living (ADLs) and quality of life (QOL). Seeing a PT and OT routinely is recommended, and always if there is difficulty you should request your neuromuscular doctor to refer you to PT and OT for assistance including appropriate exercises, home adaptations, and/or equipment.

Areas PT and OT can advise on:	
Mobility aides	Home aids and adaptions
Splints / bracing/ orthoses	Activity and exercise
Fall management	Breathing / respiratory management (not always a PT, may be a Respiratory therapist or physician)
Pain and fatigue	Maintaining movement of joint

What to Expect in Clinic

Although there is no cure for LGMD, acquired secondary conditions can be minimised and functional abilities maximized. Individuals with LGMD should have access to an individualised plan of care management from a multidisciplinary team. This may include core members such as Physiotherapist (PT), occupational therapist (OT), and include as needed an orthotist, neuromuscular care advisor or nurse or social worker, respiratory team, speech language pathology (SLP) and psychology support.

It is important that when you attend clinic for care a suitable health care professional such as a PT is monitoring your current upper and lower limb movement abilities, mobility status and if indicated, breathing. It is also important that you share your concerns, questions, and priorities for daily life activities with the PT and OT so that you can partner together on possible treatments.
We can use specific PT assessments in the clinic to assess your function and to understand what assistance, if any, is required to manage your daily life activities. Often mobility devices, wheelchairs, housing adaptation and specialised equipment such as home adaptations or modified vehicles can take a long time to obtain, so proactive and timely planning is crucial.

Physiotherapy may also be very important to keep you mobile and to keep your joints supple.

Regular monitoring of breathing and heart function in some subtypes of LGMD is necessary. Early detection of any problems can lead to starting treatments promptly, which can be lifesaving. It is therefore very important that all affected persons have access to this kind of regular follow-up.

Exercise

Physical activity to stay active, preserving strength and function and encouraging well-being is highly encouraged. It's important to talk with your care provider before starting any type of exercise programme. Identifying a form of physical activity that you enjoy is important for regular participation.

Whilst activity and exercise are important for those with LGMD, it is recommended that physical activity should be specific to your current level of function. Low to moderate intensity exercise has been shown to preserve function, strength, range of movement, endurance, balance, and independence with ADLs. Exercise and activity take many forms including going to the gym or home exercise programme, gardening, completing tasks of daily living such as transfers and self care, and sports.

It is important to use caution with the intensity of exercise. Muscle soreness more than 24hrs after exercise, muscle cramping or dark coloured urine after or during exercise may mean you have pushed yourself too hard. If available, exercising in water can be useful as it makes movement easier.

Useful Resources for Exercise – advice pages and exercise videos
POD-NMD Stay active advice page

https://www.pod-nmd.org/managing-nmd/staying-active/

Guidelines to exercising with a muscle wasting condition from Muscular Dystrophy UK

https://www.musculardystrophyuk.org/support/information/your-condition/exercise/?gad_source=1&gad_campaignid=22095363240&gbraid=0AAAAD6h4c619q9sTm_1h9ZDC5fuLW5m-&gclid=Cj0KCQjw097CBhDIARIsAJ3-nxcp5i-bCUILh4ciFeHqes1zun8GvDIhmnHsEjCGhICAhGxiwv7C668aAtQsEALw_wcB

Bridges programme self-management

https://nmd.bridgesselfmanagement.org.uk/professional-advice/

Pilates for people with neuromuscular conditions with demonstrations of activities in sitting/ standing/ lying down (You Tube videos) by UK Neuromuscular Physiotherapists

https://www.youtube.com/playlist?list=PLazCbfp_tqxyve043vSch45aPfMzFfHxX

Seated Pilates for people with Neuromuscular conditions – Shelley Mockler, Iowa Wellstone Centre

https://www.youtube.com/watch?v=yuk3MYkyNjs

MDA at home physical therapy for LGMD

https://www.youtube.com/watch?v=uRuWyLoaLjU

Maintaining movement of your joints

Preserving the full movement of joints and muscle flexibility assists to maintain mobility and function. When there is muscle tightening that limits movement of a joint, this is known as a contracture. Contractures may cause pain, deformity, and reduce the function of a joint, thereby impacting ability to perform daily activities.

To assist to keep joints supple for as long as possible, discuss an individualised programme with your local neuromuscular PT/OT who can advise on:

- 24-hour positioning: consider how you can incorporate positioning through your daily routines. This may include opportunities while sitting at work, standing in line at the store, relaxing to watch television, regular exercise.
- Use external environmental / routine prompts (e.g., cup of tea / cleaning teeth / smart watch reminders / commercials during tv show) to remind you to get moving or to change positions
- If you are unable to move your joint through full movement, range of motion exercises can be performed with assistance of another
- Regular preventive home stretching may help to maintain movement. Prolonged stretch is best
    - Something as simple as elevating your legs onto the coffee table
    - Elevating leg rests and reclining seat back on wheelchair
    - Use of orthotics
    - Standing stretching wedges
- Standing frames/ tilt tables for therapeutic standing
- Contracture correction devices
- Surgery may be suitable in a limited number of cases

Further information on stretching and video examples

POD-NMD: advice and video links to stretches
https://www.pod-nmd.org/managing-nmd/stretches/

Scottish muscle network benefits of stretching information
https://www.nn.nhs.scot/smn//wp-content/uploads/sites/25/2024/01/NSD610-018.37-SMN-Benefits-of-streching-patient-leaflet-1.pdf

Orthoses / bracing / splints

Orthoses, braces and splints are equipment that is prescribed to support your movement and joints when muscles or joints have become weak. These are provided by an orthotist after being prescribed by your specialist neuromuscular doctor or PT.

Orthoses are used in a variety of ways

- To help support or correct alignment of a joint
- To assist with stretches and prevent muscle tightening and joint contractures
- To reduce pain
- To improve walking pattern

In LGMD, when prescribing orthoses

- Less is more!
- Lightweight
- Compromise- comfort and benefit over restoring normal walking pattern

Managing Falls

If you are experiencing falls, it is important to discuss a fall management plan with your specialist neuromuscular team. Although falling can be common in LGMD, preventing falls is important to reduce risk of injury which could lead to decline in mobility and cause pain. Have your PT/OT assess your ability to get off the floor

Suggestions for reducing risk for and management of falls:

Environmental modifications

- Remove obstacles from your home and work environments that may cause tripping (e.g., rugs, cords).
- Keep flooring dry
- Have hallways and walkways lit for mobility in the dark

Equipment

- Consider use of non-slip mats in bathroom
- Consider grab bars or shower chair in the bathroom
- Assessment by OT for lifting cushions / hoist / Hoyer
- Seat risers

Assistive devices

- Use shoes that fasten securely to feet and have non-slip tread
- Consider use of a mobility aid such as a walking stick/cane/walking aid when outdoors as these alert the general public that you might need a little more space
- Lower leg braces/ orthoses/splints to improve ankle and foot stability
- Hiring a mobility aid such as a scooter or wheelchair on days out/ holidays may promote independence and prevent falls
- Use seat belt on wheelchair to prevent falls out of the wheelchair
- Use wheelchair brakes when transferring in and out of the chair

Communication

- Communicate clearly with caregivers assisting with transfers to avoid miscommunications that can lead to falls
- Commercial fall-alert devices such as a pendant alarm
- Training family or carers to help you
- Pay special attention the day after you exercise as falls may be more common when muscles are fatigued
- Use of smart speakers/ mobile phone to alert someone to assist you

Further information

POD-NMD managing falls resources
https://www.pod-nmd.org/managing-nmd/falls-management/#1701433438892-b6d2aea6-b586

Pain and Fatigue Management

Pain

Individuals with LGMD may experience pain intermittently or in an ongoing manner. This can be related to postural changes, sitting more, overuse activity or using your body in new ways to compensate for muscle weakness and muscle imbalance. It is important to have your pain and fatigue assessed by an PT/ OT and discuss with your neuromuscular doctor to develop an individualised management plan which is reviewed regularly.

Pain management options

- Physiotherapy
- Energy management, pacing and avoid over-exertion
- Exercise and activity
- Postural changes and stretches
- Medication
- Psychological support
- Pain management specialist services

Fatigue

Managing fatigue and energy levels, both physically and mentally is very important in LGMD. In order to be able to complete the meaningful activities in your day or week, balancing daily activities is crucial. Understanding your limits and minimising over-exertion is key.

