A Longitudinal Investigation of Hydrotherapy for Children and Adolescents with Muscular Dystrophy.

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A thesis submitted to The University of Gloucestershire in accordance with the requirements of the degree of Masters in Science by Research in the School of Applied Sports and Exercise Sciences.

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Preliminaries

Abstract

Introduction: Muscular dystrophy (MD) is characterised by progressive muscle weakness and degeneration, that can lead to cardiovascular and respiratory complications, loss of ambulation, and a significant reduction in quality of life. There is no current cure for MD, however the use of hydrotherapy has been recommended in recent guidelines for the management and delay of disease progression. Despite these guidelines, there is a paucity of evidence regarding the effectiveness of hydrotherapy. The aim of the study was to investigate the effects of hydrotherapy on respiratory function, muscle strength, and wellbeing. **Methodology:** Two males with Duchenne MD received 45-minute hydrotherapy sessions once a week for 40 weeks. Hand-held dynamometry was used to assess dominant arm and leg strength. A respiratory pressure meter for static maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), and 2-Dimentional ultrasonography for diaphragm thickness was used. The New Philanthropy Capital (NPC) Wellbeing measure (level 2) was used to assess wellbeing. These measures were taken at week 0, week 8-10, week 16 and week 40. **Results:** Out of six children recruited, three children completed the study, of which one was excluded from data analysis, due to having attended only 21.4% of available hydrotherapy sessions. Mean biceps strength decreased from baseline measures by 40.1 N in Participant 1 and 32.0 N in Participant 2 after 40 weeks of hydrotherapy. Mean quadriceps strength and MEP increased from baseline measure at each time point to week 40 in Participant 1 (33.0 N and 0.4 cm H_2O, respectively) and Participant 2 (48.6 N and 18.0 cm H_2O, respectively). In Participant 1 only, mean MIP and diaphragm thickness at week 40 was lower than baseline by 4.5 cm H_2O and 0.01 cm, respectively, but were greater than baseline at week 8-10 and week 16. Wellbeing scores in Participant 1 decreased from baseline to week 40 by 3.0. In Participant 2 only, mean MIP, diaphragm thickness, and wellbeing increased from baseline to week 40 by 6.3 cm H_2O, 0.10 cm, and 3.0 points, respectively. The rate of attendance in Participant 1 was 67.9 % and in Participant 2 was 89.3%. **Adjoining:** To address the poor recruitment, attendance, and participation rates in Study 1, a second study to investigate barriers

and motivators that may affect participation in hydrotherapy for children and adolescents with MD was implemented. **Methodology:** Sixteen parents and/or carers with a child aged 5-17-years-old and diagnosed with MD, completed an online questionnaire surrounding barriers and motivations to participation in hydrotherapy. **Results:** Participation for hydrotherapy amongst children with MD was facilitated by parent-reported perceptions that hydrotherapy could slow down MD progression, decrease pain, and increase comfort, fun, relaxation, and independence. For parents, distance and a lack of time hindered their ability to bring their child to hydrotherapy sessions, while for children (as reported by their parents) their lack of self-esteem was the main barrier preventing them from participating. **Conclusion:** Study 1 provided useful insights into the potential contribution that the use of hydrotherapy could have for the maintenance on respiratory function, quadriceps strength, and wellbeing in children with MD. There was limited evidence supporting 40 weeks of hydrotherapy for the maintenance of function, but this was based on very limited sample size and no control group to support the results. The lack of standardisation was highlighted as a limitation across both Study 1 and 2, and a requirement of further investigation. However, the further understanding of barriers and motivators for MD from Study 2, provides an explanation for the findings of Study 1 and can be applied to future studies improve the implementation of interventions. Therefore, this thesis can serve as a template to better design future studies.

Declaration

I declare that the work in this thesis was carried out in accordance with the regulations of the University of Gloucestershire and is original except where indicated by specific reference in the text. No part of the thesis has been submitted as part of any other academic award. The thesis has not been presented to any other education institution in the United Kingdom or overseas.

Any views expressed in the thesis are those of the author and in no way represent those of the University.

Signed

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Glossary

2D: 2-Dimensional

CI: Confidence Interval

EK: Egen Klassification

HRQoL: Health-Related Quality of Life

ICC: Intraclass Correlation Coefficient

ICF: International Classification of Functioning, Disability and Health

MD: Muscular Dystrophy

MEP: Maximal Expiratory Pressure

MIP: Minimal Inspiratory Pressure

MFM: Motor Function Measure

NHS: National Health Service

NICE: National Institute of Care and Excellence

NPC: New Philanthropy Capital

PAD-model: Physical Activity for people with a Disability model

SCT: Social Cognitive Theory

QoL: Quality of Life

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Chapter 1.0: Introduction

Muscular dystrophy (MD) is a group of inherited neuromuscular diseases that causes progressive muscle degeneration and weakness (Cardamone et al., 2008), resulting from mutations to genes, which are responsible for the structure and function of muscle tissues (Gumerson & Michele, 2011; Huml, 2015). The onset of MD can occur anywhere from birth to late adulthood, where patterns of inheritance, rates of progression, severity, and life expectancies differ between types of MD and individuals with the same form of MD (Guzmán et al., 2012).

Over time, the decline in muscle strength and progressive muscle damage can cause multi-system complications, decreasing respiratory and cardiovascular function and leading to impaired biomechanical and psychological health (Mercuri & Muntoni, 2013). Thus, individuals with MD suffer from a wide range of signs and symptoms (Manzur & Muntoni, 2009), including abnormal gait, difficultly walking, spinal deformities, cardiac and respiratory issues, learning and behavioural problems and pain (Gaina et al., 2019; Mercuri & Muntoni, 2013; Osorio et al., 2019). This causes a decline in activities of daily life, participation in sport and exercise, and health-related quality of life (HRQoL) (Bendixen et al., 2012; Mercuri & Muntoni, 2013). Children and adults with more severe forms of MD lose the ability to walk (Gaina et al., 2019; Osorio et al., 2019), and in severe cases respiratory insufficiency or cardiomyopathy can progress to failure and then death (LoMauro & Aliverti, 2016; Mah, 2015b).

There is currently no cure for MD, and thus effective management is especially important to preserve function and delay the deterioration of physiological, psychological, and biomechanical function (Harjpal et al., 2022; National Institute of Neurological Disorders and Stroke, 2013). Insufficient management of MD can contribute to an increased progression rate of muscle damage and weakness (Duan et al., 2021; Lombardo et al., 2021), decreasing multi-systemic function and an

individual's HRQoL (Birnkrant et al., 2018b; Osorio et al., 2019). Multi-disciplinary care is required to manage the diversity and complexity of MD (Paganoni et al., 2017), using a range of approaches such as, drug therapy, speech-language therapy, nutritional care, surgery, exon skipping, occupational therapy and physiotherapy (Birnkrant et al., 2018b; Lombardo et al., 2021). Exon skipping is a treatment that uses oligonucleotides to stop the inclusion of an exon that is next to a mutated or deleted gene (responsible for MD) by binding to pre-mRNA to make a shorter, functional version of the protein, decreasing severity (Takeda et al., 2021). As of 2021, this treatment is still within the trial phase, focusing on its application to Duchenne MD by creating functional protein to produce more dystrophin (National Health Service, 2021). While found to be feasible for 30.0% of individuals (Eser & Topaloğlu, 2022), the long-term effects have not been investigated and so rehabilitating management is still needed to preserve overall physical function (Case et al., 2018). Practitioners are often hesitant to prescribe exercise for those with MD, as they do not want to exacerbate pain, induce injury, or cause further damage to muscles. Thus, low-moderate intensity aerobic activity with plenty of rest is often recommended, such as the incorporation of water-based exercises (Case et al., 2018; Lombardo et al., 2021). Additionally, existing guidelines surrounding physical rehabilitation and current management research for MD is limited, mainly focusing on Duchenne MD (Lombardo et al., 2021), ambulant individuals (Bendixen et al., 2016; Peay et al., 2018), and medications and drug therapy (Matthews et al., 2021). Those people with more severe symptom presentation find participation in land-based physical therapy difficult due to an inability to weight-bear but wanting to maintain muscle strength (Case et al., 2018). Thus, the use of hydrotherapy has been recommended in practise for the management of MD (Lombardo et al., 2021).

Hydrotherapy utilises the properties of water and has been suggested to have several benefits for children and adults with MD (Adams et al., 2017; Hind et al., 2017; Ogonowska-Slodownik et al., 2022). For example, systematic reviews surrounding MD has found hydrotherapy to be advantageous for improving pain, stiffness, muscle weakness, respiratory function, and HRQoL (Lima & Cordeiro,

2020). This has been attributed to the resistance from drag and viscosity of water, which may contribute to increased or maintained muscle strength (Torres-Ronda & Schelling i del Alcázar, 2014). The buoyancy of water can also reduce gravitational load and promote relaxation (Mooventhan & Nivethitha, 2014). The safer environment has also been found to provide a more inclusive environment for non-ambulant individuals, whereby improved mental health has been reported due to the decrease in social isolation (Atamturk & Atamturk, 2018). Unfortunately, despite its potential importance and benefits, limited studies have investigated the effectiveness of hydrotherapy for children and adolescents with MD. Of those studies that have, most are short-term case studies, lasting between 8 (Adams et al., 2017) and 12 weeks (Santos et al., 2016). Despite these studies finding improvements in HRQoL scores, respiratory function, and motor function, they were unable to identify longitudinal changes that is essential to MD due to it being an ongoing progressive disorder (Duan et al., 2021). Few long-term studies were completed, lasting between 6 months (Hind et al., 2017) and 5 years (Sanders & Torres, 2010), however data was either subjective or focused on one or two consequences of MD, which provides limited insight into the maintenance of the complex and multi-system nature of MD. For example, two studies investigated motor function only (Ferreira et al, 2015; Honório et al, 2013), and one investigated functional activity performance and respiratory function (Huguet-Rodríguez et al., 2020). Whereas those that did investigated a mixture of consequences, such as reduced quality of life (QoL), ambulation and muscle strength, were subjective, being a case study (Sanders & Torres, 2010) and pilot feasibility study (Hind et al., 2017). Thus, it is unknown whether long-term hydrotherapy can delay the progression of psychological, respiratory, and functional consequences in those with MD. As a result of limited research in this area, hydrotherapy is not currently recommended under the National Health Service (NHS) National Institute for Health and Care Excellence (NICE) guidelines making access to it limited.

This thesis aims to advance our understanding about the longitudinal effects of hydrotherapy on MD strength, wellbeing, and respiratory function in children and adolescents. If found effective,

this would allow practitioners to prescribe hydrotherapy appropriately and more effectively to children and adolescents with MD. To further build on our understanding, influences on hydrotherapy participation amongst these children and adolescents will also be sought. This would contribute to strengthening the design of future therapies and clinical interventions. Therefore, to effectively investigate each aspect, the thesis will consist of two studies:

1) The overall aim of **Study 1** is to investigate the effects of 40-weeks of hydrotherapy on muscle strength, wellbeing (physical, mental, and social), and respiratory function in children and adolescents (5-17 years old) with MD.
2) The overall aim of **Study 2** is to investigate the barriers and motivators that influence participation in hydrotherapy in children and adolescents (5-17 years old) with MD from the perspective of their carer.

Chapter 2.0: Literature Review

2.1 Background into Muscular Dystrophy

2.1.1 Aetiology and Prevalence

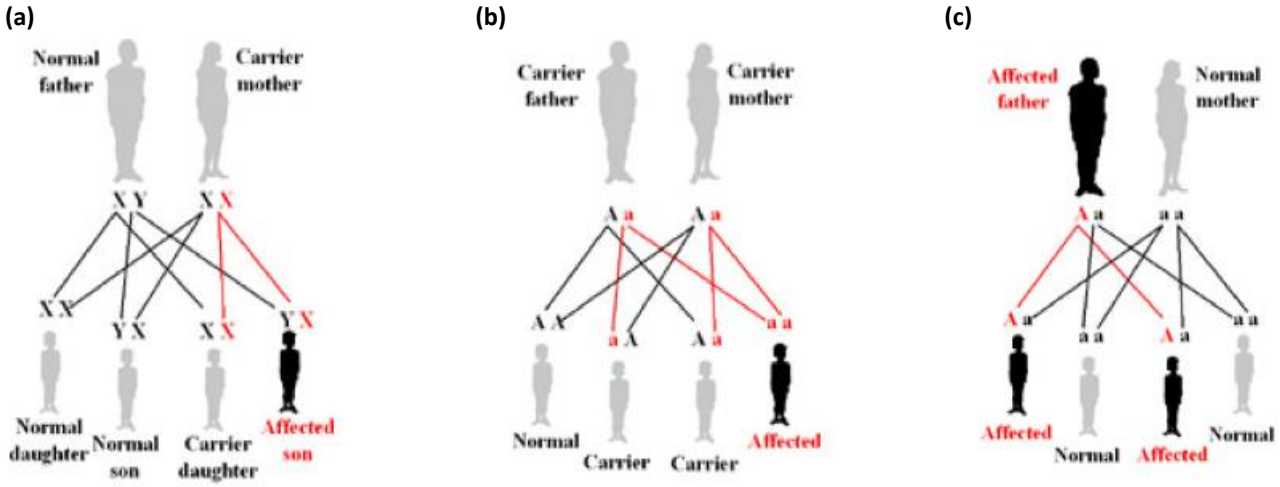
MD is a relatively rare disorder, with an estimated prevalence of 29.5 per 100,000 persons in 2019 and incidence of 1.16 per 100,00 person years from 2015-2019 in the United Kingdom (Carey et al., 2021). There are around 30 forms of MD that can be summarised into nine overall types: Duchenne, Becker, Congenital, Distal, Emery-Dreifuss, Facioscapulohumeral, Limb-Girdle, Myotonic, and Oculopharyngeal (National Institute of Neurological Disorders and Stroke, 2013). The most common forms of MD in childhood and adulthood are Duchenne MD and myotonic MD, respectively (Liao et al., 2022; van Ruiten et al., 2014), as well as facioscapulohumeral MD (Theadom et al., 2014).

MD results from mutations and/or deletions in genes responsible for the structure and functioning of muscles, which causes defects in different supporting proteins, enzymes, and/or the extracellular matrix (Guzmán et al., 2012; Rahimov & Kunkel, 2013). These mutations, such as to the dystrophin-glycoprotein complex, affect muscle fibre or sarcolemma (muscle membrane) integrity by providing less protection and increasing susceptibility to damage and tears during muscle contractions (Wilson et al., 2022). This increases the membrane's permeability of calcium, ions, and small molecules, leading to cell death and muscle degeneration (Gumerson & Michele, 2011). For example, in some types of MD, the leaking of creatine kinase out of the muscle membrane can cause an excess in calcium within the muscle that harms the muscle fibres (Guzmán et al., 2012; National Institute of Neurological Disorders and Stroke, 2013), resulting in fibre death branching and splitting, or phagocytosis (Huml, 2015). Since creatine kinase is responsible for chemical reactions needed to produce energy for muscle contractions (Guzmán et al., 2012), this manifests as the weakening of

muscles. These alterations in genes may result from autosomal dominant, autosomal recessive and/or X-linked inheritance, although in few cases can be sporadic (Cardamone et al., 2008; Huml, 2015).

Figure 1

Patterns of Inheritance in Muscular Dystrophy



Note. (a) X-linked Recessive Inheritance. (b) Autosomal Recessive Inheritance. (c) Autosomal Dominant Inheritance. Adapted from "Clinical utility of genetic tests for inherited hypertrophic and dilated cardiomyopathies" by M. G. Colombo, N. Botto, S. Vittorini, U. Paradossi, & M. G. Andreassi, 2008, *Cardiovascular Ultrasound, 6*(62) (https://doi.org/10.1186/1476-7120-6-62).

2.2.1.1 X-Linked Recessive Inheritance

In X-linked recessive inheritance, mothers carry and pass the mutated gene to their offspring since mutations occur on the X chromosome (Huml, 2015). This means that males have a 50% chance of inheriting MD since they must receive their Y chromosome from their father and X chromosome from their mother (Basta & Pandya, 2022), as shown in Figure 1a. Females are usually less affected (approximately only 8.0%) and are more likely to be carriers only, although they may still exhibit milder symptoms (Song et al., 2011). Although females also have a 50% chance of receiving the gene (Basta & Pandya, 2022), as shown in Figure 1a, unless the father has MD they will receive a healthy X chromosome from the father, which typically produces enough protein to compensate for the defect and counteract the effects of MD (Nozoe et al., 2016).

X-linked recessive inheritance is most associated with Duchenne and Becker MD, which both belong to a group of X-linked muscle diseases (dystrophinopathies) that result from mutations to the DMD or dystrophin gene (Morales & Mahajan, 2021). As a result, functional dystrophin is not produced in Duchenne MD, due to a nonsense or frameshift mutation, while dystrophin is only partially functional in Becker MD, due to a missense mutation (Okubo et al., 2020). Dystrophin is responsible for stabilising the sarcolemma and protects the muscle cells from contraction-induced damage (Gao & McNally, 2015; Rahimov & Kunkel, 2013). Thus, as the disease progresses, the muscle membrane becomes more unstable and susceptible to damage, causing muscle degeneration and weakness (Duan et al., 2021; Gumerson & Michele, 2011). Notably, Emery-Dreifuss MD can also result from X-linked inheritance by defects in the FHL1 or EMD gene and emerin protein production, although it is more commonly associated with autosomal inheritance (Wang & Peng, 2019).

2.2.1.2 Autosomal Recessive Inheritance

In autosomal recessive inheritance, MD occurs from one copy of a mutated gene coming from each parent, although the parents do not usually suffer from MD themselves (Huml, 2015). Males and females have an equal 25% chance of receiving both copies of the faulty gene and inheriting MD (Colombo et al., 2008), as shown in Figure 1b. This pattern of inheritance is seen in congenital, distal (early-onset), Emery-Dreifuss, and limb-girdle MD (Lovering et al., 2005). The specific gene affected is dependent on the subtype of MD an individual suffers from. For example, Limb-Girdle MD may be caused by mutations in calpain-3 (type 2A), deficiencies of dysferlin (type 2B) or deficiencies in specific structural sarcoglycan protein genes (all other types) (Lovering et al., 2005; Rocha & Hoffman, 2010). Types of Emery-Dreifuss MD may be caused by defects in the LMNA gene (Wang & Peng, 2019), while types of congenital MD may be caused by disruptions to α-dystroglycan (part of the dystrophin-glycoprotein complex) (Rocha & Hoffman, 2010).

2.2.1.3 Autosomal Dominant Inheritance

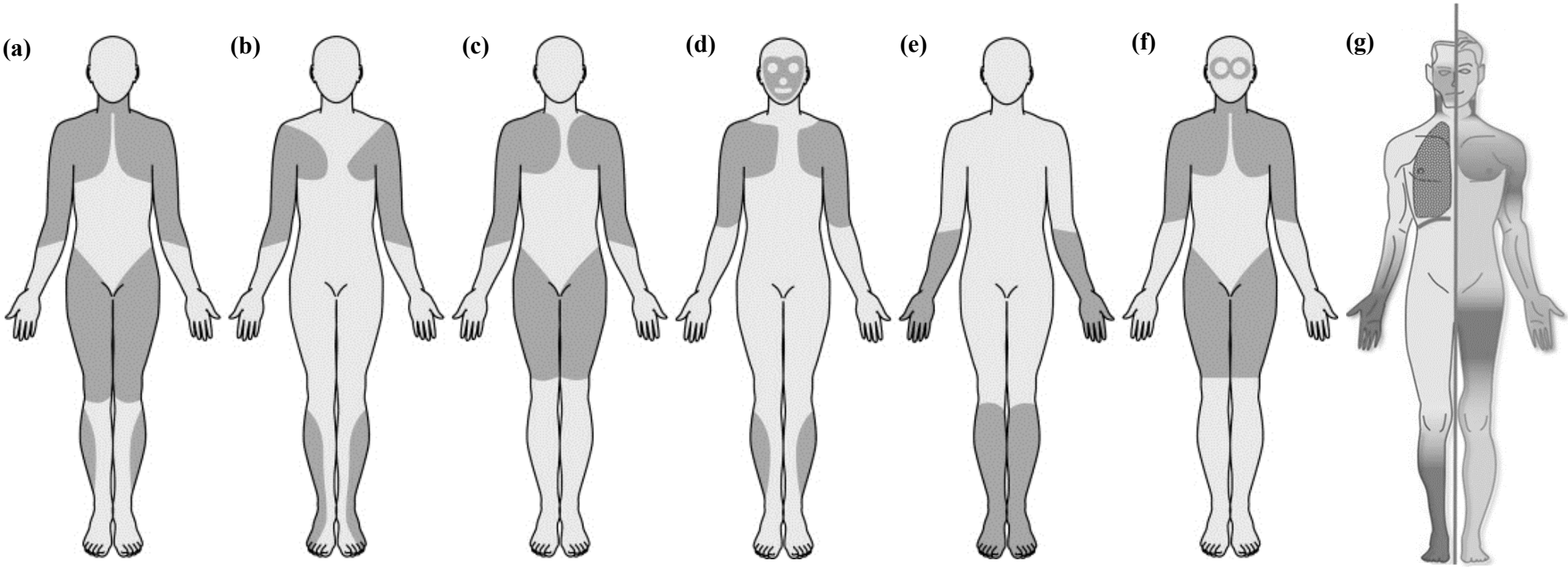
In autosomal dominant inheritance, MD occurs from one copy of a mutated gene coming from a single parent (Huml, 2015). Males and females have an equal 50% chance of receiving the affected gene and inheriting MD (Huml & Perez, 2015), as shown in Figure 1c. This form of inheritance is associated with distal (late-onset), facioscapulohumeral, myotonic, oculopharyngeal, Emery-Dreifuss and limb-girdle MD (Lovering et al., 2005). Different genes can be affected that is also dependent on the subtype of MD an individual suffers from. For example, types of Emery-Dreifuss MD can be caused by defects in the LMNA, SYNE1, STNE2, or TMEM43 gene (Wang & Peng, 2019), while oculopharyngeal MD can be caused by abnormal GCG trinucleotide repeats in the PABPN1 gene, myotonic by expansion of a CTG trinucleotide repeat in a gene for an enzyme (the DMPK gene), and facioscapulohumeral by associations with the deletion of 3.3 kb repeats (D4Z4) (Lovering et al., 2005).

2.2.2 Clinical Presentation

Individuals with MD may suffer from a diverse range of symptoms because of the involvement of multiple systems that can be affected by the impact of muscle damage on surrounding tissues and structures (Carter et al., 2018; Manzur & Muntoni, 2009; Mercuri & Muntoni, 2013). Each type of MD can be distinguished from one another, not only through differences in the patterns of inheritance and/or family history, but also by the muscles affected, age of onset, life expectancy, severity, progression rate, and comorbidities (Huml, 2015; Mercuri & Muntoni, 2013), as outlined below:

Figure 2

Main Muscles Affected in Different Forms of Muscular Dystrophy



Note. (a) Duchenne and Becker muscular dystrophy. (b) Emery-Dreifuss muscular dystrophy. (c) Limb-girdle muscular dystrophy. (d) Facioscapulohumeral muscular dystrophy. (e) Distal muscular dystrophy. (f) Oculopharyngeal muscular dystrophy. (g) Myotonic muscular dystrophy. Shading represents the most common affected areas. From "Muscular Dystrophies," by E. Mercuri, and F. Muntoni, 2013, *The Lancet, 381*(9869), p. 850 (https://doi.org/10.1016/S0140-6736(12)61897-2) *and* "Core Clinical Phenotypes in Myotonic Dystrophies," by Wenninger, F. Montagnese, and B. Schoser, 2018, *Frontiers in Neurology, 9*(303), p. 1-9 (https://doi.org/10.3389/fneur.2018.00303).

1. **Duchenne MD** occurs in early childhood, around 2-3 years old, and is rapidly progressive (Duan et al., 2021), where most individuals are symptomatic between the ages of two and four years old (Guzmán et al., 2012). Muscle weakness usually affects the pelvis and upper legs first, before spreading to the arms and later the shoulders, calf, and gluteal muscles (National Institute of Neurological Disorders and Stroke, 2013), as shown in Figure 2a. Children often show a Gower's sign, where they rise from a supine position using their arms (Gaina et al., 2019). Advances in management interventions have resulted in an increased life expectancy, increasing to 28.1 years (95% confidence interval (CI) [25.1, 30.3 years]) in those with MD born after 1990 (Broomfield et al., 2021).

2. **Becker MD** has a similar clinical presentation to Duchenne MD (Figure 2a), however is less severe and progresses slower (Guzmán et al., 2012). This is due to partially functional dystrophin still being produced (Rahmawati et al., 2021). Thus, onset occurs later, usually between 5 and 15 years old (Ciafaloni et al., 2016; Rahmawati et al., 2021), although it can begin in early adulthood, and the life expectancy is increased to around 40 to 50 years old (Thada et al., 2022).

3. **Congenital MD** typically occurs form birth or within the first six months of life (Mah et al., 2015a), where infants present with hypotonia, weakness, and in more severe forms are described as "floppy baby" (Bertini et al., 2011). Individuals with congenital MD may have a reduced life expectancy, with severity differing between each subtype (Bertini et al., 2011). At birth, children may present with pes cavus, sucking and swallowing difficulty, joint contractures, reduced patella reflexes, and skin dimples (Falsaperla et al., 2016).

4. **Distal MD** typically occurs between the ages of 40-and-60-years-old in both males and females, although can occur in early childhood (National Institute of Neurological Disorders

and Stroke, 2013). In general, it is typically less severe and slow in progression compared to other forms of MD (Savarese et al., 2020). As shown in Figure 2e, muscle weakness usually affects distal muscles first, including the hands, feet, forearm, and lower leg (Dimachkie & Barohn, 2014), with proximal, cardiac, and respiratory muscles being affected in later progressions (Savarese et al., 2020).

5. **Emery-Dreifuss MD** usually occurs between five-and-ten-years-old, with slow progression (Bonne et al., 2019), although some individuals have a milder phenotype that causes later onset (Kovalchuk et al., 2021). This type of MD often follows a triad of characteristics; 1) early contractures before significant weakness of the elbows, Achilles tendon and posterior cervical muscles, 2) slowly progressive muscle weakening and wasting beginning with a humero-peroneal distribution, and 3) cardiac abnormalities and problems, such as cardiomyopathy and arrhythmias (Emery, 2000), as shown in Figure 2b.

6. **Facioscapulohumeral MD** can occur at any point from childhood to early adulthood, prior to the age of 5 years or ranging between 15 and 30 years old (Goselink et al., 2019). Life expectancy usually remains similar to that of an unaffected individual (Sacconi et al., 2015), because overall progression is slow and steady, although there are intermittent periods of rapid muscle deterioration (National Institute of Neurological Disorders and Stroke, 2013), followed by periods of little to no progression (Statland & Tawil, 2016). As shown in Figure 2d, muscle weakness often begins in the face (mimetic muscles), shoulder girdle (serratus anterior and rhomboid), and upper arms (biceps and triceps) (Sacconi et al., 2015; Statland, 2020). This later progresses to the trunk, distal lower extremities (tibialis anterior and gastrocnemius), and eventually to more proximal muscles (quadriceps and hamstrings) and the pelvic girdle (Statland, 2020). A positive Beevor's sign, characterised by lower abdominal weakness but not upper abdominal weakness may also be seen (Huml & Perez, 2015).

7. **Limb-Girdle MD** usually occurs around the age of 15-years-old, although it can occur before the age of 12 and after the age of 30 (Strafella et al., 2019). Progression can be rapid with severe consequences or slow with minimal disability and can often pause then resume (National Institute of Neurological Disorders and Stroke, 2013). Muscle weakness starts at the hips, then affects the shoulders, legs, and neck (Rocha & Hoffman, 2010), as shown in Figure 2c. Early signs include, frequent falling, a waddling gait, tiptoe walking, difficulty with running, climbing stairs, and/or carrying heavy objects, and scapular winging (Rocha & Hoffman, 2010; Strafella et al., 2019).

8. **Myotonic MD** can have a congenital onset, childhood onset, or adulthood onset (Meola & Cardani, 2015a). Life expectancy often remains within normal range for type 2 but is reduced for type 1 (Meola & Cardani, 2015b). Slow weakening of muscles around the neck and face usually occurs first, followed by weakened foot extensors, finger flexors and wrist flexors in type 1 or neck flexors, hip flexors and hip extensors in type 2 (Wenninger et al., 2018), as shown in Figure 2g.

9. **Oculopharyngeal MD** onset is later in adulthood, typically occurring between 40-and-70-years-old (National Institute of Neurological Disorders and Stroke, 2013). As shown in Figure 2f, weakness affects the extraocular, upper facial, neck, and proximal upper and lower limb muscles, which do not typically affect the respiratory muscles, although obstructive sleep apnoea may occur (LoMauro & Aliverti, 2016).

Signs, symptoms, and the clinical presentation of MD can overlap between types of MD but may vary between the individual and stage of progression (Carter et al., 2018). It is recommended that the assessment and management of MD follow the International Classification of Functioning, Disability

and Health (ICF) (Case et al., 2018). By considering the components of the ICF framework, including body function and structure, activity and participation limitations, and environmental and personal factors, it allows for the evaluation and understanding of impairments in MD (Conway et al., 2018).

2.2.2.1 Body Function and Structure Impairments

Progressive muscle weakness occurs in all types of MD (National Institute of Neurological Disorders and Stroke, 2013), due to the integrity of muscle fibres mainly being affected which causes muscle wasting (Huml, 2015). This muscle weakness may present as side-to-side asymmetry in some forms of MD, such as facioscapulohumeral MD (Huml & Perez, 2015). Consequently, muscle fibres may respond ineffectively, leading to diminished reflexes in individuals with MD, such as distal MD (Dimachkie & Barohn, 2014). Strength and reflexes may further decrease or be lost over time as muscles become replaced by connective tissue and fat (Huml, 2015). The accumulation of fat and connective tissue replacing muscles often can make a muscle appear larger and healthier than it actually is, resulting in pseudohypertrophy (Walters, 2017), often found in lower leg muscles of children and adolescents with Duchenne and Becker MD (Kornegay et al., 2012).

In the early stage of life, Duchenne MD becomes apparent from delayed motor milestones (i.e., sitting, standing independently, and walking), gait problems (i.e., waddling, toe walking, and flat footedness), learning difficulties and speech problems (Brandsema & Darras, 2020; Darras et al., 2015). Similarly, infants with congenital MD may fail to display any signs of motor development (Falsaperla et al., 2016) and muscle control – poor head control. Several subtypes of congenital MD present with spasticity, causing motor function to deteriorate, in which walking is rarely achieved (Bertini et al., 2011).

In some cases, tendons and muscles may become chronically or permanently shortened (Huml, 2015), further impacting the production of movements and overall strength. This can result in

joint contractures, due to the prevention of movements occurring freely (Udd, 2011), that may be further reduced by continually decreasing mobility and muscle fibrosis, and increasing muscle imbalance (Lombardo et al., 2021). For example, Achilles contractures with toe walking, elbow contractures (Popeye arms) and severe lumbar lordosis, were all found in Emery-Dreifuss MD (Gaina et al., 2019). Following sudden contractures, myotonia is often seen in type 1 Myotonic MD in which muscles are unable to relax (National Institute of Neurological Disorders and Stroke, 2013), whilst muscle imbalances may result in changes to muscles supporting the spine and trunk, leading to the development of scoliosis (Archer et al., 2016). Scoliosis may be seen in individuals with facioscapulohumeral (Huml & Perez, 2015), Duchenne (Archer et al., 2016), congenital (Mercuri & Muntoni, 2013), and distal MD (Udd, 2011). As scoliosis progresses, changes in posture and positioning, costo-iliac impingements, pelvic obliquity, and discomfort can occur, contributing to further discomfort in non-ambulant individuals using wheelchairs (Archer et al., 2016).