Fatigue can present in different ways including:

- Overwhelming exhaustion, lacking physical energy
- Feeling unmotivated
- Not having enough energy to get through all the activities in a day, like you can't charge your battery or if runs flat quickly
- 'brain fog' or struggling to remember things
- Tired / cramp / ache in muscles
- Difficulty getting up in the morning

Fatigue may not be related to the physical severity of your LGMD. Fatigue may be caused by a combination of factors including lifestyle, breathing, medication, pain, mood, sleep, activity, environment. Discuss with your neuromuscular team who might suggest:

- Pacing your activity levels
- Every day is different and it is important to listen to your body and consider how you are feeling today and what you have planned
- Avoid over-exertion and doing too much on one day
- Plan your week's activities ensuring appropriate rest

Further Information

POD-NMD: Fatigue management
https://www.pod-nmd.org/managing-nmd/fatigue-management/

Scottish Muscle Network: Fatigue management in neuromuscular disorders
https://www.nn.nhs.scot/smn//wp-content/uploads/sites/25/2024/01/NSD610-018.38-SMN-Fatigue-management-in-muscle-disorders.pdf

Muscular Dystrophy UK fatigue help document
https://www.musculardystrophyuk.org/app/uploads/2024/04/INF81-Fatigue-document.online.update0123-min-1.pdf

Mobility Equipment

The prescription and training of assistive devices such as canes or wheelchairs varies depending on symptoms and progression of disease but can help to facilitate independence in daily tasks. An added benefit of taking a walking aid with you when out in the community is that people may give you a little more space, reducing risk of loss of balance and falls in crowded areas. Based on your evaluation by your PT/OT or specialist doctor, recommendations and referrals can be made for suitable equipment. You will likely need to see a specialist PT/OT/ Orthotist or Wheelchair therapist so that the equipment can be fitted specifically to you.

A variety of walking aides are available. These could include

- Walking stick or cane
- Elbow crutches
- 3 or 4 wheeled walker
- Walking/hiking poles

Wheelchairs and scooters

If walking is causing fatigue or pain, or there is risk of falling, a wheelchair or mobility scooter may be suitable. There are many options, and the prescription is advised by your specialist neuromuscular team. One important consideration is your ability to get in and out of the seat. Often people with LGMD have difficulty getting off a standard height chair, and a seat riser function can be a critical part of a wheelchair prescription to ensure your independence getting out of the chair.

Features of a wheelchair that individuals with LGMD have found useful include:
- seat riser
- head rest
- ability to recline back rest
- ability to tilt to help shift weight
- thigh strap or knee blocks to stop legs splaying
- electric elevating leg rests

What do you sit in and more importantly, how do you get out again?

In LGMD, getting up from a chair may become difficult even when you are walking well. Often just raising a surface a little higher, can make the difference between being able to stand up by yourself or not. Some suggestions of equipment to assist the ability to stand up from sitting includes
- Portable seat riser
- Over toilet chair
- Powered toilet seat riser
- Shower chair
- Bar stools
- Riser / recliner chairs - not all built equal - look for one that rises before tipping you out
- Riser blocks under the settee/ sofa
- Rolling / wheeled walker with higher seat

Home adaptations and equipment

It is important to consider the home environment and what your needs may be in the future. A discussion with your specialist team, particularly an OT will assist to guide recommendations for adaptations and equipment in the home to maximise your independence.

Adaptations in the home could include:
- Altering access to the house
- Ramps/rails at front and back door
- Environmental controls such as keyless door operation
- Altering room layout
- Widening doorways to accommodate a wheelchair
- Stair lifts/ through floor lifts (elevator)
- Ceiling track lift systems
- Portable Hoyer/ hoist
- Building a downstairs extension with bedroom/bathroom
- Suitable heating/cooling system

Bathroom Considerations

There are a wide variety of bathroom adaptations and equipment available to promote independence and safety including
- Wash and dry function toilets
- Powered Toilet Lifts to assist into a standing position
- Walk-in or Roll-in Showers
- Grab Bars
- Shower benches/chairs
- Bathtub lift
- Handheld Showerhead
- Placement of ceiling tracking
- Hoist type-standing sling/ commode sling

It is important to consider what may assist toileting outside the home. Portable equipment to assist accessing the toilet is available and can be discussed with specialist team. -This may include female and male urinals, portable and disposable devices such as a bridge/ Shewee, travel jane/john for example. Access to a seat riser on a wheelchair or a portable seat riser can also assist moving from sitting into standing to access the toilet.

Driving Considerations

The progressive nature of LGMD means driving or getting in and out of a car may become difficult over time. Different muscles can be affected, often including those in the lower leg, which can affect safe pedal operation. A driver assessment and input of an OT is an important part of planning the correct vehicle modifications.

Vehicle modifications can be made such as a specialized steering wheel to make steering easier when lifting arms above shoulder is difficult or hand controls if lower extremities use is difficult. Drivers may also find a wheelchair accessible vehicle helpful. Discuss with your neuromuscular team and ask for a referral to a specialist driver assessment area.

Other equipment that may be useful for LGMD:	**Other equipment suggestions to assist tasks of daily life:**
· Transfer devices- Hoyer, ceiling lift, slide sheets, slide boards · Electric bed/ turning bed · Transfer boards · Walking belts · Voice Command Devices- environmental control options · Other environmental controls · Converted Vehicles for independent driving or being a passenger	· Sock aid to assist putting on socks · Straws: Plastic/Metal/Silicone · Lap tray for wheelchairs · Button Hooks · Reaching aids / pick up sticks / grabbers · Adaptive plates, utensils, cups · Non-slip matting · Raised chairs and sofas and bar stools · Dressing Sticks · Long shoehorns · Low stool for resting feet on · Office chair with electric seat riser

Bone Density

Bone density refers to the amount of minerals, such as calcium, present in your bones. It is a key indicator of bone strength and overall bone health. Essentially, the higher your bone density, the stronger and denser your bones are, making them less likely to fracture or break.

Here's why bone density is important:

1. **Bone Strength:** Strong bones are less prone to fractures. When bone density is low, bones become weaker, which increases the risk of breaking, even from minor falls or injuries.

2. **Fracture Risk:** Low bone density significantly raises the chances of fractures. For individuals with conditions like LGMD, which can cause muscle weakness and put additional strain on bones, this becomes a serious concern.

3. **Age and Disease Impact:** As you age, bone density naturally decreases, but conditions like LGMD can accelerate this loss. Regular monitoring helps catch any changes early, allowing your healthcare team to manage bone health proactively.

4. **Long-Term Health:** In neuromuscular diseases, low bone density can lead to complications like scoliosis or joint deformities, further limiting mobility. Keeping bone density in check and taking steps to strengthen bones can help manage these risks.

Considerations for promoting bone density

If possible and safe, discuss options for supported standing, where you are taking some weight through the legs, with your local team.

Equipment options include

· Standing frame
· Tilt table
· Seat riser on powered wheelchair
· Standing and walking in water if unable on land
· Standing or walking slings
· Use of sit to stand transfer devices

Depending on the region in which you live, your physician may recommend supplementation with calcium and vitamin D. In some instances, they may prescribe bisphosphonates to treat osteopenia or osteoporosis. The treatment of osteopenia or osteoporosis should follow the recommendations for the general population.

Top tips Iowa Wellstone Dystroglycanopathy Patient Conference

https://wellstone.medicine.uiowa.edu/sites/wellstone.medicine.uiowa.edu/files/2024-02/Life%20Hacks%202023.pdf

https://wellstone.medicine.uiowa.edu/resources-and-links/resources-patients-and-families#:~:text=Life%20Hacks%202023-,Home%20Hacks%202020,-Muscular%20Dystrophy%20Life

https://wellstone.medicine.uiowa.edu/resources-and-links/resources-patients-and-families

Muscular Dystrophy UK website- support and information

https://www.musculardystrophyuk.org/support/

Bridges self-management of neuromuscular disorders

https://nmd.bridgesselfmanagement.org.uk

Iowa Wellstone Dystroglycanopathy Patient resources

https://wellstone.medicine.uiowa.edu/resources-and-links/resources-patients-and-families

Scottish muscle network patient and families resources

https://www.nn.nhs.scot/smn/patients-and-families/

POD-NMD for healthcare professionals and individuals with Neuromuscular disorders

07

Psychosocial Management

Time of diagnosis and emotional reactions (adults and parents)

Receiving a diagnosis of LGMD may have a marked impact on the affected individuals' lives as well as those of their families', Not just in terms of the physical limitations but also psychologically and socially. Thus, it is important that health professionals pay attention to psychosocial issues both for the person with the diagnosis and the person's family.

The impact of the diagnosis may vary greatly between individuals depending on the age and developmental stage at diagnosis, but also on other factors such as life circumstances, personality, coping strategies, and social support networks. There are no wrong reactions. We do not control how we react.

Emotional reactions to the diagnosis that you or your family may experience are shock, anger, sadness, hopelessness, despair, loss of control and guilt among other feelings. Some experience physical reactions such as headache, stomach ache, nausea and muscle tensions. It is also normal to experience restlessness, irritability and feelings of injustice. What is happening may be perceived by you as unreal, and you may have trouble concentrating, remembering things and making decisions. Life may feel meaningless for a while. These are all normal reactions. It is also normal to not really react, and some may even feel relief, perhaps because they have long worried about what was wrong with themselves or their child and finally have an answer.

Often the above reactions are an expression of grief over the loss of something that is important e.g., the loss of a healthy you, a healthy child, the loss of ability to carry out various tasks, the loss of who you used to be, the loss of being an ordinary family or the loss of future plans and dreams.