The risk of fractures is also increased in neuromuscular diseases, including MD, where 30% of individuals had sustained at least one fracture post-diagnosis, with the reduction of ambulation being a major risk facture (Vestergaard et al., 2001). The reduction in bone structure and density in MD, often in individuals on steroid therapy treatments, can increase the susceptibility to fractures, often in the vertebras (19%) and long bones (25%) (Feder et al., 2017). In those using knee-ankle-foot orthoses, upper-limb fractures were most common (65%), whilst in those who were independent or wheelchair bound, lower-limb fractures were most common (54% and 68% respectively) (McDonald et al., 2002).

Additionally, progressive muscle weakness and fatigue can affect muscles involved in inspiration and expiration, including the diaphragm, abdominal, and intercostal muscles (LoMauro & Aliverti, 2016; Pennati et al., 2021). In many types of MD this can lead to respiratory failure, defined as an “inability of the respiratory system to provide proper oxygenation and carbon dioxide

elimination" (LoMauro & Aliverti, 2016). Additional signs of respiratory failure in MD include: loss of lung volume, sleep-disordered breathing, chest infections (Simonds, 2002), restrictive pulmonary function, inefficient coughing, impaired regulation of breathing, hypoventilation, altered thoracoabdominal patterns, dyspnoea, and hypercapnia (LoMauro & Aliverti, 2016). Respiratory complications can be detrimental in many cases of MD as it decreases life expectancy, with respiratory failure being one of the main causes of death in MD (Pennati et al., 2021). Non-ambulant individuals may have further stress on the respiratory system if they use a wheelchair, as the position may restrict the airways or lung space, which may reduce breathing rate, oxygenation to the body and lung vital capacity (Simonds, 2002; Strafella et al., 2019). Additionally, the presence of scoliosis may further stress the respiratory system (LoMauro & Aliverti, 2016; Takaso et al., 2010).

Some types of MD may have progressive weakness of the heart and surrounding muscles that can hinder the ability of the heart to pump blood to the rest of the body (National Institute of Neurological Disorders and Stroke, 2013). This may lead to ventricular arrhythmias, heart failure, cardiomyopathy, or any other cardiac irregularities (Bourke et al., 2018), with significant pulmonary and cardiac failure resulting in short life-expectancies and early death in some individuals (Feingold et al., 2017; Verhaert et al., 2011). For example, the most common cause of death in Duchenne MD is progressive cardiomyopathy and respiratory complications (Gaina et al., 2019), that may begin to develop at age 5 and 25-30, respectively (Guzmán et al., 2012). Unlike Duchenne MD, respiratory involvement is less common in Becker MD (Brandsema & Darras, 2020), however heart failure is a common cause of death in Becker MD, often occurring around mid-40s (Gaina et al., 2019).

The different involvement of multiple systems, such as the central nervous system, can result in structural changes affecting vision, cognitive function, hearing, and psychological wellbeing (Huml & Perez, 2015; Messina et al., 2010). Psychological (or mental) wellbeing as defined by Tang et al. (2019) is an aspect of mental health focusing on emotional regulation, coping (resilience), and

happiness (hedonic (enjoyment) and eudaimonic (fulfilment)). For example, individuals with oculopharyngeal MD experience swallowing problems, dysphagia, and ptosis (Yamashita, 2021), while those with myotonic MD experience ptosis (Longman, 2006) and high levels of abdominal and musculoskeletal pain (Meola & Cardani, 2015b). Hearing loss was also apparent in individuals suffering with early onset facioscapulohumeral MD, affecting 80% of individuals between the ages of 18 and 84 years old (Goselink et al., 2019).

Children and adolescents with neuromuscular disorders are more susceptible to various degrees of cognitive impairment and emotional, social, and behavioural dysfunction (Paganoni et al., 2017). This is evident in Duchenne MD, whereby 32.0%, 27.0%, and 15.0% of individuals reported suffering from an attention-deficit hyperactivity disorder, anxiety, and an autism spectrum disorder, respectively (Ricotti et al., 2016). Additionally, approximately 58% of individuals with congenital MD suffer from cognitive impairment (Messina et al., 2010).

2.2.2.2 Activity and Participation Limitations

The progressive physical and mental complications within multiple systems (as outlined above) may contribute to decreased participation in MD (Bendixen et al., 2012; Mercuri & Muntoni, 2013). As muscle weakness increases and mobility decreases, this can impact gait, functional movements and eventually the ability to walk (Kennedy et al., 2020). Research found that as the age of onset at first signs and symptoms increased by a year, loss of ambulation annual risk decreased by 10% (hazard ratio = 0.90, 95% CI [0.87-0.94]) (Ciafaloni et al., 2016). Thus, more severe forms and childhood onset of MD are likely to result in loss of ambulation. As a result, more severe forms of MD have reduced rates of participation in activities of daily life and physical sporting activities (Bendixen et al., 2014), seen at in both early and later stages of life, in older children and adults who lose ambulation as their disease progresses (Strafella et al., 2019). To support individuals, joint-stabilising orthotics may be used around the age of 10 for Duchenne MD, before individuals are then

confined to a wheelchair by the age of 11-13-years-old (Darras et al., 2015), thus reducing participation in activities. In other forms of MD, such as facioscapulohumeral, individuals' participation may only reduce later in life, where approximately 20.0% people aged 50-years-old and over required a wheelchair (Statland & Tawil, 2016). However, early signs of facioscapulohumeral MD include difficulty reaching above shoulder level, scapular winging, facial weakness, an inability to run, and loss of power (Huml & Perez, 2015), further hindering participation levels. Additionally, signs of limb-girdle MD, such as frequent falling, gait disruptions, an inability to carry heavy objects, and scapula winging (Strafella et al., 2019; Takahashi et al., 2013), may also hinder participation in daily activities and sports.

In boys (aged 6-15) with Duchenne MD, participation in physical activities had moderate negative correlations with timed functional performance tests, including a 10-meter run ($r = -0.35$, ≤ 0.01), supine to stand rise from the floor ($r = -0.42$, $p \leq 0.001$), and four stair climb ($r = -0.44$, $p \leq 0.001$); however, had a positive correlation with quadriceps strength ($r = 0.32$, $p < 0.01$) (Bendixen et al., 2014). This demonstrates how changes in physical function may influence participation levels in children and adolescents with MD, whereby decreases in function were associated with decreased participation. Additionally, increased age was found to be associated with decreased function, where Bushby and Connor (2011) found that non-ambulant children all had motor function scores below 50% as they reached the age of 10. This suggests an association between increased age, decreased function, and decreased participation levels. For example, older boys (aged 10-15) had weaker lower limb muscle strength, significantly slower completion times of functional performance tests, lower levels of participation in skill-based, recreational, and social activities, and lower social engagement outside of their home when compared to younger boys (aged 6-9) (Bendixen et al., 2014). This is supported by Bendixen et al. (2012) who found that participation levels were lower in older boys ($\geq$ 10 years old) with Duchenne MD compared to younger boys ($<$ 10 years old), with a significant difference in social participation levels. Additionally in adults with myotonic MD, myotonia is first

seen in grip (Longman, 2006), then the jaw and tongue (Wenninger et al., 2018), hindering many daily activities and fine motor functioning, especially when in the hand, affecting the ability to use tools and doorknobs (Ho et al., 2019; Longman, 2006).

As a result, HRQoL tends to decline with the increased progression of MD (Jacques et al., 2019; Uzark et al., 2012), where HRQoL can encompasses physical, psychological, social and wellbeing domains (Uttley et al., 2018). Non-ambulant boys with Duchenne MD at later stages of progression had lower HRQoL scores (Szabo et al., 2022), limiting their performance and participation in activities and sports. This was supported by boys with Duchenne MD found to have worsened QoL scores (total, physical, social, and school-related) and physical activity participation levels than unaffected boys ($p < 0.001$) (Bendixen et al., 2012). In children with Duchenne MD, 16.7% presented with high anxiety risk and 41.7% presented with a comorbid psychiatric disorder (combined depression, generalised anxiety disorder, and/or obsessive-compulsive disorder (Ozer & Tufan, 2019). Based on a meta-analysis, depression, anxiety, autism, attention-deficit hyperactivity disorders, and obsessive-compulsive disorders were present in Duchenne MD (11.0%, 24.0%, 7.0%, 18.0%, and 12.0%, respectively) and Becker MD (7.0%, 25.0%, 6.0%, 28.0%, and 7.0%, respectively), of which scores where greater than those of the healthy population (Pascual-Morena et al., 2022). The presence of these mental health disorders can negatively impact HRQoL, and as a result further hinder participation in daily activities and sport, as well as social participation.

2.3 Management and Treatments for Muscular Dystrophy

Early diagnosis of MD allows for "early access to standards of care", where innovative clinical trials and optimised care may be more accessible for families, allowing them to make informed decisions on their child's care (van Ruiten et al., 2014). Since there is no current cure for MD, effective management and treatment is essential for delaying progression that would otherwise have detrimental effects on an individual's HRQoL and life expectancy (Lombardo et al., 2021; Sun et al.,

2020). By addressing the primary and secondary consequences of MD as they present (Case et al., 2018; Lombardo et al., 2021), a holistic management can be done to prolong ambulation and function and improve HRQoL (Wei et al., 2015). Thus, multidisciplinary care is required for "anticipatory, preventative care and optimal management" of MD (Bushby et al., 2010a). Different healthcare specialists are needed to manage the multi-systemic nature and diverse range of symptoms associated with MD, such as physiotherapists, occupational therapists, medical doctors, speech and language pathologists, social workers, and nurse practitioners (Paganoni et al., 2017).

Guidelines on the management of different forms of MD are based on expert consensus and standard of care literature, however the majority available surround Duchenne MD (Case et al., 2018; Lombardo et al., 2021). The aim of treatments for MD is to maintain independence for as long as possible (National Institute of Neurological Disorders and Stroke, 2013), promote overall health, preserve motor function, prevent secondary complications, improve autonomy and HRQoL (Lombardo et al., 2021), and improve longevity (Bushby et al., 2010a). General treatments can be used to address the common characteristics of muscle weakness, contractures, bone fragility, fractures, and spinal deformities (Lombardo et al., 2021), however optimal management often varies between MD types and individuals with the same MD types (Carter et al., 2018). Thus, a combination of the following approaches may be used to address symptoms as they present:

1. ***Drug therapy and/or medication*** may be used to delay muscle degeneration, and assist with cardiovascular and respiratory function, with the medication type varying depending on the type of MD and requirement of the individual (National Institute of Neurological Disorders and Stroke, 2013). For example, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and β-adrenergic blockade have been effective for the use of cardiomyopathy (Feingold et al., 2017). Additionally, glucocorticoids have been found to further delay the loss of ambulation in Duchenne MD (Henricson et al., 2013).

2. ***Speech-Language therapy*** may be used in MD where dysphagia is present and progressive (Birnkrant et al., 2018b).
3. ***Nutritional care*** from a dietitian nutritionist may be required to assist with promoting a healthy, balanced diet to monitor growth and weight, and prevent individuals becoming overweight or underweight (Birnkrant et al., 2018b). Nutritional care aids in preventing malnutrition that can be caused by gastrointestinal dysfunction, chewing, and swallowing difficulties in ambulant and non-ambulant DMD patients (Guzmán et al., 2012).
4. ***Corrective surgery*** may be required in severe cases of MD, such as for correcting progressive scoliosis, contractures, and foot positioning, however there may be risk of cardiac and respiratory decompensation during and after surgery (Birnkrant et al., 2018a). Despite the risks, surgery has been found to improve function, sitting balance and QoL, especially in those with MD types presenting with scoliosis (Archer et al., 2016; Takaso et al., 2010). However, Archer et al. (2016) also stated that life has also been prolonged when non-invasive ventilation for scoliosis was used, since surgery cannot improve or slow the deterioration of respiratory function.
5. ***Gene replacement therapy*** may allow for the production of missing proteins in MD, as seen in advancements of research into using adeno-associated viral vector for the restoration of dystrophin (Elangkovan & Dickson, 2021).
6. ***Exon skipping trials***, as defined in *Chapter 1.0: Introduction*, may be used for the correction of dystrophin mutations in Duchenne and Becker MD, by restoring "the frame of an out-of-frame dystriohin mutation" (Takeda et al., 2021). Four exon skipping drugs have been conditionally approved for Duchenne MD, that has been found to benefit at least 30% of individuals (Eser & Topaloğlu, 2022).
7. ***Physiotherapy and Occupational therapy*** using Manual therapy programmes, pain management, splinting and orthotic intervention, gait and standing rehabilitation, adaptive equipment, and fall and fracture management are often implemented for individuals with MD

(Case et al., 2018). Stretching between four to six days per week, based on recent guidelines, for muscles and joints susceptible to hypo-extensibility, may be incorporated into these therapies to prevent and minimise contractures (Case et al., 2018).

8. ***Orthoses*** may be used to provide support at different stages of MD, such as ankle-foot orthoses that are appropriate to use throughout different stages of MD and knee-ankle orthoses that are used for late-ambulatory and early non-ambulatory stages (Case et al., 2018).
9. ***Cardiorespiratory Care***, other than medications, using diuretic agents, assisted ventilation, Cardioverter-Defibrillator and Resynchronization Therapy have also been found to be beneficial depending on the condition being evaluated and/or stage of MD (Feingold et al., 2017).

Current management for MD within research focuses on medication and drug interventions. For example, available clinical trials between 2000 and 2015 in the United States of America found that 61.5% of studies involved some form of drug therapy (Matthews et al., 2021). Drug therapy often aims to restore function of mutated genes, such as dystrophin in Duchenne MD, or target any consequential pathological changes (Yao et al., 2021). While medication can have a beneficial effect, there are side effects that can occur and need to be controlled, such as weight gain, behavioural changes, and cataracts (Henricson et al., 2013). Thus, rehabilitative management is required to protect muscles and preserve overall individual function (Case et al., 2018) and is needed for psychophysical wellbeing (Lombardo et al., 2021).

The importance of physical therapy must not be dismissed, as activities are required to maintain muscle strength (Case et al., 2018). However, land-based physical therapy may limit the number of activities that individuals with severe forms of MD can complete that still allow for the maintenance of muscle strength. Repetitive movements and high intensity exercise on land may increase the susceptibility to injury and muscle damage (Lott et al., 2021; Siciliano et al., 2015). This

means practitioners and/or individuals may be hesitant to complete intensive land-based exercises and therapies. There is a reliance on the ability of individuals with MD to weight-bear during land-based exercise (Lombardo et al., 2021), however this excludes non-ambulant individuals from participating. Therefore, individuals with MD should be made aware of and given access to alternative physical rehabilitation that does not rely on weight bearing.

An alternative to land-based physical therapy is hydrotherapy, also referred to as aquatic (physio)therapy, defined as a therapeutic modality that utilises the properties of water to treat injuries or diseases, carried out by trained professionals (i.e., physiotherapists) in an appropriately heated pool (Pattman et al., 2021). The use of gentle, aerobic aquatic exercises has been recommended in guidelines of physical rehabilitation for MD (Lombardo et al., 2021), supporting the use of hydrotherapy for MD. The properties of water, including buoyancy, hydrostatic pressure, drag, and metacentric effects, have been found to provide advantageous psychological, physiological, and biomechanical benefits for several clinical populations (An et al., 2019), such as children with cerebral palsy (Adar et al., 2017; Ballington & Naidoo, 2018) and juvenile arthritis (Osama et al., 2020). Thus, hydrotherapy may benefit children and adolescents with MD by helping to manage complications that occur across multiple systems, such as the cardiovascular, musculoskeletal, respiratory, renal, and sympathetic and central nervous system (Mooventhan & Nivethitha, 2014; Wratten et al., 2019).