Many experience pendulating between everyday life and the grief over the diagnosis. Perhaps you also experience this. Sometimes you may be able to go about doing everyday tasks and enjoy a good time with friends and family, almost forgetting the diagnosis, while other times you may be occupied with thoughts about the diagnosis and the emotional reactions. Moving in and out of the grief can be seen as a way of processing the new life circumstances and is a natural reaction.

Due to the progressive nature of the conditions, it is also normal to worry about the future and to experience the future as more uncertain and unpredictable. If you and/or your family have questions and concerns about the future, it is important that you contact the neuromuscular specialists. Although they may not have answers to all your questions, getting some answers may be very helpful.

It is also important that you contact your GP or the neuromuscular specialists if you feel overwhelmed by the situation and/or have difficulty coping with everyday life, or if you are worried about your child's or your own reaction. They can help you get the relevant help. Some people find that talking to a psychologist helps them deal with their new situation. You do not need to be psychologically unwell to benefit from sessions with a psychologist. Perhaps your specialist neurology team has a psychologist or can provide advice on how to find one.

Time of diagnosis (children/adolescents)

Receiving the diagnosis as a child or adolescent may be experienced very differently to receiving the diagnosis as an adult. The child/adolescent may not fully comprehend the meaning and potential consequences of the diagnosis but may experience that they have difficulty keeping up with their peers. Children are usually more occupied with the present rather than future scenarios unlike adults.

It is often a very personal choice how parents choose to deliver the news to their child/adolescent. However, talking to your child about his/her experiences and being honest about the diagnosis is important. This way your child knows that you can be trusted and that he/she can come back to talk to you about any worries they may have. Delivering the news to your child must be done in a way that is age appropriate and in a way that takes into consideration your child's emotional readiness and ability to reflect. Most parents fear making their child sad or worried by talking about the diagnosis and its consequences. However, not talking about it, may leave your child alone with his/her thoughts and worries, and your child may imagine even worse scenarios than reality. Therefore, it is important that you show your child that this is something you can handle talking about. Children often model their parents' behaviors, also in terms of coping with difficult situations and emotions. If you are open and show emotions, it will also be easier for your child.

Nonetheless, some children may still avoid talking about it to protect their parents. Thus, it is important that you repeatedly invite your child to talk about their worries and that you again and again show you can handle talking about it. Children may quickly sense when something cannot be talked about. Listening may be needed more than advice. Make sure your child understands that it is okay to be emotionally affected.

Avoid trying to cheer up your child by statements such as 'don't be sad, there's other things you can do'. Although well-intended, the child may be left with the impression that his/her emotional reactions are inappropriate. Such assertions rarely reduce the emotional distress and merely leaves the child alone with his/her feelings. Being given the space to share their feelings and thoughts with someone who listens without advice often provides very effective emotional relief. Some children may benefit from talking to an adult other than their parents e.g., a grandparent or a teacher. If the child is capable, then invite the child to talk about what support they would find the most helpful. Consider contacting your neuromuscular team if you need more information on how to engage in these difficult conversations with your child or if you are worried about your child's reactions.

Furthermore, it is important to explain to the child everything they are asking for, clearly, without adding things that they have not asked for; summary and incomplete answers, attitudes that sems to ignore the problems must be avoided, always using language appropriate to their age.

Everyday Life

The diagnosis and its consequences may penetrate all areas of life and increasingly so with progression of the condition. Behavioral and emotional issues may arise when your child reacts to physical limitations or social problems. Children may react with sadness, frustrations, anger, aggressivity, passivity and/or competitiveness as well as regression to earlier developmental stages. They may also experience physical symptoms such as headache, speech problems, stomachache and nausea and withdrawal from social activities and/or school.

Children spend a large part of their time in daycare/school with adults other than their parents. Close collaboration between parents and teachers or institutional staff is usually necessary. Even when symptoms are mild and/or your child is psychologically well, the staff at your child's school or daycare should be informed about the diagnosis so they can support your child. Your child may need extra attention and may behave differently or more easily become upset or angry.

Knowing about your child's situation and diagnosis means that the staff may better understand and can provide adequate support for your child. It is possible that your child may need more breaks/rest than other children or assistive devices. It may be beneficial both for your child and for the other pupils that the other pupils know why your child is getting extra support. Professional help may be necessary to help with any learning or behavioral issues that may arise due to your child's physical limitations or tiredness. It is important to be aware of any difficulties in socializing with the other children that may arise and take care of these. Everything possible should be done to make the child feel an equal part of social life as the other children which means that the best possible measures should be taken not to remove the child from the classroom setting and the other pupils e.g., resting in the back of the classroom instead of in a separate room or participating in gym class on different terms instead of missing out on gym. In the instance of sports where there is contact, or crowded rooms with activity, be particularly mindful to prevent falls.

It is important that you contact your neuromuscular team, if your child is having any issues related to social interactions/making friendships, problems in school (e.g., tiredness, aches and pain, learning difficulties, withdrawal from school), psychological distress (e.g., anger, behavioral outbursts, excessive worry, anxiety or depression). You and your child should be asked about psychological and social problems at every neuromuscular visit and be referred for evaluation and treatment as soon as possible.

Consider helping your child get in contact with other children in a similar situation. Perhaps your neuromuscular team or the patient organization may be able to help you with this. Some children may also benefit from having an adult with the same or similar diagnosis as a role model.

Preparing your child for adulthood starts in early childhood

Just like any other children, your child should grow up and become an independent adult. Thus, your child needs to be met with similar expectations as other children in terms of contributing to chores in the home, attending school, learning new skills, making friendships and romantic relationships. Your child should also be expected to become a sexually active individual just like any other children. Showing your child that you have these expectations should begin in early childhood and be adjusted according to your child's age just like for any other children. This way you help your child prepare for adulthood and to gain the skills necessary to take control of their own lives.

If your child cannot physically perform chores in the household (cooking, cleaning, washing clothes etc), he/she needs to learn how to guide you on how to do these chores in order to gain the necessary skills to one day guide personal assistants on their own. As your child grows older, your child also needs to get increasingly involved in medical conversations and decisions, so he/she learns how to engage in the medical aspects related to the diagnosis.

Supporting your child in the development of social skills, organizational skills and creative ways of thinking will help prepare your child for the skills necessary to engage in work, social activities and to maintain connections with friends. Relationships with other people are very important for our emotional and physical wellbeing and quality of life and may require a bigger effort for people with physical limitations to develop and maintain.

Adolescence

During adolescence, your body undergoes a lot of change, and it is normal to become more occupied with your own appearance and capabilities in relation to your friends. Some experience that their friends can do things they may struggle with because of physical limitations or tiredness. Some adolescents may develop feelings of inferiority and inadequacy or of being left behind. It is also normal to think more about the diagnosis and to worry more about the future regarding progression of the diagnosis and consequences of the diagnosis for the ability to develop romantic relationships and have children. Some react with frustration, anger, depression, anxiety and feelings of loneliness and/or isolation. It is important to reach out to your parents and your neuromuscular team so they can support you in getting the best possible help. Perhaps a new assistive device can help you better keep up with your friends or perhaps you need to talk to a psychologist to process your emotional reactions and cope with the challenges. Many also find it very helpful to meet up with other young people who are in a similar situation. Perhaps, someone from your neuromuscular team can help you with this.

It is also normal to become more sexually oriented during this time of life. Most neuromuscular teams have a person you can talk to about masturbation, having sex, the possibilities of becoming a future parent, or other intimate topics.

For Parents

During transition through adolescence to adulthood, some children face the reality of becoming more and more dependent on help at the same time as their peers grow and gain skills and increase their independence. Promoting more and more independence from you as a parent is important irrespective of your child's physical limitations to support the natural teenage-need for breaking free from parents and gaining independence. This may become more difficult if your child has been dependent on you for personal assistance, but your child should now be encouraged to receive this help from people other than yourself. Few teenagers want to bring their parents along to social gatherings with other young people. Being reliant on you as a parent may mean withdrawal from such activities. Peers are more important to teenagers than their parents and connecting with peers without the presence of parents is important for identity formation. You can help your child in this process by promoting autonomy and self-advocacy. Just like other young people, your child will also become more sexually oriented at this stage and need to be met with similar expectations regarding this as other young people.

Transition to adulthood

As an adolescent you should start thinking about your future goals so that you and your family can start out working on a plan with your school. This should include thinking about your educational goals, and how you would like to live, study and work. It is important that such plans include thoughts on how you can maintain independence and engage in activities that matter the most to you. You may ask yourself questions such as 'what types of activities do I enjoy'? 'What do I find most meaningful in life?' 'When do I feel I am living life my way?' 'What inspires me?' 'What is realistic for me to engage in?'

Together with school professionals, you and your family can work to organize the education and training needed to obtain these goals. Your neuromuscular team and social workers may assist with conversations on important considerations regarding your diagnosis and how to plan your future including advice on potential support measures that may be considered to support you in your achievements in life and in new educational settings. It is important that emphasis at this time is not only on educational support but also on the importance of continuing social engagement and independence of living.

Young adulthood and adulthood

Living a good adult life with LGMD is possible, although living with LGMD may affect all aspects of life. Your ability to perform daily activities, as well as work, personal and family life may be affected. In general, people with LGMD do well in school and graduate. They are generally employed in office or remote jobs. Life may sometimes be experienced as unpredictable as it may be difficult to determine same day or next day's energy levels and capabilities. The inability to live life as one had imagined or wanted may cause emotional distress and frustration. It is normal to worry about the consequences for your family, your work situation and your finances.

As the condition progresses, you may experience new losses and physical limitations that may affect you emotionally causing sadness, frustration, anger, feelings of hopelessness and/or worries about further progression. Such reactions are completely normal. Perhaps you also have a partner and/or children that you are concerned about the consequences for. Some people with LGMD may feel guilt or that they are a burden, but it is important to remember that it is the diagnosis and not you that is burdensome. It is important that you contact your local GP or the neuromuscular team if you feel overwhelmed emotionally so you can get the best possible help. Screening for anxiety and depression should be done at each neuromuscular visit and treated early and appropriately, if present.

Some may experience an urge to withdraw from social activities due to the unpredictability of the condition or obstacles in accessibility and the planning needed. Some also withdraw from social activities because they fear they will get too fatigued or experience pain. If you tend to do this, it is important to consider whether you are losing or missing out on more than need be. For some, receiving a new assistive device such as a wheelchair may free up extra energy and relieve pain. Others may overuse their bodies and work long hours as they refuse to let the physical limitations set the boundaries for what they can do. Finding a balance in activity levels and prioritizing the things that matters most to you in life may improve your quality of life. Some may need professional help to find out what matters most to them in life and to learn how to manage their activity levels. Your neuromuscular team may be able to help you with this process.

During this time of life, it may also be beneficial to meet up with others who are in a similar situation to share experiences on how to cope with everyday challenges including being a parent with LGMD.
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Living with LGMD is multifaceted. With time, some people come to see that the diagnosis, besides the losses, also has brought them something positive in life. Perhaps cutting down on work hours or early retirement has resulted in more time with your children or grandchildren, perhaps you have met some great people with a condition like yours that you would not otherwise have met, or perhaps you have become more emotionally attached to your family because of your situation

Being a relative / caregiving

A diagnosis of LGMD affects the whole family. Partners, parents, children and siblings may also be at risk of psychological distress and social isolation. Relationships and family roles may change as the condition progresses and the person with LGMD loses functional abilities and develops a greater need for physical support. Balancing caregiving with other chores and work life is a challenging task. There is a risk that caregivers become overwhelmed and stop doing the types of things that provide them with joy and energy in their desire to help and have their family live a happy life.

Although there may be an increased need for you as a care partner to take care of various problems and tasks, it is important to pay attention to whether all the things you are doing are needed or whether you are doing some of the things to escape negative emotions such as feeling powerless. If you are doing some of the things to escape difficult emotions, it may be worthwhile allowing yourself to feel sad, angry and so on or to seek emotional support. Thoughts and worries may arise that you may not feel comfortable talking to your spouse or friends or family about. Consider whether there is someone you can talk to, and, if not, you may want to consider contacting a psychologist, perhaps through the neuromuscular team.

Your emotional burden may also depend on the expectations that you are met with by your surroundings. These largely depend on cultural values and the local support measures available. It is also important to pay attention to what you expect from yourself. It may be difficult to live up to all these expectations. If you feel you do not have the energy or ability to cope with the expectations, there is a risk that you may become overburdened and/or overwhelmed. It may be helpful to talk to those around you about what they can expect from you even if it may not always be possible for them to reduce their expectations. This may make it easier for you to notice when your boundaries are being crossed or when you need to call for external assistance and support.

Consider meeting up with other relatives like yourself with whom you can share your experiences, concerns and advice on how to deal with the role as relative/ caregiver.

Siblings

Growing up as a sibling to someone with LGMD may be difficult. Siblings may also be emotionally affected by the situation. As a parent it is important to pay attention to the challenges and dilemmas that siblings may experience as they may sometimes need extra support. Siblings usually understand and accept that the child with LGMD needs more parental support than they do, but even so there is a risk that siblings may feel overlooked or under prioritized. If you find it hard to take care of the needs of all of your children, consider involving other adults in your life such as grandparents. If possible, prioritize spending time alone with each of your children.

Siblings may also attempt to protect you from further worries or sadness by keeping their own problems, worries and needs to themselves. Repeatedly inviting your child to talk about their concerns and letting your child know that you are capable of handling it, may increase the chances that your child talks to you. Be also wary of siblings taking on too much responsibility and setting aside their own interests or time with friends. Siblings should not be expected to take on the responsibility of caring for their sister or brother with LGMD in the same way as an adult.

It is also important that you pay attention to having a near equal expectation of all children in terms of contributing to household chores. Although the child with LGMD may not physically be able to perform chores, he/she may take on other tasks such as finding the cooking recipe and guiding the cooking.
As the healthy child, siblings may feel a pressure to do well in life. This does not have to be expectations that you have expressed but something that comes from within. It may be a good idea to talk to siblings about this to relieve the pressure.
In general, it is important that you pay attention to changes in behaviour or mood of siblings and help them cope. Seek help if you are worried about their reactions.

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Sexuality

Intimacy and sexuality are basic needs and important aspects of life with or without LGMD. The importance of these may vary during various phases of life and may also differ from person to person. For most people intimacy and sexuality are, nonetheless, important. It is possible to have a sexually active life and to build and enjoy romantic relationships with LGMD.

Our sexual drive may be influenced by multiple factors including our emotional state, stress levels, health and relationship problems. Having physical limitations, may mean that you have to think creatively in terms of how to have your sexual drive fulfilled or how to be intimate with a partner. Several assistive devices exist that may aid in overcoming some of the potential physical barriers and that will allow you to experience sexual pleasure on your own or with a partner. It may also be necessary to think of different ways of positioning yourself and your partner.
It is important to remember that sexual intimacy is more than intercourse. It also includes other types of physical closeness such as a gentle touch, a hug, kissing or lying close in bed. Talking to someone in your neuromuscular team, a marriage- or relationship counsellor or a sexuality counsellor, perhaps together with your partner, may be helpful if you need advice.

For consideration regarding pregnancy see section on pregnancy.

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Cardiac Management

I was just diagnosed with LGMD - what do I need to know about my heart?

First, not all LGMD subtypes carry the same risk for your heart. Some do not have any additional risk for heart disease than people living without LGMD. Others carry an increased risk for development of conduction system problems, abnormal heart rhythms, and/or cardiomyopathy. And some of the more recently discovered subtypes do not have enough information yet to decide of the potential cardiovascular risk.

There are several different gene variations that can lead to LGMD. These affect proteins that are involved in skeletal and/or cardiac muscle function. While the exact mechanisms differ depending on the gene involved, ultimately, they alter the ability of the muscle cells to contract. For heart muscle, this can be a particularly difficult problem as the heart beats continuously, but it has a very limited ability to regenerate new heart muscle cells. Thus, over time, as muscle cells become more damaged and undergo cell death, the heart's ability to contract and pump blood to the rest of the body can become compromised. There are likely many modifying factors that determine the timing and severity of heart involvement for individual LGMD patients, such as other genetic factors, other underlying diseases, or lifestyle effects. Together, this is why the heart disease in LGMD tends to be variable in nature.

Important Recommendations or Questions You May Have if you are living with LGMD:

1. **Get your baseline measurements.**
    a. Make a cardiology appointment - Ideally with a provider familiar with neuromuscular diseases and their related complications.
    b. ECG - An ECG (or EKG) is an electrocardiogram. It is a 3 second snapshot of the electrical activity in the heart. This test is used to look for problems like heart block, where the normal pacemaker cells of the heart from the upper chambers (atria) don't communicate to the other cells in the lower pumping chambers (ventricles) correctly. We can also use an ECG to diagnose electrical problems that can predispose you to arrhythmias (abnormal heart rhythms).
    c. Echocardiogram - An echocardiogram uses high-frequency sound waves to take pictures of the heart. This allows us to make sure that the structure of the heart is normal and also allows for the assessment of the function of the heart. This is usually expressed as the ejection fraction (EF), with normal values ranging from 55-75% in the left ventricle. Sometimes other measures of function may be looked at, such as fractional shortening or longitudinal/circumferential strain.
    d. Cardiac MRI - An MRI uses a strong magnetic field to take detailed pictures of the heart without being exposed to radiation. This modality of cardiac imaging has a few benefits. It is the gold standard for determining the volume and quantifying the function of the ventricles. It also allows for characterization of the cardiac muscle to look for evidence of early disease, such as scar formation or inflammation. This is an advantage over echocardiography, as in many cardiomyopathies (heart muscle disease) we can see these changes in tissue characterization well before we see a decrease in ventricular function and intervene earlier.
    e. Holter monitor - A Holter monitor is like an ECG, except it looks at all of the heart beats over a period of time, usually one to ten days. This allows your cardiologist to see if there are underlying abnormal rhythms while you are going about your normal activities, including sleeping.
    f. Event monitor - An event monitor is similar to a Holter, but instead of looking at all the heart beats during a period of time, it looks at the heart beats when you are having symptoms. Since it isn't always recording, it can be used over longer time periods (one to three months) to try to capture the heart rhythm when there are infrequent symptoms.