2.4 The Use of Hydrotherapy for Muscular Dystrophy

2.4.1 Outcome Measures: Measure Strength, Respiratory Function, and Wellbeing

Several studies have investigated postural control, functional performance, pulmonary changes, and HRQoL in individuals with MD (Lima & Cordeiro, 2020). A wide range of outcome measures were identified across 12 studies that investigated the use of hydrotherapy in MD, demonstrating a comprehensive view of symptoms experienced by those with MD. Most studies

concluded that hydrotherapy was beneficial for improving and/or maintaining respiratory function, biomechanical function, and psychological health in MD (Adams et al., 2017; Atamturk & Atamturk, 2018; DiBiasio et al., 2015; Sanders & Torres, 2010; Santos et al., 2016; Silva et al., 2012); however, the effects of hydrotherapy on similar outcomes is debated between studies. For example, motor function and/or muscle strength in some studies were found to improve after hydrotherapy (Luz et al., 2021; Santos et al., 2016), however in other studies worsened (Honório et al., 2013) or remained the same (Silva et al., 2012). Similarly, forced vital capacity was found to increase after hydrotherapy interventions in some studies (Abo-zaid et al., 2021) but decrease in other studies (Huguet-Rodríguez et al., 2020; Voos et al., 2020) or had no change (Silva et al., 2012). Notably, several studies could not be evaluated because articles were written in another language and/or only had the abstract available.

2.4.1.1 Biomechanical Function

Regarding functional performance, score improvements and maintenance in the Motor Function Measure (MFM) (Santos et al., 2016) and the Vignos scale and Egen Klassification (EK) scale (Silva et al., 2012) were found after hydrotherapy. Motor function involves performing an activity that involves specific muscle movements, defined by the American Physical Therapy Association (2014) as "the ability to learn or demonstrate the skillful and efficient assumption, maintenance, modification, and control of voluntary postures and movement patterns" (as cited in Hallemans et al., 2020). Motor function is one of the main outcome measures used for monitoring biomechanical functioning in children and adults with MD (Nunes et al., 2016). Thus, most studies used motor function as an outcome measure to report the effects of hydrotherapy (Ferreira et al., 2015; Honório et al., 2013; Santos et al., 2016; Silva et al., 2012).

Motor function remained the same after 10 weeks (Silva et al., 2012) and improved by 4.3% after 12 weeks of hydrotherapy (Santos et al., 2016), suggesting that the addition of hydrotherapy for

durations longer than 10 weeks improves and/or maintains function in MD. However, this is conflicting with motor function found to worsen after two years of hydrotherapy and physical activity combined, indicated by an increase of nine in the EK Scale (Honório et al, 2013). Similarly, Ferreira et al. (2015) found that after two years of hydrotherapy and physiotherapy combined, motor function diminished when performed on land. It is uncertain whether improvements in motor function plateau after a certain point after 12 weeks of hydrotherapy and prior to two years. Research should consider using multiple time points to monitor progression more precisely, since there may be little reason to continue hydrotherapy sessions after improvements plateau and before they begin to decline. However, greater declines in motor function were also found in participants who received no form of physical activity compared to those who received hydrotherapy in Honório et al. (2013). This suggests that hydrotherapy may contribute to slowing the decline in motor function in MD, although it may not outweigh natural disease progression.

Inconsistencies between studies may be attributed to the differences in motor function outcome measures used and the stage of disease that participants were in. Several studies used the EK scale (Ferreira et al., 2015; Honório et al, 2013; Silva et al., 2012), while only a few used the MFM (Santos et al., 2016). Those that used the EK scale had participants between 8 and 14 years old. At this stage, children are in or near to the point where they are losing the ability to walk, and so the use of a wheelchair becomes more prominent (Duan et al., 2021; Wahlgren et al., 2022). Thus, motor function would have been already decreasing, and whilst hydrotherapy may have been able to slow this down, it would likely not have prevented decreases from happening. The MFM scale was found to be a reliable and valid measure for upper- and lower-limb function in ambulant and non-ambulant people with neuromuscular diseases, including MD, between 6 and 62 years old (Bérard, et al., 2005), whereas the EK scale was found to be valid and reliable for use in older, non-ambulant children (Darras et al., 2015; Werlauff & Steffensen, 2014). This explains why studies may have used these measures. However, the MFM does widely assess antigravity function in the upper limb (only 25%

of item), which is clinically important for children with Duchenne MD after they have lost ambulation (Mazzone et al., 2012). Nonetheless, decreases in motor function were found to be strongly correlated with decreased muscle strength (Nunes et al., 2016), so it could be suggested from Santos et al. (2016) and Silva et al. (2012) that muscle strength was also maintained. An issue with motor function is that it does not use manual resistance or focus on contraction of specific muscles, thus monitoring progression of muscle strength is not know from these measures (Nunes et al., 2016).

The maintenance or improvement of motor function could be attributed to muscle strength being maintained (DiBiasio et al., 2015), which may be the result of resistance from the drag and viscosity of water strengthening the muscles (Torres-Ronda & Schelling i del Alcázar, 2014). Progressive muscle weakness is the main characteristic common to all types of MD and is responsible for many secondary consequences of MD, such cardiomyopathy, respiratory and psychiatric disorders (Gaina et al., 2019). Unlike motor function, muscle strength is "the ability to exert force on an external resistance" (Jones & Comfort, 2020). Despite the importance of muscle strength in relation to the progression of MD, limited studies investigating the use of hydrotherapy for MD have included muscle strength itself as an outcome measure. One study investigating 32 weeks of hydrotherapy on a child with limb-girdle MD found decreased leg muscle strength during left-sided hip abduction, right-sided hip abduction, left-sided knee extension and right-sided knee flexion by 11.3%, 23.4%, 35.8% and 39.2%, respectively (DiBiasio et al., 2015). Decreased muscle strength could be attributed to progressive weakness outweighing the effects of hydrotherapy, especially in more severe forms of MD where the progression rate is fast (Mercuri & Muntoni, 2013). Since MD continually worsens overtime, an overall maintenance of function (i.e., muscle strength) is as equally important as improving function. Even if small decreases occur, this can indicate a delay in the rate of MD progression that would otherwise occur during normal progression (Silva et al., 2012). In the same study by DiBiasio et al. (2015), 84.0% of overall combined lower-limb strength was maintained, suggesting a potential benefit in the use of hydrotherapy for MD. This is supported by greater overall

lower- and upper-limb strength being found in a woman with congenital MD after four months of hydrotherapy and land-based sessions combined, that diminished after six months when hydrotherapy participation stopped (Sanders & Torres, 2010). This suggests that hydrotherapy may contribute towards a delay in progression, since without it the rate of MD progression increased. Therefore, considering muscle strength as an outcome measure rather than motor function during hydrotherapy may be more beneficial.

2.4.1.2 Respiratory Function

Declines in muscle strength also affect the respiratory muscles in MD (LoMauro & Aliverti, 2016). Multiple outcome measures have been used to assess respiratory function in MD. Several studies support the use of hydrotherapy for the maintenance of respiratory function in MD, however results within research are contradicting. Hydrotherapy was also found to increase inspiratory volume and ventilatory pressures (Abo-zaid et al., 2021) that indicated increases in strength and oxygen saturation, and increased function and HRQoL in children with MD (Huguet-Rodríguez et al., 2020). This could be attributed to the hydrostatic pressure of water, where exercises in water increases cardiac output (between muscles and time for oxygen transport to fatigued muscles), strengthens lungs, and reduces muscle damage (Torres-Ronda & Schelling i del Alcázar, 2014).

Hydrotherapy had no change on forced vital capacity and minimal improvements (between 3.0% and 11.6%) in oxygen saturation, maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), minute ventilation and peak cough flow (DiBiasio et al., 2015; Huguet-Rodríguez et al., 2020; Silva et al., 2012). Additionally, other studies found small decreases in forced vital capacity post-hydrotherapy by 0.75% (Hind et al., 2017) and 6.15% (Huguet-Rodríguez et al., 2020). Even though these indicate a slight worsening, the differences in each study were insignificant, suggesting the maintenance of respiratory function. In many forms of MD respiratory function continues to

decrease in MD (Kinane et al., 2018), thus it is unlikely that treatments would improve function but rather would contribute to maintaining or slowing the progression.

On the other hand, respiratory frequency, peak cough flow, minute volume, and flow volume were all found to worsen by between 8% and 29% after 10 sessions of hydrotherapy (Silva et al., 2012). These may have worsened more compared to other studies because of the stage of progression the child was in. The child being 12 years old in this study may have affected the results where they were non-ambulant and had DMD, meaning they likely already had a worsened respiratory function. This is supported by Adams et al. (2017) who found respiratory function differed with age, in which chest expansion, inspiratory capacity and peak flow are more likely to increase in the younger, ambulant male compared to the older, non-ambulant male. Age must be considered during interventions for MD, as in Duchenne MD natural worsening of the respiratory system began around 10-12 years, and after age 16 was less than 50% of predicted values of healthy age-matched children (Henricson et al., 2013). This suggests that a comparison of improvements should not be made between individuals of different ages due to the natural progression and worsened function in older children. Additionally, without a comparison between natural progression and the addition of hydrotherapy, it cannot be determined if function is being maintained because of hydrotherapy, thus a control group would be required to determine this.

Respiratory function outcomes improved slightly more in those who received hydrotherapy compared to those who received land-based therapy (Abo-zaid et al., 2021). This suggests that improvements in function may be attributed to hydrotherapy, although since no control group was used, caution must be used. Improvements in outcomes, such as MIP and MEP, indicate improved respiratory muscle strength (Watson et al., 2022). However, diaphragm muscle strength was not measured, which would provide greater insight into the effects of hydrotherapy on respiratory muscle strength, something that has not been investigated before. Diaphragmatic muscle strength is

responsible for effective breathing (Laviola et al., 2018; LoMauro & Alverti, 2016), making it important as natural declines in respiratory function, such as altered breathing patterns, occur in MD. Thus, since there is no research that has investigated the effects of interventions on diaphragmatic thickness, further investigation could contribute to better understanding of respiratory function and the effects of hydrotherapy participation.

2.4.1.3 Psychological Function

Finally, self-efficacy, mental relaxation, and HRQoL was also found to improve in MD after receiving hydrotherapy (DiBiasio et al., 2015; Hind et al., 2017; Sanders & Torres, 2010). The buoyancy of water reduces load of muscles, joints, and bones, and increases the range of movement, whilst reducing pain and muscles damage (Mooventhan & Nivethitha, 2014), suggesting a safer environment. Participation in water-based exercises could decrease social isolation and be completed alongside their peers, which could benefit non-ambulant individuals (common in MD) and increase mental health.

Declines in muscle strength, alongside primary and secondary consequences of MD, increases the likelihood of a poor HRQoL and lack of participation in activities of daily life (Jacques et al., 2019; Powell & Carlton, 2023). Several studies found that HRQoL improved after two to six months of hydrotherapy. A parent-reported interview found that eight hydrotherapy sessions twice a week improved HRQoL, relaxation, socialisation, and self-perception in a child with Duchenne MD (Atamturk & Atamturk, 2018). This was supported by parent-reported Pediatric QoL surveys that found significant improvements in daily activities, treatment, and worry dimensions by ≥ 4.5 points after eight weeks of hydrotherapy (Adams et al., 2017), and improved child-reported QoL scores by 5.9 after ten weeks of hydrotherapy (Huguet-Rodríguez et al., 2020). Six months of hydrotherapy was also found to contribute to the maintenance of HRQoL by improved scores of 8.1 and 0.07 as reported by carers using the carer QoL questionnaire and children using the Child Health Utility 9-Dimension

Index, respectively (Hind et al., 2017). These suggest that hydrotherapy can be beneficial for improving psychological function and wellbeing in individuals with MD.

Notably, the outcome measures may have monitored different aspects of HRQoL and wellbeing. For example, Huguet-Rodríguez et al. (2020) used the Pediatric QoL Neuromuscular Module (Huguet-Rodríguez et al., 2020) that monitors social and physical wellbeing through questions surrounding problems caused by the disease, communication difficulties, and problems on family functioning, whereas Adams et al. (2017) used the Pediatric QoL Generic Core Scale and Hind et al. (2017) used the Child Health Utility 9-Dimension Index that both consists of questions surrounding a child's physical, emotional, social and school functioning and wellbeing. Thus, research should apply an outcome measure that considers the aspect of HRQoL they would like to monitor.

2.4.2 Considerations of Age and Ambulation

Of the available studies, 72.7% investigated hydrotherapy on children under 18 years old only (Abo-zaid et al., 2021; Adams et al., 2017; Atamturk & Atamturk, 2018; Ferreira et al., 2015; Hind et al., 2017; Honório et al., 2013; Santos et al., 2016; Silva et al., 2012). Research guidelines encourages early intervention for the management of MD (Bushby et al., 2010a), which could contribute to why most hydrotherapy studies used children and adolescents as the sample population. An issue with this is that previous research found the inclusion criteria for clinical studies often prevented parents from letting their non-ambulant child participate in research (Bendixen et al., 2016). This may impact the willingness of individuals participating in future research, as if they constantly do not meet the criteria, it is unlikely they will consider joining clinical trials. There is evidence to suggest that hydrotherapy may be more beneficial for older, non-ambulant children and adolescents, who cannot perform land-based exercises, where the buoyancy and properties of water allow for more freedom and independence without a wheelchair (Ogonowska-Slodownik et al., 2022;

Torres-Ronda & Schelling i del Alcázar, 2014). Hydrotherapy is more inclusive and can encourage people with MD to participate alongside their peers. Therefore, research on hydrotherapy should be inclusive to both ambulant and non-ambulant individuals.

2.4.3 Considerations of Study Duration and Design

Many studies are short-term, with most hydrotherapy sessions lasting between 8 weeks (Adams et al., 2017; Atamturk & Atamturk, 2018) and 12 weeks (Santos et al., 2016). Whilst these studies suggest that there are benefits of hydrotherapy for MD, short-term research may have overlooked and/or missed patterns or changes which may have been identified using longitudinal research. Few long-term studies were completed, lasting between six months (Hind et al., 2017) and five years (Sanders & Torres, 2010), however data was either subjective or focused on one or two consequences of MD, such as only focusing on motor function or respiratory function. Thus, it is unknown whether long-term hydrotherapy can delay the progression of psychological, respiratory, and functional consequences in MD.

The majority of studies available were case studies, making generalisation to the wider MD population more difficult. Of the MD hydrotherapy studies, six (50.0%) were case studies or series with ≤ 5 participants (Adams et al., 2017; Atamturk & Atamturk, 2018; DiBiasio et al., 2015; Sanders & Torres, 2010; Santos et al., 2016; Silva et al., 2012). Case studies allow for an in-depth exploration of variables for patients in real-life settings, with suggested educational value that contributes to the advancement of medical knowledge (Sayre et al., 2017). However, case studies and series have been described as weaker designs among the hierarchy of evidence-based practice (Murad et al., 2016), often used to inform evidence-based practice in physiotherapy (Hoffmann et al., 2013). The lack of control groups, mean causal effects cannot be confirmed between hydrotherapy and improvements in function (Sayre et al., 2017). Although it cannot be confirmed that these case studies were planned, several studies did report difficulty with recruitment and attendance of their intervention sessions

(Abo-zaid et al., 2021; Hind et al., 2017). Thus, caution must be used with the results from these studies due to the individuality amongst people with MD, making it harder for generalisation between the types of MD and individuals. Alongside individuality, it is important to consider the age of onset, muscles affected, progression rate and severity that differentiate types of MD (Huml, 2015; Mercuri & Muntoni, 2013), as it may affect the outcome measures chosen or the age group chosen in the design of the study.