2. What to expect? What's the difference between these different assessments?

a. ECG - It is performed by placing a series of sticker electrodes (usually 12 of them) on your limbs and chest. The test usually takes less than five minutes.

b. Echo - It is performed while laying on an exam table. A small amount of gel is applied to the chest to improve the conduction of the sound waves and improve picture quality. Then the ultrasound probe is moved to different positions on the chest to get a complete study of the heart. This test usually takes 45-60 minutes.

c. MRI - This test requires going to a center that has an MRI machine that is capable of cardiac imaging with tissue characterization (this includes most academic centers). An IV will need to be placed to give the contrast. Contrast is gadolinium-based and while there is very low risk of allergic reaction, some people may feel nauseated during contrast administration. This can usually be mitigated by slowing down the rate the contrast is injected. Most MRI scanners are shaped like a doughnut with a table in the middle, so they are not completely enclosed. However, some people with severe claustrophobia may have difficulty with this test. The test is not ideal for very young children as it requires the patient to hold still and follow breath-holding instructions. Most children's hospitals have entertainment aids available, such as music, videos, and/or Child Life specialists to help. However, usually this test isn't done without anesthesia before the age of 8 years or so. This test can take 45-90 minutes, depending on the images needed and the skill of the staff.

d. Holter and Event Monitors - There are many different types of monitors available, but the most commonly used today are patch monitors that go on the skin on the chest over the heart. The monitors can usually get wet although they cannot be submerged in water, so showering is fine but bathing or swimming should be avoided in most cases. The equipment is used at home over the allotted time period and either brought back to the office or sent back via mail.

Type of Test	Pros	Cons
Electrocardiogram	Quick, in the office	Need to wear stickers
Echocardiogram	Quick, in the office	Can not detect heart disease before it affects heart function
Cardiac MRI	Best assessment of heart function, can detect heart disease early	Need appointment with radiology team, longer time needed, need IV contrast
Holter Monitor	Longer time to get "big picture", may reveal "silent" arrhyth-mias	Need to wear stickers - no baths/swimming, older monitors can be uncomfortable to carry around the for 24+ hours
Event Monitor	Longer time for infre-quent, symptomatic arrhythmias	Need to keep it with you for 30+ days to be effective

3. What is cardiomyopathy?

This is a disease of the heart muscle itself. This may be due to muscle cells dying and being replaced by scar or by chronic inflammatory changes. Over time, enough muscle is affected so that the function of the muscle starts to be compromised and the heart cannot pump blood as efficiently as it normally would. This reduction in function is called heart failure. Sometimes it is accompanied by thickening of the muscle walls due to hypertrophy of the remaining cells, although more often it is accompanied by thinning of the ventricular wall and dilation of the normal chamber size. Usually medicines are used to treat heart failure effects, including muscle changes and symptoms. In severe cases, surgical interventions may be required including a device to pump for the left ventricle (called a ventricular assist device) or ultimately a heart transplant.

4. What is myocarditis?

This is inflammation of the heart muscle, typically in the acute setting. Often myocarditis is associated with chest pain, fatigue, and shortness of breath, depending on the severity. The extent of inflammation can vary anywhere from mild, reversible effects on the cardiac muscle to severe, non-reversible involvement with concomitant decreased function (heart failure). Usually this is treated with anti-inflammatory therapies, such as steroids or immunoglobulins to decrease the inflammatory cell activation. In more severe cases, heart failure medications may be required also.

5. What is conduction disease?

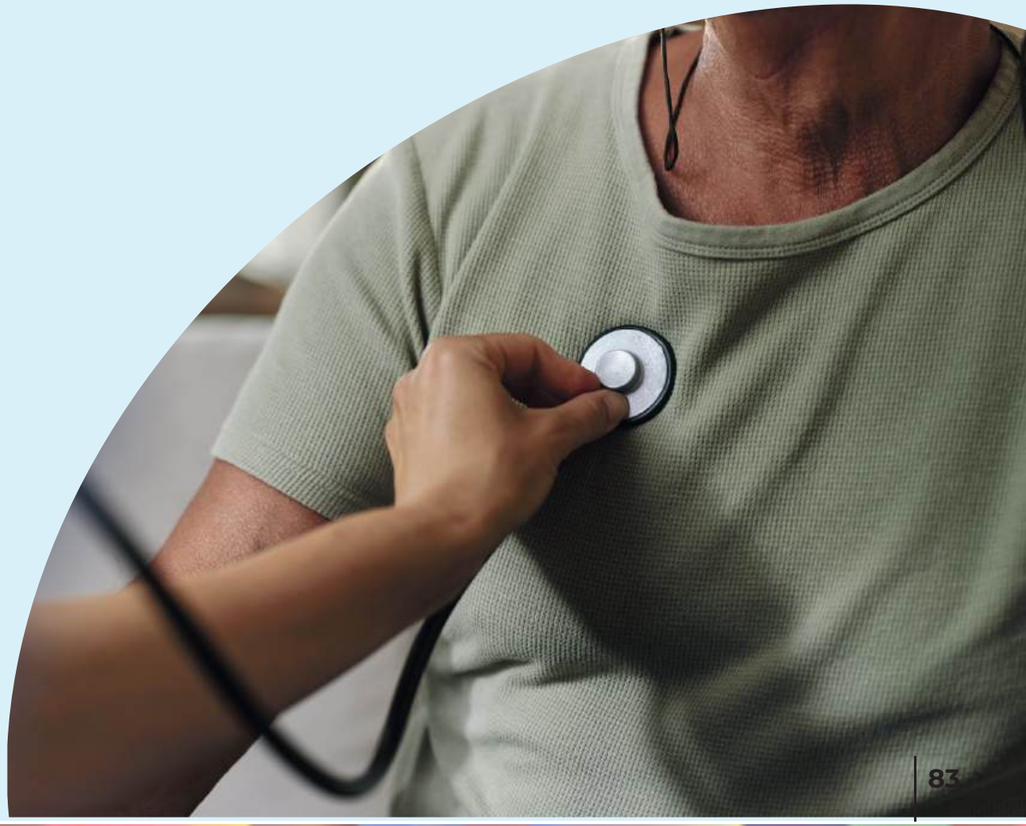
This is a disturbance in the normal communication between the pacemaker cells of the heart (the sino-atrial node) and the lower chambers via the common conduction pathway (atrio-ventricular node and His-Purkinje system).
This type of disease can be progressive over time and may lead to complete block, which is a complete dissociation between the upper and lower chamber electrical signals. Most cases of complete heart block would require implantation of a pacemaker.

6. What is arrhythmia?

This is an abnormal heart rhythm. There is a broad range of different types of arrhythmias, some are mostly benign while others are potentially dangerous. They can arise from the upper chambers (atria) or the lower chambers (ventricles).

7. Cardiac Medications:

There are a number of medications that may be used for cardiac disease in LGMD. One of the major goals, especially of early therapy, is to prevent muscle cell damage and cell death. This is usually referred to as cardiac remodeling. Other medicines may be used to decrease the risk of arrhythmia or to help preserve cardiac function in patients with heart failure



Medication Class	Medication Class	Common Side Effects	Examples
Angiotensin-converting enzyme inhibitors (ACEi)	Work on the angiotensin pathway; shown to have a positive cardiac remodeling effect	Dizziness, fatigue, low blood pressure; less commonly chronic cough	lisinopril, enalapril, perindopril
Angiotensin receptor blockers (ARB)	Work on the angiotensin pathway; shown to have a positive cardiac remodeling effect	Dizziness, fatigue, low blood pressure	valsartan, losartan, eprosartan
Mineralocorticoid receptor antagonists (MRA)	Exact mechanism unclear, may be multifactorial; shown to delay scar progression and dysfunction in neuromuscu-lar disease	Dizziness, fatigue, low blood pressure (less common), weak diuretic effect, can cause electrolyte disturbance with dehydration and / or kidney disease	spironolactone, eplerenone, finerenone
Beta blockers	Slow the baseline heart rate to decrease arrhythmia susceptibility; also have a positive cardiac remodeling effect	Dizziness, fatigue, low blood pressure, can blunt heart rate response to exercise; can exacerbate lung disease in asthmatics	metoprolol, carvedilol, propranolol

Medication Class	Medication Class	Common Side Effects	Examples
Neprilysin inhibitors	Blocks the action of the neurohormone neprilysin, which reduces the negative “stretch response” in the heart; usually used in combination with an ARB, the combination has been shown to improve LVEF in heart failure patients	Most side effects are due to combination use with ARB, can cause electrolyte disturbance with dehydration and /or kidney disease	sacubitril
Sodium-glucose cotransporter-2 inhibitors (SGLT2i)	Exact cardiac mechanism unclear, may be multifactorial in-cluding reduced inflammation, reduced fibrosis, and improved function	Fatigue, low blood sugar, increased risk for UTI	dapagliflozin, empagliflozin, canagliflozin

The table below is meant to be inclusive, however it only represents a snapshot in time. Some of the more newly identified LGMD subtypes may not have enough information to adequately assess the risk of cardiac involvement. Additionally, as we develop better treatments and diagnostic methods, previously unrecognized cardiovascular disease may be unmasked in other subtypes as well. For this reason, we would typically recommend getting a baseline echocardiogram and ECG at the time of diagnosis to ensure normal anatomy and function and a baseline MRI and Holter by at least 18 years of age (or at diagnosis for older patients) to evaluate for subclinical (asymptomatic) heart involvement in all LGMD subtypes. More frequent cardiology follow-up is required for those patients with higher risk of cardiac involvement.

LGMD Subtype	Inheritance	Gene	Protein Product	Cardiac Involvement			When should I begin cardiac appts?	Suggested tests	When should I begin meds?
				Cardiomyopathy	Arrhythmia	Conduction			
1A (z-disk proteinopathy, myofibrillar myopathy)	Autosomal Dominant	DNAJB6	DNAJ/HSP 40 homolog, subfamily B, member 6	Rare	Rare	Rare	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
1B (nuclear envelopathy, Emery-Dreifuss muscular dystrophy)	Autosomal Dominant	TNP03	Transportin-3	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
1C (rippling muscle disease, caveo-lae-associated muscular dystrophy)	Autosomal Dominant	HNRNPDL	Heterogeneous nuclear ribonu-cleoproteins	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms

LGMD Subtype	Inheritance	Gene	Protein Product	Cardiac Involvement			When should I begin cardiac appts?	Suggested tests	When should I begin meds?
				Cardiomyopathy	Arrhythmia	Conduction			
1D (z-disk proteinopathy, LGMDD1)	Autosomal Dominant	DES	Desmin	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
1E (z-disk proteinopathy, myofibrillar myopathy)	Autosomal Dominant	DNAJB6	DNAJ/HSP 40 homolog, subfamily B, member 6	Rare	Rare	Rare	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
1F (nuclear envelopathy, LGMDD2)	Autosomal Dominant	TNP03	Transportin-3	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
1G (LGMDD3)	Autosomal Dominant	HNRNPDL	Heterogeneous nuclear ribonu-cleoproteins	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
1H	Autosomal Dominant	Chromosome 3p23-p25.1	unknown	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
2A (calpainopathy, LGMDR1)	Autosomal Recessive	CAPN3	Calpain 3	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms

LGMD Subtype	Inheritance	Gene	Protein Product	Cardiac Involvement			When should I begin cardiac appts?	Suggested tests	When should I begin meds?
				Cardiomyopathy	Arrhythmia	Conduction			
2B (dysferlinopathy, LGMDR2)	Autosomal Recessive	DYSF	Dysferlin	Rare	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
2C (gamma sarco-glycanopathy, LGMDR5)	Autosomal Recessive	SGCG	γ-Sarcoglycan	Common	Rare	Rare	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2D (alpha sarco-glycanopathy, LGMDR3)	Autosomal Recessive	SGCA	α-Sarcoglycan	Common	Rare	Rare	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2E (beta sarco-glycanopathy, LGMDR4)	Autosomal Recessive	SGCB	β-Sarcoglycan	Common	Common	Common	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG, Holter (every 3 years if no symptoms)	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2F (delta sarco-glycanopathy, LGMDR6)	Autosomal Recessive	SGCD	δ-Sarcoglycan	Rare	Rare	Rare	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Hotler	If cardiac abnormalities or symptoms
2G (z-disk pro-teinopathy, LGMDR7)	Autosomal Recessive	TCAP	Telethonin	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac a bnormalities or symptoms
2H (LGMDR8)	Autosomal Recessive	TRIM32	Tripartite motif-containing protein 32	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
2I (alpha dystro-glycanopathy, LGMDR9)	Autosomal Recessive	FKRP	Fukutin related protein	Common	Rare	Rare	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2J (z-disk proteinopathy, LGMDR10)	Autosomal Recessive	TTN	Titin	Common (may be pathogenic variation specific)	Rare	Not reported	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2K (alpha dystro-glycanopathy, LGMDR11)	Autosomal Recessive	POMT1	Protein O-man-nosyltransferase 1	Rare (may be higher for certain pathogenic variations)	Rare	Rare	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms

LGMD Subtype	Inheritance	Gene	Protein Product	Cardiac Involvement			When should I begin cardiac appts?	Suggested tests	When should I begin meds?
				Cardiomyopathy	Arrhythmia	Conduction			
2L (anoctaminopathy, LGMDR12)	Autosomal Recessive	ANO5	Anoctamin 5	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
2M (alpha dystroglycanopathy, LGMDR13)	Autosomal Recessive	FKTN	Fukutin	Reported	Reported	Reported	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
2N (alpha dystroglycanopathy, LGMDR14)	Autosomal Recessive	POMT2	Protein O-mannosyltransferase 2	Not reported	Reported	Reported	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
2O (alpha dystroglycanopathy, LGMDR15)	Autosomal Recessive	POMGnT1	Protein O-mannose beta-1,2-N-acetylglucosaminyltransferase	Reported	Reported	Not reported	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG,	If cardiac abnormalities or symptoms
2P (alpha dystroglycanopathy, LGMDR16)	Autosomal Recessive	DAG1	Dystroglycan	Not reported	Reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
2Q (z-disk proteinopathy, LGMDR17)	Autosomal Recessive	PLEC1	Plectin 1f	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms

LGMD Subtype	Inheritance	Gene	Protein Product	Cardiac Involvement			When should I begin cardiac appts?	Suggested tests	When should I begin meds?
				Cardiomyopathy	Arrhythmia	Conduction			
2Q (z-disk proteinopathy, LGMDR17)	Autosomal Recessive	PLEC1	Plectin 1f	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms

2R (z-disk proteinopathy, myofibrillar myopathy)	Autosomal Recessive	DES	Desmin	Not reported	Rare	Common	Baseline evaluation at diagnosis or young adulthood, every 1-3 years for ECG/ Holter	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
2S (alpha dystroglycanopathy, LGMDR18)	Autosomal Recessive	TRAPPC11	Trafficking protein particle complex subunit 11	Not reported	Not reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms
2T (alpha dystroglycanopathy, LGMDR19)	Autosomal Recessive	GMPPB	GDP-mannose pyrophosphorylase B	Rare (more common in late onset patients)	Rare	Not reported	Baseline evaluation at diagnosis or young adulthood, then every 3-5 years	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
2U (alpha dystroglycanopathy, LGMDR20)	Autosomal Recessive	ISPD	isoprenoid synthase domain	Common	Common	Common	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG, Holter (every 3 years if no symptoms)	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations

LGMD Subtype	Inheritance	Gene	Protein Product	Cardiac Involvement			When should I begin cardiac appts?	Suggested tests	When should I begin meds?
				Cardiomyopathy	Arrhythmia	Conduction			
2V (Pompe disease)	Autosomal Recessive	GAA	alpha 1,4-glucosidase	Common early onset, less common late onset	Common	Common	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG, Holter (every 3 years if no symptoms)	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2W (PINCH-2 related myopathy)	Autosomal Recessive	LIMS2	lim and senescent cell antigen-like domains 2	Common	Common	Common	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG, Holter (every 3 years if no symptoms)	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2X (nuclear envelopathy, BVES related myopathy	Autosomal Recessive	BVES	Blood vessel epicardial substance	Not reported	Common	Common	Baseline evaluation at diagnosis or young adulthood, every 1-3 years for ECG/ Holter	Echocardiogram or MRI, ECG, Holter	If cardiac abnormalities or symptoms
2Y (nuclear envelopathy, TOR1ASIP1 related myopathy)	Autosomal Recessive	TOR1A1P	Torsin A-interaction protein 1	Common	Common	Rare	Baseline evaluation at diagnosis, every 1-3 years or more frequently with cardiac abnormalities	Echocardiogram or MRI, ECG, Holter (every 3 years if no symptoms)	If cardiac abnormalities or symptoms; may be a role for prophylactic meds in some pathogenic variations
2Z (alpha dystroglycanopathy)	Autosomal Recessive	POGLUT1	Protein O-glucosyl-transferease 1	Not reported reduction in NOTCH1 signaling, which is associated with forms of congenital heart disease)	Not Reported	Not reported	Baseline evaluation at diagnosis or young adulthood.	Echocardiogram or MRI, ECG	If cardiac abnormalities or symptoms

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09

Considerations for Surgery

People living with LGMD may need to undergo different types of surgical interventions. These can be either related to their condition, such as those for muscle biopsies, correction of joint contractures or spinal deformities, or non-related, such as caesarean sections, or following traumas or acute abdomen.