2.4.4 Considerations of Participation

The uptake in adherence to participation in available management interventions and/or research projects has been a common problem throughout MD research (Abo-zaid et al., 2021; Matthews et al., 2021). This is consistent with low recruitment and attendance rates in hydrotherapy research for MD (Hind et al., 2017). There is a greater challenge in recruiting and retaining individuals with rare diseases, such as MD, because of the smaller clinical population, complexity and burden of the disease, and commitment required in planning, understanding, and support from families, practitioners, and the community (Bendixen et al., 2016). Thus, identifying barriers and motivators was suggested in previous research to justify the use of hydrotherapy (Hind et al., 2017).

Participation in physical activity is important yet significantly reduced in children with MD compared to their healthy peers (Bendixen et al., 2014). There are an abundance of themes, barriers, and motivators for participation amongst children with neuromuscular diseases, including those children and adolescents with MD (Shields et al., 2012). Understanding the facilitators and barriers to participation is "essential for the design and implementation of effective interventions and strategies" (Shields & Synnot, 2016). If individuals do not want to attend intervention sessions, then potential funding, efforts and/or time into planning sessions may be wasted. Whereas, if there are external factors stopping individuals who would like to attend, then identifying and addressing these solutions can be made possible, optimising participation rates (Peay et al., 2018). Despite the

importance of identifying barriers and facilitators to participation in MD, existing research has only investigated neuromuscular diseases as a group for physical activity and clinical trial participation (Peay et al., 2018) or in cerebral palsy (Abid et al., 2022).

Research found that barriers and motivators to participation are person-specific, with children focusing on personal factors and parents focusing on policy and programme, familial or social factors (Shields et al., 2012). Motivations from parents' perspective mostly surrounded "hope for significant improvement in strength, endurance, school performance, and/or QoL" (Peay et al., 2014). This was supported by parents reporting improvements surrounding their child needs, such as in improved motor skills, confidence (Brown et al., 2022), altruism and the potential for better care (Peay et al., 2018), as motivators for participation. Several studies have identified parental perspectives as being essential for enhancing attendance and participation rate in children (Brown et al., 2022). Therefore, further understanding of possible facilitators and barriers for children and adolescents with MD from the perspective of parents may contribute to the effective implementation of hydrotherapy and additional interventions in future studies. Notably, barriers to participation are more predominantly studied compared to facilitators (Shields et al., 2012), thus research should investigate both variables as both are influential on participation for children.

Personal, social, environmental, and policy and programme factors are commonly reported forms of barriers and motivators in childhood-onset of physical disabilities (Mckenzie et al., 2021; Shields et al., 2012). The use of these factors is consistent with the Physical Activity for people with a Disability model (PAD-model) for understanding limitations to participation in physical activities (Buffart et al., 2009; van der Ploeg et al., 2004). Within this model, it is an individuals' intention that influences the personal and environmental factors (Abid et al., 2022), which with self-efficacy and health conditions, then influence physical activity behaviour (van der Ploeg et al., 2004). Alternatively, the social cognitive theory (SCT) model explains that personal and environmental

factors influence behaviour (Brown et al., 2022). Based on the SCT, if individuals feel in control of their behaviour, can cope with the demands, and have self-regulatory strategies then people are likely to continue being motivated to participate in sporting activities and therapy interventions (Mailey et al., 2016). Both models have been used as a framework for exploring factors that facilitate or hinder participation (Abid et al., 2022; Brown et al., 2022). Therefore, the use of the models should be considered to assist with the exploration of barrier and motivators to participation.

2.5 Summary

All forms of MD cause progressive degeneration and weakness, that results in the deterioration of function in multiple systems, such as the cardiorespiratory, musculoskeletal, gastrointestinal, neurological, and psychological systems (Birnkrant et al., 2018a; Birnkrant et al., 2018b; Birnkrant et al., 2018c). Although advancements in treatments have occurred, there is still no cure for MD (Lombardo et al., 2021; Manzur & Muntoni, 2009); therefore, effective management is important to maintain function and slow down the progression of MD. The use of hydrotherapy has been recommended within guidelines for the management of MD (Lombardo et al., 2021). Reasons for its use are attributed to the effects that buoyancy, drag, viscosity, and hydrostatic pressure can have on physical, physiological, and psychological functioning (An et al., 2019). However, several gaps in knowledge surrounding the use of hydrotherapy for MD were identified throughout Chapter 2.

The design of previous studies indicates some considerations for the present study. A lack of long-term studies exist, meaning it is unknown whether the progression of psychological, respiratory, and biomechanical consequences of MD are delayed after the addition of hydrotherapy in studies that last over three months. Multiple time points should be considered throughout a period of longitudinal research to identify whether any effects plateau after a certain length of time. Additionally, the inclusion criteria within hydrotherapy research largely included ambulant individuals, despite the

potential benefit of buoyancy allowing for non-ambulant individuals to be more independent. Furthermore, muscle strength has not been widely used as outcome measures in studies on hydrotherapy for MD, while diaphragm thickness has not been used. Thus, incorporating these outcome measures, a longer study durations and multiple time points, may assist with a more effective study design towards providing further insight in the effectiveness of hydrotherapy.

Broadly speaking, this thesis sought to answer two questions, 1) Does hydrotherapy contribute to delaying the progression of muscle weakness, declining respiratory function, and declining wellbeing in children and adolescents with MD? and, 2) What are the barriers and motivators to hydrotherapy participation in children and adolescents with MD? Low recruitment and attendance rates in physical activity and clinical trial participation were found as a gap within previous research within Chapter 2 and our first study reinforced this finding. Therefore, an overall sequential research design was conducted, in which to gain further insight and understanding into the results of Study 1, a second study was designed and completed.

In summary, Chapter 1.0 outlined the justification for investigating the effects of hydrotherapy within the MD paediatric population. It highlighted the need for longitudinal research to understand whether hydrotherapy can contribute to delaying MD progression, due to a lack of knowledge and no existing recommendations within NHS NICE guidelines. Chapter 2.0 explored the background of MD, including the aetiology, prevalence, clinical presentation, and available treatments, as well as provided an analysis of the current gaps within literature, providing direction to Study 1 and Study 2. Chapter 3.0 to Chapter 5.0 comprises of part 1 to the thesis, *'The effects of hydrotherapy on respiratory function, strength, and wellbeing in children and adolescents with Muscular Dystrophy'*. Chapter 6.0 to Chapter 8.0 comprises of part 2 to the thesis, *'An investigation into barriers and motivators that may affect participation in hydrotherapy for children and adolescents with Muscular*

Dystrophy'. Finally, Chapter 9.0 draws both studies together and provides a summary of the overall thesis, highlighting the implications for future research.

Study 1

Existing research specific to hydrotherapy for MD is limited and results are often contradicting, with little research on long-term effects. Contradictions can be attributed to no existing set definition or outcomes to assess the improvements or maintenance for MD. To understand whether hydrotherapy can contribute to a delay in MD disease progression, it is necessary to monitor common symptoms that can be present in each form of MD. However, as explored in Chapter 2.0, it is not feasible to monitor all possible symptoms and consequences associated with MD throughout treatments, due to the multi-systemic nature of MD, individuality in clinical presentations, and continued worsening of symptoms (Birnkrant et al., 2018a; Birnkrant et al., 2018b; Ohlendieck & Swandulla, 2021; Tsuda, 2018). Therefore, Chapter 3.0 explores the justification of the chosen measures that captured respiratory, biomechanical, and psychological function, as well as aiming to address the gaps in current knowledge, as previously highlighted.

The aims of Study 1 were to answer the following questions:

1) Is there an effect after 40-weeks of hydrotherapy on biceps and quadriceps muscle strength in children and adolescents with MD?
2) Is there an effect after 40-weeks of hydrotherapy on physical, social, and mental wellbeing in children and adolescents with MD?
3) Is there an effect after 40-weeks of hydrotherapy on MIP, MEP, and diaphragm thickness in children and adolescents with MD?

Chapter 3.0: Methodology

3.1 Participants

Six males with MD, aged 11.2 ± 2.9 years, were recruited for the study. Out of the six participants, two rejected participating in the study prior to baseline testing, one withdrew post-baseline testing, and one was excluded from analysis despite participating in the study. Reasons for rejecting and withdrawing from the study included ongoing surgery and recurrent illness of the child preventing the ability to commit to hydrotherapy sessions, the child not wanting to complete group sessions with younger children and/or the child being unmotivated to attend sessions. The participant that was excluded had missing data and a low attendance rate. The participants all met the following inclusion criteria:

- Be a male or female between the ages of 5-to-17-years-old.
- Have been diagnosed with Becker, Congenital, Distal, Duchenne, Emery-Dreifuss, Facioscapulohumeral, Limb-Girdle, Myotonic, or Oculopharyngeal MD for at least three months (with diagnosis confirmed by the Physiotherapist at the Chamwell Centre).
- Be able to travel to the Chamwell Centre within the Gloucestershire area.

The participants were aged 8 and 11 at the start of the study, and suffered from Duchenne MD. Both males were at a different stage of disease progression, with the younger participant being ambulant and the older participant being non-ambulant. Throughout this study the ambulant participant began to use a wheelchair to assist in completing longer land-based activities. Physical activity levels also varied among participants, ranging from one regularly participating in sports to one not participating in any other exercises (except for any prescribed from their physiotherapist). Additionally, it was reported that the participants suffered from anxiety, and one was on the autism spectrum. All participants continued with their usual care throughout the duration of the study, due to ethical reasons, and had not received hydrotherapy for at least 18 months (due to the COVID-19 pandemic).

Participants were excluded from the study if they had one or more of the following:

- Could not be given written consent from a parent or guardian.
- Could not understand information sheets in English or adhere to study protocol.
- Violate hydrotherapy contraindications, where absolute contraindications are present, or participants are advised not to take part by their physiotherapist or the physiotherapist at the Chamwell Centre due to precautions flagged up.
- Had any serious health conditions or comorbidities unrelated to a form of MD, which may influence study outcomes (Huguet-Rodríguez et al., 2020).
- Are currently or have recently (within the last six months) been part of another study.

3.2 Recruitment

The study was completed in collaboration with the Chamwell Centre. During the COVID-19 pandemic, hydrotherapy sessions for multiple clinical populations were stopped, and only began to reopen in 2021. The Chamwell Centre opened and began putting in place hydrotherapy sessions for these clinical populations, including MD. Individuals with MD were made aware of and able to enquire about hydrotherapy sessions through local physiotherapists, paediatricians, neuromuscular advisors and in few cases through self-referral. Prior to joining any sessions, individuals were assessed by physiotherapists at the centre.

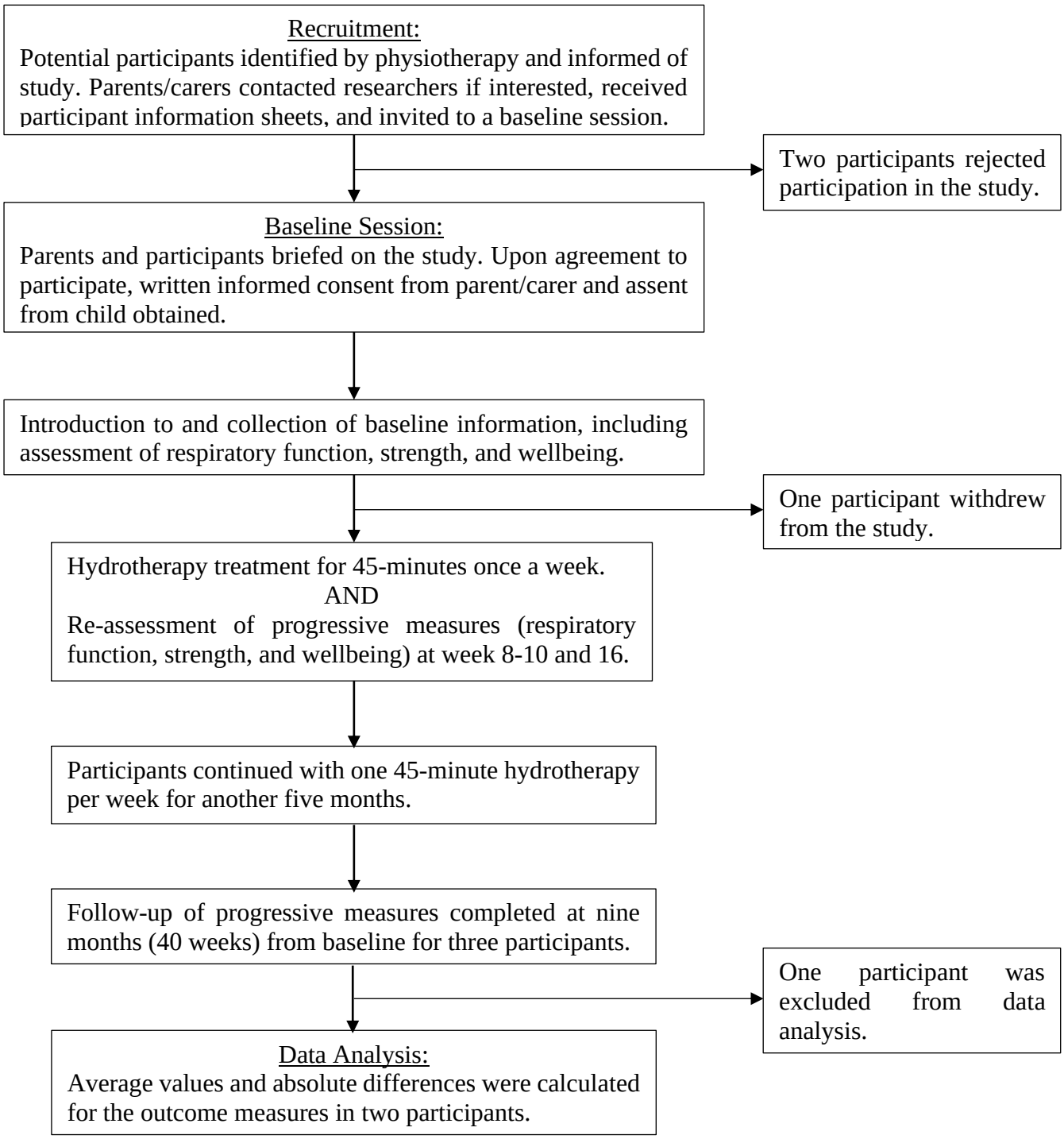
Participant recruitment was completed by the Physiotherapist in charge of MD hydrotherapy at the centre who identified potential participants and informed them of the study. If interested, parents and/or carers of these potential participants contacted the research team who provided them with participant information sheets. If interest was still shown, the parents/carers and their child were then invited to a baseline session with the researchers.

3.3 Study Overview

Ethical approval was granted from the University of Gloucestershire Research Ethics Committee (REC.18.85.8, see Appendix A). Participants and their parents and/or carers attended a baseline session, where they were briefed on the study requirements and written informed consent from the participants' parent was obtained upon agreement to participate (see Appendix B and Appendix C). Information regarding the participants' type of MD and their age was collected, however anthropometric measurements of height and weight were not taken due to a participant being non-ambulant. Participants were then introduced to the outcome measures to be collected that monitored progression, described in '*3.4 Study Procedure*'. These outcome measures were collected at baseline (week 0), week 8-10, and week 16, and during a follow-up at week 40. An outline of the study can be seen in Figure 3.

Figure 3

Flowchart Illustrating an Overview of Study 1



Participants were offered 45-minute hydrotherapy sessions once a week over a nine-month period. However, several complications limited this to a total of 28 out of 40 sessions available, equating to a little over six months of hydrotherapy over the nine months. These complications

consisted of three public holidays, five separate weeks of staff illness (COVID-19) and chlorine or pH concentrations being too high or low in the pool preventing its use. Researchers were not involved in carrying out hydrotherapy sessions but assessed its potential benefits. The hydrotherapy sessions were provided by the Chamwell Centre and conducted by a physiotherapist, trained in aquatic physiotherapy by the Aquatic Therapy Association of Chartered Physiotherapists, with prior experience in MD. The sessions were funded for by Muscular Dystrophy UK.

3.4 Study Procedure

All measures were taken at the Chamwell Centre by the same researcher, with each data collection session lasting between 30 to 40 minutes. Prior to each session, the outcome measures were explained to the participants and verbal assent was obtained. At week 0, 8-10, 16 and 40, the following outcome measures were taken:

3.4.1 Respiratory Function

1. Diaphragm Thickness was assessed using 2-Dimentional (2D) ultrasonography (uSmart 3300, Ultrasound system, Terason, Burlington, MA, USA), which provides non-invasive and time-efficient imaging through sound waves travelling from a transducer (Fayssoil et al., 2018). Measuring diaphragm thickness using an ultrasound has been suggested as an assessment of respiratory function for MD (LoMauro et al., 2015), but it has not yet been validated in MD (Laviola et al., 2018). However, it has been validated in individuals with cervical spinal cord injury (Zhu et al., 2021) and in the supine position (Baldwin et al., 2011). Caution must be used with thickness measures as an increase in diaphragm thickness does not always equate to increased respiratory function, but could indicate excess fat or collagenous tissue, known as pseudohypertrophy (Laviola et al., 2018). Additionally, a study concluded that 2D ultrasonography had excellent specificity and sensitivity and was feasible and reliable for diagnosing neuromuscular diaphragm dysfunction (Boon et al., 2014). Prior to the participants' arrival, the machine setting was inputted and a frequency of approximately

17 MHz was chosen. The participants were placed in a supine position, because it was found to result in less overall variability and greater reproducibility (Intraclass Correlation Coefficient (ICC) = 0.93, 95% CI [0.75, 0.98]) (Zhu et al., 2021), be the best posture to show diaphragmatic impairment and it was not practicable to hold the probe perpendicular to the chest wall in seated positions (Laviola et al., 2018). Ambulant participants laid supine on a plinth, however the non-ambulant participant opted to recline their wheelchair back to a nearly supine position, due to the time of transfer that would be required and their comfort. Ultrasound gel was placed on the transducer probe, which was then placed in the zone of apposition along the anterior axillary line between the 7^{th} and 9^{th} intercostal space. Participants were instructed to take a deep breath in and out, while a few recordings using the software on the ultrasonography system was completed. The recordings were viewed and three different measures along the diaphragm, between the diaphragmatic pleura and peritoneal membrane, was recorded and the average taken. These measures were taken at the end of inspiration at tidal volume (*and end of expiration at functional residual capacity*).

2. Respiratory Muscle Strength, using static MIP and MEP, was measured using a respiratory pressure meter (MicroRPM, Micro Medical, Kent, United Kingdom). They have been suggested as an assessment of respiratory function according to guidelines for respiratory management in children with neuromuscular weakness, including MD (Hull et al., 2012), in which MIP and MEP "measures at the mouth provide a global index of inspiratory and expiratory muscle strength, respectively" (LoMauro et al., 2015). The MicroRMP respiratory pressure meter has also been found to reliably measure MIP and MEP in a seated position in healthy individuals (ICC = 0.86 – 0.90) (Dimitriadis et al., 2011). Measures were completed in a seated and upright position either on a chair or wheelchair. Whilst some studies indicated that MEP and MIP may differ between body positions, the American Thoracic Society guidelines and research state that standing or seated positions can be used, with seated (on a chair or wheelchair with backrest at 90°) being better for safety reasons and comfort (Katz et al., 2018). Participants practiced forcefully breathing out and in

while the mouthpiece was not connected to the machine, being instructed to keep their lips around the mouthpiece to create a 'seal'. The mouthpiece was then connected to the machine. To collect MEP, the researcher stood behind the seated participant with their hands placed on the individual's cheeks. The participant was then told to breathe out forcefully as the researcher applied a gentle force on their cheeks to assist. To collect MIP, participants were asked to forcefully breath in as if sucking through a straw. Both measures were repeated three times and the average was taken.

3.4.2 Biomechanical Function

1. Bicep and Quadricep Strength was collected using a hand-held dynamometer (Lafayette Manual Muscle Test (MMT) System 01165: Lafayette, Indiana, USA). Assessing isometric upper-limb and lower-limb strength, in healthy 4-17-year-olds, using hand-held dynamometry was moderately to greatly reliable (ICC = 0.82 to 0.98 and ICC = 0.67 to 0.98, respectively) and valid (ICC = 0.78 to 0.94 and ICC = 0.48 to 0.93, respectively) (Hébert et al., 2011). Hand-held dynamometry was previously used in the assessment of MD (Lu & Lue, 2012). In 4-14-year-olds with Duchenne and Becker MD, hand-held dynamometry was moderately to greatly reliable for measuring lower-limb (ankle, knee, and hip) strength, where ICC was 0.69 to 0.94 and inter-tester ICC was 0.76 to 0.98 (Shi et al., 2015). This is supported by Knak et al. (2020) who found good to great inter-rater reliability in adults with myotonic MD (ICC = 0.88 to 0.97) and Brussock et al. (1992) who found great test-retest and inter-tester reliability in 6-14-year-olds with Duchenne MD (ICC = 0.90 to 0.99). Hand-held dynamometry was also found to have good to great reliability for measuring upper-limb strength in 6-14-year-olds with Duchenne MD (ICC 0.74 to 0.98) (Brussock et al., 1992) and 10-32-year-old males with Duchenne MD (ICC 0.87 to 0.97) (Connolly et al., 2015). Although the muscles affected differs between types of MD and stages of progression (National Institute of Neurological Disorders and Stroke, 2013), proximal muscles such as the biceps and quadriceps are affected at some point in most MD types and are needed in many activities of daily life. Participants were seated or remained in their wheelchair (with footrest and armrests moved to the side). To collect

bicep strength, participants bent their elbow to 90°, keeping their elbow to their side. The researcher stabilised the top of the shoulder with one hand and with the other held the hand-held dynamometer against the participants' wrist. Participants were instructed to push against the dynamometer as hard as they can for a few seconds, before being told to relax. The researcher resisted this maximal contraction, i.e., the make method, as research found this to be the best method for MD when using hand-held dynamometry (Lu & Lue, 2012). This was repeated three times. To collect quadricep (group) strength, participants remained seated with their feet not touching the floor and their knees bent to 90°. The researcher used one hand to stabilise above the participants' knee and with the other held the dynamometer against their shin. The participant was then instructed to 'kick' their leg forward against the dynamometer as hard as they can for a few seconds, before being told to relax. This was repeated three times.

3.4.3 Health-Related Quality of Life

1. The NPC's Wellbeing Measure (Level 2) is a shorted questionnaire that measures the well-being of young people with special educational needs, suitable for individuals aged 7-16 with medium-to-complex needs (Sabri et al., 2015). It consists of 14 questions that covers self-esteem, resilience, emotional wellbeing, relationships with friends and family, school, and overall life satisfaction. These questions are based on Marsh's self-description questionnaire, Wagnild and Young's resilience scale, Goodman's strength and difficulties questionnaire, Huebner's multidimensional life satisfaction score, and Cantrill's Ladder (0-10 scale, where 0 is not happy at all and 10 is happy). Since participant may also experience psychological, behavioural, and neurodevelopmental problems alongside different types of MD (Ferrero & Rossi, 2022; Ricotti et al., 2016), the NPC's questionnaire was chosen as it may be easily understood by more children and adolescents. Participants were asked to complete the questionnaire, but parents were able to explain the questions if required to.

3.5 Data Analysis

The results in muscle strength and respiratory function for each individual was input into an excel spreadsheet, and the average value for each individual was calculated. The scores of the NPC's Wellbeing Measure were calculated using the provided scoring system for each questionnaire that formed the measure, Marsh's self-description questionnaire, Wagnild and Young's resilience scale, Goodman's strength and difficulties questionnaire, Huebner's multidimensional life satisfaction score, and Cantrill's Ladder (Sabri et al., 2015). Based on these, higher scores indicated greater levels of wellbeing. All outcomes of strength, wellbeing, and respiratory function were presented in line graphs to demonstrate the change in participants' results over 40 weeks of hydrotherapy. Percentage change for each outcome measure between week 0, week 8-10, week 16, and week 40 were also calculated (see Appendix D). Finally, attendance rates were calculated for hydrotherapy sessions throughout the 40-week study duration for each participant.

Chapter 4.0: Results

4.1 Muscle Strength

4.1.1 Participant 1

As presented in Figure 4a, an overall 40.1 N decrease in biceps strength from baseline to week 40 was found in Participant 1. Biceps strength decreased from baseline to week 8-10 (-28.5 N) and from week 16 to week 40 (-33.7 N). Whilst an increase in biceps strength from week 8-10 to week 16 was found (22.1 N), this remained lower than baseline.

As presented in Figure 4b, an overall 33.0 N increase in quadriceps strength from baseline to week 40 was found in Participant 1. Quadriceps strength increased from baseline to week 8-10 (38.5 N), however decreased from week 8-10 to week 16 by 9.1 N. An increase in quadriceps strength from week 16 to week 40 was found (3.6 N), which was greater than baseline but remained lower than week 8-10.

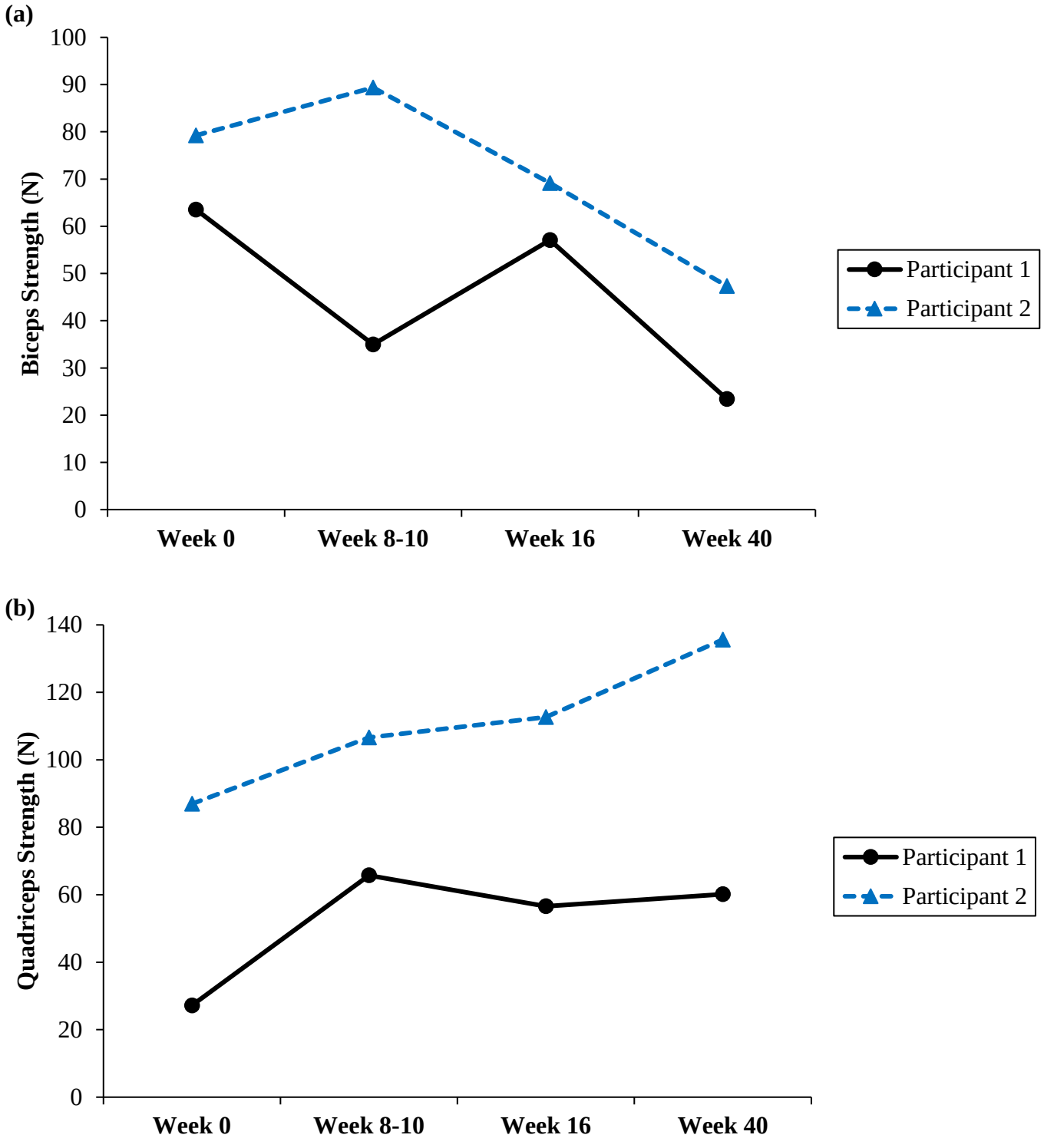
4.1.2 Participant 2

As presented in Figure 4a, an overall 32.0 N decrease in biceps strength from baseline to week 40 was found in Participant 2. Whist an increase was found from baseline to week 8-10 (10.1 N), biceps strength decreased from week 8-10 to week 16 (20.3 N), and further decreased at week 40 (21.8 N).

As presented in Figure 4b, an overall 48.6 N increase in quadriceps strength from baseline to week 40 in Participant 2. Compared to baseline, quadriceps strength increased by 19.6 N at week 8-10 and further increased by 6.0 N at week 16.

Figure 4

Changes in Muscle Strength over 40 Weeks for Each Participant



Note. These figures demonstrate the difference in change in (a) Biceps Strength and (b) Quadriceps Strength over 40 weeks of hydrotherapy for each individual participant.

4.2 Respiratory Function

4.2.1 Participant 1

As presented in Figure 5a, an overall 4.5 cm H_2O decrease in MIP from baseline to week 40 was found in Participant 1. Whilst an increase was found from baseline to week 8-10 (14.3 cm H_2O), MIP decreased from week 8-10 to week 16 (3.0 cm H_2O) and further decreased at week 40 (15.8 cm H_2O).

As presented in Figure 5b, an overall 0.4 cm H_2O increase in MEP from baseline to week 40 was found in Participant 1. MEP increased from baseline to week 8-10 (18.3 cm H_2O). MEP then decreased at week 16 (-12.0 cm H_2O) and further decreased at week 40 (-6.0 cm H_2O), however this remained greater than baseline.

As presented in Figure 5c, overall diaphragm thickness in Participant 1 remained similar from baseline to week 40 (-0.01 cm). Diaphragm thickness increased from baseline to week 8-10 (0.11 cm) and remained the same at week 16, before decreasing from week 16 to week 40 (-0.12 cm).