For people with LGMDs, undergoing surgery is generally safe provided that specific measures are implemented. However, in some circumstances, there could be an increased risk of perioperative complications compared with the general population, and it is important that you are informed about it.

It is also important that you always carry a medical alert card (a link is provided in the Pulmonary Management chapter) with information about your disease and management in case of emergency.

The neuromuscular team responsible for your regular care should be notified beforehand about any planned surgical procedure and as soon as possible in case of unplanned surgery (such as in case of fracture or other traumatic events), to provide input to the surgical team and set appropriate rehabilitation goals.

Possible Risks

· People with LGMD may have increased sensitivity to the effect of sedatives, general anaesthetics and neuromuscular blocking agents. To reduce associated risks, some drugs are preferred over others, and specific drugs (such as succinylcholine) must be avoided.

· Prolonged periods of immobilization could lead to significant impact on mobility for patients with LGMD with limited ambulation.

Preoperative Recommendations

For the patient:

· Inform the neuromuscular team that sees you regularly of your upcoming procedure

· Inform the surgical team of your condition

· The hospital personnel in charge should be familiar with your conditions and its risks

For the surgical team:

· Careful assessment is needed, to have a clear understanding of whether an exact genetic diagnosis is available, of the extent of muscle weakness, presence of cardiorespiratory involvement, previous complications during anaesthesia, potential difficulties with airway management caused by enlarged tongue.

· Consider that the majority of individuals living with LGMD present with elevated creatine kinase (CK) at baseline, for subsequent monitoring.

· Regional anaesthesia is preferred whenever possible.

· Major surgery requiring sedation or general anaesthesia should be performed in the setting of a 24-hour high-care facility.

· Refer to the most recent guidelines on anaesthesia in muscular dystrophies for detailed management.

· Consider the surgical options that minimise periods of immobilisation.

Post-operative recommendations

· Support recovery with early rehabilitation access to reduce the impact of prolonged periods of immobilisation.

Key Points

For the patient:

· Carry with you an updated alert card or equivalent with information about your disease

· Inform the surgical team about your condition

For the surgical team:

· Acquire information on the exact genetic diagnosis if available, as some LGMD types may be associated with cardiorespiratory involvement or specific risks in case of general anaesthesia or sedation

· Cardiac and respiratory investigations should be performed if LGMD type is known to affect with those systems or if no molecular diagnosis is available

· Major surgery should only be performed where 24-hour intensive care unit is available

· Refer to the most recent guidelines on anaesthesia for detailed recommendations

· Restart medications and ensure mobilisation early after surgery

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Emerging Treatments

Developing safe and effective treatments for LGMDs is a vital and multi-faceted endeavor. With numerous innovative approaches on the horizon, such as gene and cell therapies and small-molecule treatments, the potential for transformative care is within reach. This chapter emphasizes the essential steps needed for thoughtful consideration in the development process for these emerging treatments, paving the way for breakthroughs that can change patients' lives.

Multidisciplinary clinics (Clinical, PT, OT, etc)

As outlined in previous chapters, multidisciplinary clinics are essential for the health and well-being of LGMD patients, as well as the support in treatment advancements. Multidisciplinary clinics for LGMD are often selected as the locations for natural history study research and clinical trials as they offer the expertise needed to oversee this research. Academic centers are ideal locations for multidisciplinary clinics due to institutional oversight for the safety of the patients while being examined.

Some of the care you can receive when visiting a multidisciplinary clinic include:

- **Physical Therapy** can help manage the symptoms of LGMD and enhance your mobility. Although it cannot halt disease progression or repair damaged muscles, it plays a vital role in maintaining the function of healthy muscles, delaying contractures, and improving your range of motion.

- **Occupational Therapy** is designed for those who find daily activities challenging due to LGMD. This therapy equips you with essential skills for independent living and simplifies everyday tasks through personalized strategies and specially designed tools, maximizing your physical capabilities.

- **Speech Therapy** enhances your ability to express thoughts and comprehend language. Tailored to your specific needs, it focuses on improving communication skills based on age and the unique speech challenges posed by your condition. Additionally, they can help with any changes in swallowing function and can provide strategies and accommodations to support your nutritional intake for safety and efficiency. Your dedicated speech-language pathologist will curate the ideal treatment plan just for you.

- **Respiratory Therapy** focuses on exercises that enhance and sustain lung function. During your appointment, your respiratory therapist will take the time to understand your medical history, conduct thorough assessments, and partner with you to create a customized treatment plan that effectively meets your needs.

- **Genetic Counselling** gives you information about your genetic condition and how it might affect you or your family. Genetic counselors will go over questions that you have based on your genetic testing results to provide you with more insight on your diagnosis.

- **Wheelchair Services** are provided by your care team to help you understand and pick a mobility device that is best for you, if and when the time comes for needed assistance. These services promote independence and support optimal posture, breathing, digestion considerations, while actively helping to prevent skin issues.

Taking part in clinical studies can be an integral part of your care, offering opportunities to access innovative treatments and contribute to the advancement of medical knowledge. Embrace a healthcare approach that prioritizes you and your well-being—because your health journey matters.

Patient Advocacy Organizations and Patient Registries

Patient advocacy organizations play a crucial role in supporting individuals diagnosed with a specific disease or condition. Organizations, often non-profit foundations, help patients, their caregivers and families navigate resources available to them; keep them informed on information regarding the disease; provide updates on research or clinical trial opportunities; connect individuals and groups across the community; raise disease awareness; and ensure patient voices are heard through advocacy opportunities.

There are several patient advocacy organizations dedicated to LGMD across the globe. Some of these organizations educate about and support all LGMD subtypes, while others are subtype-specific. Upon diagnosis of LGMD, it is important to connect with these foundations to begin engaging with the community, find important resources, and complete a patient registry.

Patient registries are a collection of information about individuals, typically focused on those living with a specific diagnosis or condition. Registries are critical for understanding how many patients are within a rare disease population. There are many LGMD patient registries offered through patient advocacy organizations, healthcare facilities, pharmaceutical companies or private companies. It is important to check who sponsors the registry you sign up for and understand their privacy policies.

Patient registries are generally free to join and voluntary. Common details an LGMD patient or caregiver may provide include:

- Name
- Current age
- Contact details (address, phone, email)
- Age of onset
- If the diagnosis was genetically confirmed
- LGMD subtype
- Variant type

Contributing to an LGMD registry can enhance the understanding of these muscular dystrophies, help healthcare professionals develop and improve treatments, and enable researchers to design better studies. Registries can also be used during clinical trial recruitment to contact potentially eligible participants.

An up to date list of LGMD Patient Registries and Patient Advocacy Organisations is maintained by the LGMD Awareness Foundation.
https://www.lgmd-info.org/knowledge-base/navigating-lgmd/for-patients/international-lgmd-patient-registries/

Natural History Studies

Action Item: Where to get study / trial info:
https://clinicaltrials.gov/

Natural history studies are designed to gather information from patients to enhance understanding of diseases, particularly rare ones like the LGMDs. According to the U.S. National Institutes of Health (NIH), “The natural history of a disease is traditionally defined as the course a disease takes in the absence of intervention in individuals with the disease, from the disease’s onset until either the disease’s resolution or the individual’s death.”* These comprehensive observational studies aim to monitor the progression of the disease over several years, helping to identify various factors, such as demographics, genetic influences, and physical outcomes that may be linked to the disease’s development and progression. The data obtained is used to help better understand how a disease impacts a person throughout their lifetime. In the case of rare diseases, this information is particularly valuable, as it can lead to new insights, breakthroughs, and treatments.

By joining any natural history studies available to you, you may need to share diagnosis, treatment details and historical medical records, provide sample testing, and take surveys to share details on your quality of life. Natural history studies for LGMD often include site visits to conduct bloodwork, urine samples, physical therapy assessments, cardiology scans, bone density scans, skeletal MRIs, muscle biopsies and questionnaires. Some of these tests are optional, while others are required. There may also be phone call follow-ups with the clinical site in between visits. The length of natural history studies varies depending on the criteria developed by the sponsor. Participating in a natural history study may also help your doctor identify clinical trials in which you may be eligible to participate.

Having a comprehensive set of data on a rare disease, like LGMD, accelerates the search for potential treatments, allowing researchers to build on existing knowledge rather than starting from the ground up

To create safe and effective treatments for LGMD we need patients to be involved in research like natural history studies. By being involved you are helping to evolve science.

Biomarkers

Throughout natural history studies and clinical intervention treatment trials, patients’ biomarkers are collected and analysed. Biomarkers, short for biological markers, refer to a broad subcategory of medical signs – that is, objective indications of medical state observed from outside the patient, which can be measured accurately and reproducibly.** Biomarkers are essential for the effective and informed development of treatments, guiding toward safer and more targeted therapies. Different examples of biomarkers for muscular dystrophies, including LGMD, are:

- Blood based including Creatine Kinase (CK)
- Muscle biopsies
- Muscle imaging

Interventional Studies

Clinical trials and other research studies are conducted to evaluate the safety, efficacy, and potential benefits of new medical interventions, including drugs, devices, and treatments. These trials are systematically divided into four distinct phases, each with specific objectives and characteristics.