4.2.2 Participant 2

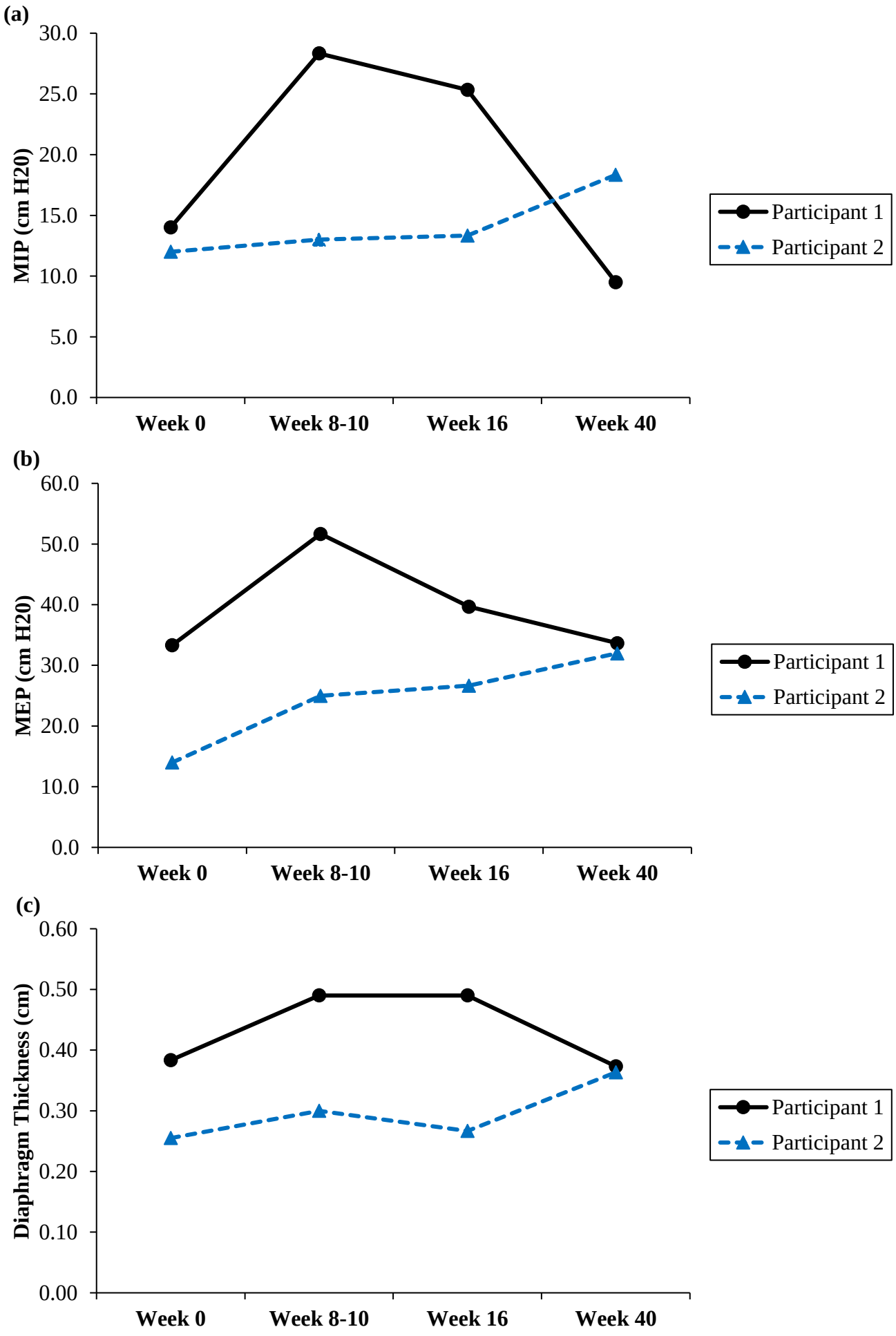
As presented in Figure 5a, an overall 6.3 cm H_2O increase in MIP from baseline to week 40 was found in Participant 2. MIP increased from baseline to week 8-10 by 1.0 cm H_2O and further increased at week 16 (0.3 cm H_2O) and week 40 (5.0 cm H_2O).

As presented in Figure 5b, an overall 18.0 cm H_2O increase in MEP from baseline to week 40 was found in Participant 2. MEP increased from baseline to week 8-10 by 11.0 cm H_2O and further increased at week 16 (1.7 cm H_2O) and week 40 (5.3 cm H_2O).

As presented in Figure 5c, an overall 0.10 cm increase in diaphragm thickness from baseline to week 40 was found in Participant 2. Diaphragm thickness increased from baseline to week 8-10 (0.04 cm) and from week 16 to week 40 (0.09 cm). Whilst a decrease was found from week 8-10 to week 16 (-0.03 cm), this remained greater than baseline.

Figure 5

Changes in Respiratory Function over 40 Weeks for Each Participant



Note. These figures demonstrate the difference in change in (a) MIP, (b) MEP, and (c) diaphragm thickness between each individual participant over 40 weeks of hydrotherapy. MEP = maximal expiratory pressure; MIP = maximal inspiratory.

4.3 Health-Related Quality of Life

4.3.1 Participant 1

As presented in Figure 6, the Wellbeing Measure score decreased from baseline to week 40 in Participant 1 by 4.0. The Wellbeing Measure score remained the same at week 8-10, however decreased by a score of 23.0 at week 16. Whilst the score then increased from week 16 to week 40 by 19.0, this remained lower than baseline.

At the end of the NPC's Wellbeing Measure, when prompted by the question "Is there anything else you'd like to say?", Participant 1 reported feeling "tired" and "struggling at school" at week 16 but left no other comments at the other data collection points.

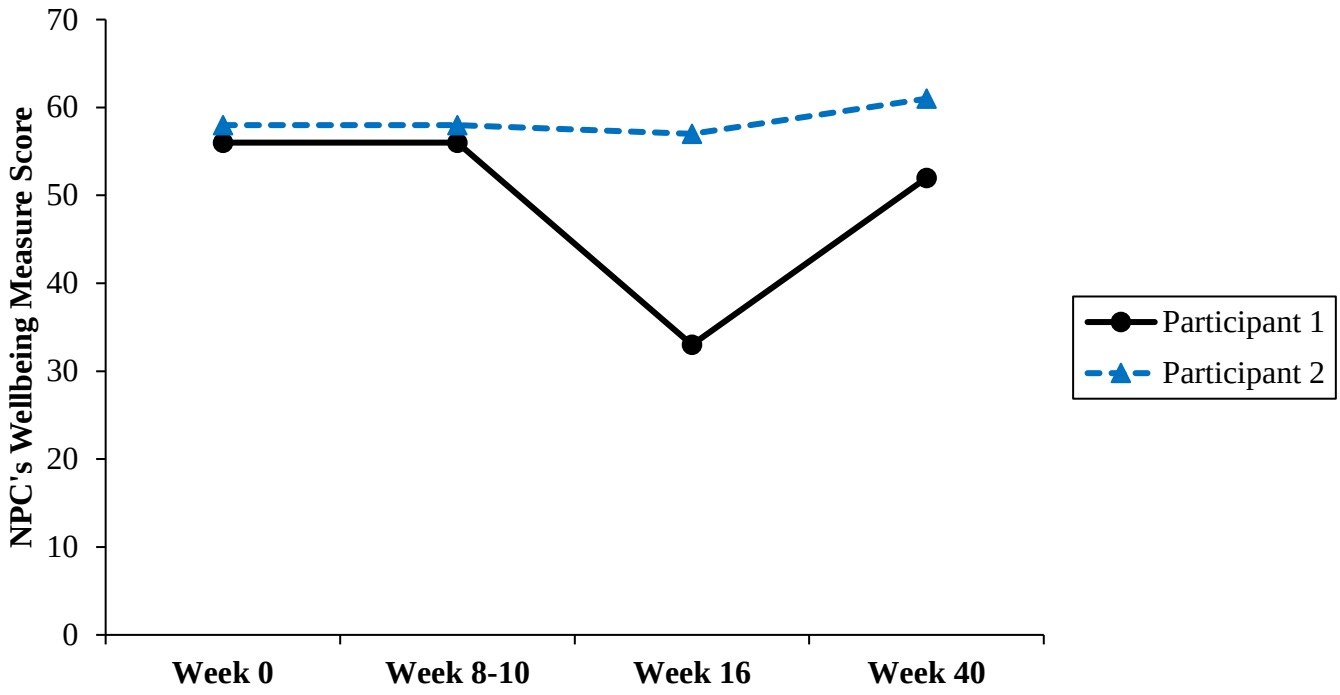
4.3.2 Participant 2

As presented in Figure 6, the Wellbeing Measure score increased from baseline to week 40 in Participant 2 by 3.0. The Wellbeing Measure score remained the same at week 8-10, however decreased by a score of 1.0 at week 16, before increasing by a score of 4.0 from week 16 to week 40.

At the end of the NPC's Wellbeing Measure, when prompted by the question "Is there anything else you'd like to say?", Participant 2 reported the following: "I like helping other people" at baseline and "Both legs can be stiff and have pains now and then" at week 16.

Figure 6

Changes in NPC's Wellbeing Scores over 40 Weeks for Each Participant



Note. This figure demonstrates the difference in change in Wellbeing Scores for each individual participant over 40 weeks of hydrotherapy. NPC = New Philanthropy Capital.

4.4 Attendance

Participant 2 attended a greater number of hydrotherapy sessions (89.3%) compared to Participant 1 (67.9%), as shown in Table 1.

Table 1

Participant Attendance Throughout the 40-Week Study Duration

	Overall		Week 0 to Week 16		Week 17 to Week 40	
	***n* (/28)**	**%**	***n* (/12)**	**%**	***n* (/16)**	**%**
Participant 1	19	67.9	11	91.7	8	50.5
Participant 2	25	89.3	10	83.3	15	93.8

Chapter 5.0: Discussion

The purpose of this study was to investigate the effects of hydrotherapy on respiratory function, muscle strength and wellbeing in children and adolescents with MD. The main findings of this study were that 1) recruitment and participation rates were poor, 2) mean quadriceps strength and MEP measure exceeded baseline measures at two, four and nine months of hydrotherapy, 3) mean biceps strength was greatest at baseline (with the exception of week 8-10 for Participant 2), 4) mean MIP, diaphragm thickness and wellbeing scores in Participant 1 remained similar after nine months, and 5) mean MIP, diaphragm thickness and wellbeing scores in Participant 2 increased after nine months.

5.1 Strengths and Limitations

MD is a limited and difficult research area because of the small population that suffers with this rare disease. Several short-term studies investigating hydrotherapy for MD are available, however they lack any useful longitudinal data (Adams et al., 2017; Santos et al., 2016; Silva et al., 2012). The few long-term studies that are available only report results from one outcome and/or report subjective findings (Ferreira et al., 2015; Honório et al., 2013; Sanders & Torres, 2010; Voos et al., 2020). We were the first study to objectively monitor the effects of 40 weeks of hydrotherapy on respiratory function, muscle strength and wellbeing within a single study. Additionally, most studies investigating hydrotherapy in MD are case studies (Santos et al., 2016; Silva et al., 2012), with only one study being a feasibility randomised-controlled trial (Hind et al., 2017). This was no different from our current study design being that of a case study. Despite our attempt to progress from a case study to group intervention, this was not feasible with the exclusion of data from the third child who participated in the study, as well as the small sample size after recruitment. To fully understand the findings of the present study, it is important to highlight the strengths and limitations.

Firstly, Laviola et al. (2018) suggests progressive diaphragm measurements should be considered as an outcome measure for monitoring the effects of interventions on respiratory function in MD because weakness of this muscle can cause respiratory failure. As of yet, this has never been monitored during interventions for MD; we were the first to include diaphragm thickness measurements in a hydrotherapy interventions study. However, there were some weaknesses. In one participant diaphragm thickness was measured while they remained in their wheelchair, due to equipment and manual handling constraints, which despite being able to recline the chair slightly, the chair was still in the way of the probe. This went against the recommended supine position for those with cervical spinal cord injuries (Zhu et al., 2021), however this same position was used for this participant across all timepoints of data collection. This systematic error may have affected the internal validity of their results. To effectively gain results, participants may need to be transferred to a plinth in future studies, different positions for measuring diaphragm thickness in MD should be investigated and validated. Additionally, one participant was self-conscious of their body and in one assessment did not want to lift his top, so the placement of the probe was limited because the probe had to be placed under the top. Nonetheless, measures of diaphragm thickness were still important to collect.

Secondly, many studies investigating hydrotherapy for MD struggled with recruitment (Abo-zaid et al., 2021; Hind et al., 2017), which was no different from the present study. Only data from two participants who completed the study could be used, and this therefore limited our ability to complete more complex statistical analysis and generalise results to the wider MD population. This was further hampered by the restrictions surrounding COVID-19, whereby NHS hydrotherapy services were still limited and not being offered to patients with MD at the start of the study. However, the data remains a useful insight into the effects of hydrotherapy on respiratory function, muscle strength and wellbeing in children with MD, as well as providing guidance for future studies.

As it's known that MD is a difficult group to recruit from, we needed to include all recruited participants in the hydrotherapy intervention group, due to the small sample size. Unfortunately, with the exclusion of one participant's findings, this meant that the study was treated as a case study and so had no control group, meaning we could not compare changes in data over time relative to whether there had been no intervention at all. Usual care was continued during the study due to ethical reasoning and to reflect everyday life, but without a control group we cannot be certain of the form of care that caused the results; further highlighting the need for a control group. Additionally, without further statistical analysis, we cannot be certain of any trends or patterns in results, further highlighting the need for a greater sample size. Therefore, our research questions could not be answered with certainty.

Thirdly, recent guidelines stated that the water temperature of hydrotherapy pools should aim to be kept within a thermoneutral range between 34.0°C – 35.5 °C (optimal range) to allow for the therapeutic effects to take place, although it can range between 32.0°C – 35.5°C (Pattman et al., 2021). Remaining within the thermoneutral range means that an individual's normal core body temperature can maintained, often for up to an hour (Bieuzen, 2013). However, during the first few weeks of the present study, the water temperature was lower ranging from 30.0°C to 33.0°C, due to an issue with the temperature controls. Although this was promptly fixed, this slightly lower temperature would have meant that it would have been more likely for children with MD to have over-cooled during these sessions, increasing their susceptibility to increased tone, thus preventing relaxation and improved circulation of the body (Carerea & Orr, 2016). Warm water immersion, especially at thermoneutral range, has physiological changes such as increased vasodilation of peripheral blood vessels, blood flow, and oxygen carrying capacity, that when combined with hydrostatic pressure reduces pain and muscle spasm (An et al., 2019; Carerea & Orr, 2016). Therefore, results produced from the first few weeks of the present study may be sightly incorrect,

highlighting the importance of monitoring the temperature at each session throughout a study. Additionally, not all studies surrounding hydrotherapy for MD reported their temperatures (Atamturk & Atamturk, 2018; Huguet-Rodríguez et al., 2020), with other temperatures varying between 32.8°C (Adams et al., 2016) and 36.0°C (Hind et al., 2017), so it cannot be determined whether discrepancies between these findings occurred as a result of these higher or lower temperatures. Future studies should consider reporting these results to allow for a comparison of results and identification of patterns in temperatures and effects.

Finally, there was a lack of standardisation during the measurements of muscle strength during the study. Participants were instructed to 'kick' (for quadriceps strength) and 'push' (for biceps strength) against the hand-held dynamometer as hard as they can for a few seconds before relaxing however, there was no set script or specified number of seconds stated out loud to the participants for how long they needed to push or kick for. The standardisation of procedure is important to "reduce the influence of any extraneous variable" and if not achieved can cause results to be unreliable, threatening the validity of the test (Fischer, 2010). Previous research found that when using the hand-held dynamometer, verbal direction significantly increased maximal strength by 5.6 lb (right-sided) and 5.7 lb (left-sided) (Walsh & Potvin, 2019). Although this was used for grip strength in healthy females, this demonstrates how differences in encouragement, verbal cues and/or instructions given during data collection sessions, may lead to different outcomes in strength. Despite the same researcher measuring these outcomes for each participant at each time point, this still may have affected the participants' muscle strength performance, in turn reducing the reliability of these results. Therefore, future studies should ensure there is a set standardisation of instructions for the researcher to relay to participants.

5.2 Attendance and Participation

The present study had difficulty with recruitment, data completeness, and adherence to hydrotherapy sessions, which is consistent with reports from previous studies (Adams et al., 2017; Hind et al., 2017). Unlike the present study, most failed to report their recruitment process, rates of attendance and/or dropout rates (Santos et al., 2016; Silva et al., 2012). Thus, the use of three or less participants within previous studies alongside the present study suggests that few individuals were willing or able to participate in the study.

In the present study, six potential individuals were identified, of which two (33.3%) rejected participation and one (16.7%) dropped out. Issues with recruitment in our study could be attributed to the Physiotherapist finding it hard to recruit and the fact that recruitment was based around one hydrotherapy centre in one location. However, previous studies with larger samples also reported difficulty with recruitment, despite having longer periods for recruitment at multiple centres. In a study by Hind et al. (2017), 70.7% of potential individuals were not interested in participating and 7.7% dropped out. Additionally, further studies found 7.7% (Huguet-Rodríguez et al., 2020) and 4.0% (Abo-zaid et al., 2021) of individuals rejected participation, although both studies had no dropouts. This further suggests that some individuals are not willing to participate in either hydrotherapy sessions and/or research interventions.