Pre-clinical Studies:

- Purpose: To test an intervention in an animal model or using human-derived tissue and immediately precedes Phase 1 testing in humans.

Phase 1: Safety and Dosage	Phase 2: Target Engagement, Hints of Efficacy and Side Effects	Phase 3: Confirmation and Comparison	Phase 4: Post-Market Surveillance
· **Purpose:** To assess the safety, tolerability, and pharmacokinetics (how the drug is absorbed, distributed, metabolized, and excreted) of the intervention in humans. · **Participants:** Small group (5-15) of healthy volunteers or individuals with the target disease. · **Goals:** · Determine the safest dose range. · Identify potential side effects. · Evaluate the best method of delivery (oral, injection, etc.). · **Success Criteria:** Establishment of a safe dosage and early understanding of how the drug behaves in the body| (pharmacokinetics).	· **Purpose**: To confirm the intervention interacts with its intended target (biomarker engagement), evaluate the efficacy of the intervention and gather more detailed safety data. · **Participants:** Larger group (20-100) of individuals with the target condition. · **Key Activities:** · Assess the intervention's effectiveness for the specific condition. · Monitor for adverse events and refine dosing regimens. · **Success Criteria:** Demonstration of a preliminary benefit and manageable side effect profile.	· **Purpose:** To confirm efficacy, monitor side effects, and compare the intervention to standard treatments. · **Participants:** Larger group of individuals with the target condition. · **Key Activities:** · Perform randomized, controlled trials to compare the intervention against placebos or standard care. · Collect data to support regulatory approval. · **Success Criteria:** Conclusive evidence of safety and effectiveness to support regulatory submission (e.g., FDA, EMA).	· **Purpose:** To monitor the long-term effectiveness and safety of the intervention after it has been approved and is on the market. · **Participants:** General population or specific subgroups using the approved treatment. · **Key Activities:** · Detect rare or long-term adverse effects. · Study the intervention's performance in real-world settings. · Explore additional indications or patient populations. · **Success Criteria:** Continuous confirmation of a positive benefit-risk profile.

Key Considerations Across Phases

· **Ethical Oversight:** Institutional Review Boards (IRBs) ensure participant safety and ethical conduct.
· **Patient-Centric Design:** Increasing emphasis on integrating patient feedback to optimize trial design and outcomes.
· **Translational Focus:** Bridging basic research insights with clinical applications.

Key Considerations in Rare Diseases

· **Ethics of Placebo controls:** In rare diseases that have few patients, consideration of whether historical controls or changes to study design will be more ethical to patients.
· **Identifying and Powering for Efficacy during Phase II:** In cases in which the disease is rare and the timeline for disease modification may be lengthy, designing a study with efficacy end points during a phase II study may be more appropriate (Phase II/III). This is the most likely scenario in LGMD.

Clinical trials are pivotal for advancing medical science, providing the evidence needed to bring safe and effective treatments to patients. Each phase builds upon the previous, progressively refining our understanding of the intervention and its impact on human health.

Key Considerations Across Clinical Trial Phases

· Ethical Oversight: Institutional Review Boards (IRBs) ensure participant safety and ethical conduct.

· Patient-Centric Design: Increasing emphasis on integrating patient feedback to optimize trial design and outcomes.

· Translational Focus: Bridging basic research insights with clinical applications.

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Genetic Therapies

Therapies for rare muscular dystrophies target various aspects of disease pathology, from genetic variations to downstream cellular dysfunctions. The approaches can be broadly categorized into gene-specific therapies, non-disease-specific therapies and cell-based therapies:

1. Gene-Specific Therapies

These aim to correct or compensate for the underlying genetic defect:

Gene Replacement Therapy	**Gene Editing**	**Antisense Oligonucleotides (ASOs)**
· Delivers functional copies of defective genes using viral vectors (e.g., AAV) i.e. provides the body with functional copies of the missing gene. · Example: Experimental therapies for Duchenne Muscular Dystrophy and Limb Girdle Muscular Dystrophies	· CRISPR-Cas9 or similar technologies are employed to repair pathogenic variations directly (i.e. providing the body with a functional copies of repaired gene) · Challenges include efficient delivery and potential toxicity.	· Modify RNA splicing to skip exons with pathogenic variations or restore partial protein function. · Decreasing the expression of a toxic protein in the case of a dominant muscular dystrophy · Examples: Eteplirsen (DMD) and similar drugs targeting exon skipping.

2. Non-Disease Specific Therapies (Small molecule approaches)

These focus on correcting downstream effects of genetic pathogenic variations that may occur in multiple types of muscular dystrophy. Not all of the approaches below are applicable for all LGMD subtypes.

Target specific pathways to improve muscle health	**Target secondary inflammation that may be contributing to disease**
· Examples (myostatin inhibition)	· Examples (prednisone) · Mitigate Fibrosis that can occur secondary to ongoing muscle damage. · Target mitochondrial dysfunction or reduce oxidative stress.

3. Cell-Based Therapies

These approaches aim to restore muscle cells or introduce new functional cells. These approaches may use donor cells or following gene correction prior to implantation (autologous):

Stem Cell Transplantation	**Satellite Cell Augmentation**
· Mesenchymal stem cells or induced pluripotent stem cells (iPSCs) are differentiated into muscle cells.	· Enhance the activity or transplant satellite cells (muscle stem cells).

The choice of therapy depends on the type and stage of muscular dystrophy, patient specific factors, and the availability of disease modifying treatments. Many are still in experimental stages but hold great promise.

Sources and Further Information:

Establishing a framework for building multidisciplinary programs - PMC
https://pmc.ncbi.nlm.nih.gov/articles/PMC4671763/

Genetic Counseling | Genomics and Your Health | CDC
https://www.cdc.gov/genomics-and-health/about/genetic-counseling.html

Natural history study - Toolkit
https://toolkit.ncats.nih.gov/glossary/natural-history-study/

What are Biomarkers? - PMC
https://pmc.ncbi.nlm.nih.gov/articles/PMC3078627/

Questions to ask when you are considering about a clinical trial

· What phase is this trial and how much do we already know about this treatment in terms of safety and efficacy?

· What potential benefits or outcomes are being measured as part of this trial and how important are they to me?

· What are the risks and safety concerns of this trial that I should consider?

· What are the eligibility criteria for this trial and does this apply to me?

· Are there any medicines or therapies I need to stop to be eligible for this trial, and will that be a problem for me?

Other considerations

· What are the other options for management if I decide not do this trial, and what are the other options that might be emerging in the near future?

· If I take this treatment as part of a clinical trial, will it prevent me from being part of another trial at a later date?

· Will being on this trial affect any other aspects of my care or plans, such as a pending surgery, another treatment I was considering or even a travel plan I was arranging?

· Where is this trial being conducted and how will I manage any trial visits or appointments? Your treating team may be able to advise you of services to support this.

Practical matters

· How will participation in this trial affect other aspects of my life such as my work, education or family responsibilities and how should I prepare for this?

· Who can I speak to if I would like more information about this trial?

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Conclusion

We hope this guide serves as a supportive companion as you navigate life with Limb Girdle Muscular Dystrophy (LGMD). While LGMD includes a range of different subtypes, you are not alone in managing its challenges. Whether you're newly diagnosed or further along in your journey, remember that advocacy groups, neuromuscular specialists, and a community of individuals and families living with LGMD are here to walk alongside you.

Taking that first step to seek information or connect with others can feel difficult—but it's also a powerful act of strength. You are part of a wider community that understands, supports, and cares.

List of Organisations

LGMD Awareness Foundation
https://www.lgmd-info.org

The Speak Foundation
https://www.thespeakfoundation.com

Coalition to Cure Calpain 3 (C3)
https://www.curecalpain3.org

Jain Foundation
https://www.jain-foundation.org

CureLGMD2i Foundation
https://www.curelgmd2i.com

LGMD2D Foundation
https://www.lgmd2d.org

Cure SCG
https://www.curescg.org

Daniel Ferguson LGMD Foundation (Australia)
https://www.danielfergusonfoundation.org.au

AFM-Téléthon (France)
https://www.afm-telethon.fr

Conquistando Escalones (Italy/Spain)
https://www.conquistandoescalones.org

Stichting Spierkracht (Netherlands)
https://www.spierkracht.nl

Dimus Chile (Chile)
https://www.dimuschile.cl

FONDAZIONE GRUPPO FAMILIARI BETA-SARCOGLICANOPATIE
WWW.LGMD2E.ORG

Disclaimer: Every effort has been made to ensure that the information in this guide is accurate, up to date, and free from error. However, despite our best efforts, occasional inaccuracies or omissions may occur. This guide is intended for informational purposes only and should not replace professional medical advice or consultation.

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TREAT-NMD®
Neuromuscular Network

TREAT-NMD Services Limited C/O Womble Bond Dickinson (UK) Llp

The Spark, Draymans Way, Newcastle Helix, Newcastle Upon Tyne, England, NE4 5DE