Amongst individuals who agreed to participate, attendance in hydrotherapy sessions also varied. In the present study, Participant 1 and 2 attended 67.9% and 89.3% of available hydrotherapy sessions, respectively. The third participant in the study only attended 21.4% of sessions and thus their results were excluded from the data analysis. Reasons given for missed sessions amongst these participants included illness/COVID-19, fatigue, injury, family events, and post-surgery recovery. The variation of attendance amongst individuals with MD is supported by few studies. Attendance was ranged from 50.0% to 100.0% over eight weeks (Adams et al., 2017), between 47.0% and 88.0%

over six months (Hind et al., 2017), and for one individual was 96.2% over eight months of hydrotherapy (DiBiasio et al., 2015). Reduced attendance may have hindered the effectiveness of hydrotherapy for MD, where it is likely that long-term and consistent intervention is needed to combat MD, since it is a chronic and progressive disease. Additionally, the excluded participant only attended two out of four data collection sessions, due to requiring surgery midway through the present study, which would have greatly impacted the analysis of their results if it was included in the study. One study supported the difficulty with data completeness, where not all participants completed all outcomes at each time point (Hind et al., 2017). Missing data can cause issues with the analysis and interpretation of results, such as a reduced statistical power, bias, and reduced representativeness, that can lead to invalid conclusions (Kang, 2013). Thus, attendance in hydrotherapy and data collections sessions are both important. However, due to the nature of MD, in which flare ups of symptoms could occur, it should be considered that missed sessions are likely to occur in future studies, that may need to be accounted for during the design of the study. Future studies are required for a better understanding of why recruitment and participation in children and adolescents with MD is low, which could help inform further discussions surrounding the use hydrotherapy for MD.

5.3 Outcome Measures

5.3.1 Defining a delay in progression

In the present study, the mean MIP, diaphragm thickness, and wellbeing score of Participant 1, and mean biceps strength in both Participant 1 and 2 at week 40 were lower than baseline measures (Figure 4, 5, and 6). Despite these outcomes declining from baseline, this does not indicate that hydrotherapy was ineffective for the management of MD. This is supported by Silva et al. (2012) who concluded that the worsening of outcomes when monitoring the effects of hydrotherapy in MD does not necessarily mean that a negative effect has occurred due to the natural disease progression associated with MD. MD worsens over time and there is no current cure (Duan et al., 2021), so interventions aim to preserve and maintain function (Lombardo et al., 2021) rather than improve

function, meaning that maintaining similar functions would indicate a delay in MD progression. Thus, even if the outcome has a negative change, if this change is less than what would occur during the progression of the disease naturally, it suggests that the intervention or treatment used has contributed to slowing the rate of progression. As previously mentioned, the case study design and lack of control group(s) mean we cannot determine if this does or does not occur with the use of hydrotherapy for delaying respiratory function, wellbeing, and strength in MD.

There is no research available that has defined this delay in progression for MD, making it difficult to establish whether an intervention is effective in maintaining biomechanical, respiratory, or psychological function. Smaller increases and decreases, i.e., less than 30% change (based on Consolaro et al. (2016) for juvenile arthritis), shown in Table 1, could indicate a maintenance of function for that outcome. Based on this, it could be argued that a delay in progression occurred from week 8-10 to week 16 for quadriceps strength, MIP, and MEP in Participant 1 (-13.9%, -10.6%, and -23.2%, respectively) and biceps strength, diaphragm thickness and wellbeing scores for Participant 2 (-22.7%, -10.0%, and -1.7%, respectively). It could also be argued that a delay occurred from baseline week 40 for diaphragm thickness (-2.6%) and wellbeing (-7.1%) in Participant 1 (see Appendix D). Thus, this definition of delayed progression suggests that hydrotherapy may have contributed to the maintenance of respiratory function, mental and physical wellbeing, and muscle strength in these individuals. However, caution must be used with these changes as they are specific to each participant and cannot be used generalised to the wider MD population. In Consolaro et al. (2016), this definition was used in individuals and so it is unknown whether it would be suitable for monitoring group progressions in future research studies that have established control and intervention groups. Additionally, the relative percentage change can be misleading because on small numbers this change can look more significant than it is, as when your initial value gets "smaller and smaller, percentage change gets bigger and bigger" with the opposite true for bigger initial values (Curran-Evertt & Williams, 2015). Thus, caution must also be used when evaluating results using this

method, as if values are taken out of context, the intervention may appear more effective than it is, which could be wrongfully applied to justify its use. Nonetheless, Consolaro et al. (2016)'s definition of less than 30% change could be useful to monitor the progression of physiological, psychological, and biomechanical function in children with MD. However, investigation into other methods that could also define delays in progression is required. Therefore, future research needed to establish a standard definition for maintaining MD progression. This could inform clinical guidelines and would allow for a standardised method that research studies could use, which would also enable easier comparisons between studies that is applicable to usual care.

Additionally, there are no set core outcomes to monitor disease progression, unlike other clinical populations, such as juvenile arthritis (Consolaro et al., 2016), meaning comparisons between studies becomes harder due to the multiple outcomes being used in different studies. Previous research has also indicated the lack of core measures available for MD (Bushby & Connor, 2011; Lombardo et al., 2021), with different measures often being used based on the type or stage of progression for MD. Thus, as well as a definition of maintenance to fully determine a delay in progression, it may be beneficial for future studies to investigate potential core outcomes that can be used when assessing the effectiveness of clinical interventions for all types of MD.

5.3.2 Muscle Strength

Monitoring muscle strength in individuals with MD is essential as muscle weakness is the main complication in all types of MD (Theadom et al., 2014). Management programmes should be aiming to optimise and/or maintain muscle strength (Lombardo et al., 2021). Few studies have monitored changes in muscle strength (via dynamometer) during hydrotherapy intervention, with only one longer-term study (32 weeks) having monitored lower-limb strength in children with MD (DiBiasio et al., 2015). Thus, when comparing previous studies to the present study caution must be

taken as changes found in the shorter time periods cannot identify or predict patterns of change beyond their study duration, i.e., support the patterns found over 40 weeks of hydrotherapy.

The suggested improvements in mean quadriceps strength for Participant 1 and Participant 2 after 16 weeks (29.4 N and 25.6 N, respectively) and 40 weeks (33.0 N and 48.6 N, respectively) of hydrotherapy within the present study could be attributed to the higher viscosity of water causing a resistance against movements in water, that encourages muscles to work harder, and thus increasing strength (An et al., 2019). Based on Bernoulli's principle moving faster through water increases turbulence behind the body, which increases resistance to forward movements, due to moving from positive pressure to negative pressure within the water (Wratten et al., 2019). This in turn allows the body to experience a drag force that, when increasing the surface area of the limb with additional equipment or moving through the water with more force, offers more resistance, allowing the enhanced control of muscle strengthening (Becker, 2011; McIntyre, 2017). Our study was consistent with DiBiasio et al. (2015) who found 84.0% of combined lower-limb muscle strength in a 12-year-old female with limb-girdle MD type 2 was maintained after 32 weeks of hydrotherapy. This was supported by self-reported increases in lower-limb strength after receiving 16 weeks of hydrotherapy and land-based session in a 35-year-old female with congenital MD (Sanders & Torres, 2010). This was attributed to the water properties within hydrotherapy, due to increases in muscle strength being diminished once hydrotherapy was stopped, however hydrotherapy cannot be confirmed as the cause since there was no control group in Sanders and Torres (2010). Additionally, quadriceps strength, measured by grades on the Medical Research Council Scale, remained the same after six weeks (12 sessions) of hydrotherapy, while hamstrings, gluteal, iliopsoas, and hip adductor strength increased by one (Luz et al., 2021). However, compared to the present study, the use of a scale has poor functional relevance, is unable to quantify strength, and the grade difference are non-linearity, making it is important for future studies to assess which outcome measure for strength would be most beneficial for monitoring progression. Nonetheless, these support improvements in quadriceps

strength found at the shorter (16 weeks) and longer (40 weeks) time points in the present study, although due to lack of comparison to a control group this means that causality cannot be determined.

Interestingly, when only comparing measures of quadriceps strength in DiBiasio et al. (2015), right-sided strength increased by 2.0 N and left-sided strength decreased by 15.6 N. This highlights that imbalances in muscle strength within a child with MD may exist. This asymmetry between muscles may be due to the participant suffering from limb-girdle MD type 2, where asymmetry can occur (Murphy & Straub, 2015), unlike in Duchenne MD where muscles on both sides are usually affected equally (National Institute of Neurological Disorders and Stroke, 2013). However, symmetry did improve in studies investigating other types on MD. Quadratus lumborum and abdominal muscle contractions (using an EMG) in a child with congenital MD improved after 12 weeks of hydrotherapy, and differences in left and right sides decreased from 19.9 μv to 3.5 μv (Santos et al., 2016). They attributed improvements in lower-limb strength and symmetrical contractions to the individual overcoming the resistance of water that caused greater muscle activation. This is due to the motions produced within water, whereby an increased speed, decreased streamline position, change in lever length, and change in direction, increases turbulent pressure that enhance drag within water (Wratten et al., 2019). One way that different types of MD can be differentiated is by looking at the muscles affected, including the symmetry between each side of the body (Huml, 2015). Thus, the design of future interventions needs to consider whether to include all forms of MD in the inclusion criteria and as a result what specific muscles should be used in the muscle strength outcome measure.

The inclusion criteria of the present study included children and adolescents with all types of MD, however our study only monitored participants' dominant side. Although asymmetry is not commonly reported in Duchenne MD, female carriers can present with asymmetrical muscular weakness in their hip, shoulder, knee and ankle extensors, flexors, adductors and/or abductors, affecting function through using compensatory movements and posture in some females (Silva et al.,

2020). It is unknown whether the participants had improvements in both sides and is likely asymmetry could have been present if more children with MD participated in the study, which would have affected the results. This is because there may be an increase in muscle tone one side of the body that is less susceptible to the effects of drag, which would influence results when combined. Therefore, it may be more beneficial for future studies to not only report strengths on both dominant and non-dominant sides of the body separately but also to compare whether improvements in asymmetry in individual forms of MD occur with the use of hydrotherapy. This would allow for a more effective monitoring of muscle strength throughout interventions.

In contrast to quadriceps, overall biceps strength in Participant 1 and 2 decreased by 40.1 N and 32.0 N, respectively, from baseline to week 40. This was inconsistent with previous short-term research that found self-reported increases in muscle strength of the arms in a female with congenital MD after four months of hydrotherapy (Sanders & Torres, 2010). Twelve sessions of hydrotherapy supported this, finding right- and left-sided upper limb strength increased by 39.2 N and 49.0 N, respectively, in a 32-year-old female with limb-girdle MD (Luz et al., 2021). However, results from these studies were consistent with the 10.1 N increase from baseline to week 8-10 in Participant 2, and the 22.1 N increase from week 8-10 to week 16 in Participant 1, although the lower increases in our study could be attributed to sessions in Luz et al. (2021) occurred twice a week. This is supported by studies that found increased motor function after 10 weeks to 2 years of hydrotherapy (Ferreira et al., 2015; Honório et al., 2013; Silva et al., 2012). Improvements have been positively correlated with increase muscle strength (Nunes et al., 2016), meaning that any improvements in quadriceps and biceps strength in the present study could be attributed to motor function improving. This in turn may also be attributed to the drag and viscosity of water, creating resistance to increase muscle strengthening through moving against a turbulence, resulting in improved motor function (Becker, 2011; Ogonowska-Slodownik et al., 2022). These findings do not support the decrease in mean bicep strength in Participant 1 at week 8-10 and week 40, or in Participant 2 at week 16 and week 40.

Although these results could be attributed to the higher severity and stage of MD that individuals were in, shown by one male transitioning to a wheelchair, indicating decreases in strength. However, the gap of approximately five months between measures in the present study means that patterns cannot be identified between week 16 and week 40.

Notably, it can be expected that muscle strength would not return to baseline at week 40, due to the continual degression of bicep and quadricep strength associated with Duchenne MD (Osorio et al., 2019). Participants were aged 8 and 11 at the start of the study, with Participant 2 reporting greater stiffness in his legs and an increased use of a wheelchair throughout the duration of the study. This suggests that Participant 2 was in the beginning of the transitional stage, going from being ambulant to non-ambulant. At age 11-13 individuals with Duchenne MD often become less ambulant (Darras et al., 2015), which could have contributed to the decline in muscle strength. Despite Participant 2 being younger, increases in age have been correlated with decreases in motor function, with a rapid decline between 5 and 15 years old, whereby all individuals with motor function scores below 50% were non-ambulant, occurring from the age of 10 (Bushby & Connor, 2011). This supports that decreases in strength in both participants could have been due to the natural worsening of muscle strength in MD. Additionally, Sanders and Torres (2010) found that decreases in strength after stopping hydrotherapy, were attributed to diminished muscle reflex responses. Whilst they investigated congenital MD, in Duchenne MD diminished reflexes are common as the disease progresses, further contributing to muscle weakness in the biceps and quadriceps. Thus, quadriceps and biceps muscle strength not returning to baseline may not mean that hydrotherapy was ineffective for the maintenance of strength in MD. Future studies should consider stratifying results by age if a large age range is used, like in the present study, due to the potential effect that age has on physical function and performance in outcome measures in MD.

5.3.3 Respiratory Function

Another common characteristic of MD is progressive inspiratory and expiratory muscle weakness that can result in respiratory failure, in which more severe types of MD, including Duchenne MD, leads to premature morbidity and death (Guzmán et al., 2012; LoMauro & Aliverti, 2016). Thus, preserving and maintaining respiratory function in treatments for MD is of upmost importance (Laviola et al., 2018). The overall findings of the present study suggest the maintenance and/or improvement of MIP, MEP, and diaphragm thickness after 40 weeks of hydrotherapy in Participant 1 and Participant 2 (Figure 5).

Many measures for respiratory function exist, where MIP and MEP are global measures of inspiratory and expiratory strength, while forced vital capacity is a global measured of respiratory function (LoMauro et al., 2015). In the present study, mean MIP decreased by 4.5 cm H_2O in Participant 1 and increased by 6.3 cm H_2O in Participant 2 at week 40 compared to baseline, while mean MEP increased by 0.4 cm H_2O and 18.0 cm H_2O in Participant 1 and Participant 2, respectively. Few long-term hydrotherapy studies investigated respiratory function, however DiBiasio et al. (2015) found after 32 weeks forced vital capacity was unchanged and maximum ventilation volume increased by 8.0%, and suggested this could possibly be due to hydrotherapy improving respiratory muscle strength and endurance. Previous research found that MIP and MEP have a moderate positive correlation with maximum ventilation volume ($r = 0.27$, $p = 0.01$) and forced vital capacity ($r = 0.44$ to 0.47, $p = 0.01$) (Bairapareddy et al., 2021). Thus, as these outcomes improved in DiBiasio et al. (2015), it is likely that respiratory muscle strength measured by MIP and MEP also improved. This supports our findings that hydrotherapy may have contributed to the maintenance and/or improvements of MIP and MEP. It could be argued that MIP was maintained in Participant 1, as although a decreased occurred, only a small difference in absolute change was found. However, further research is needed to define a delay in progression to establish what values are maintained. The suggested maintenance of these outcomes could be attributed to the pressure of water on an

individual's chest causing resistance to inspiration during movements, which trains the respiratory muscles (Huguet-Rodríguez et al., 2020). This is due to the hydrostatic pressure based off Pascal's Law, where at any depth of liquid within a container, the pressure exerted "is transmitted equally and undiminished in all directions throughout the liquid" (Wratten et al., 2019). This in turn assists with the venous return, increasing cardiac volume, stroke volume, lowering heart rate, and strengthening respiratory muscles, due to increased blood flow (McIntyre, 2017). This attribution is supported by resistive breathing exercises shown to improve MIP (strength), vital capacity, and maximum voluntary ventilation (Koessler et al., 2001). Therefore, further supporting that hydrotherapy may contribute to the maintenance of respiratory muscle strength.

Previous studies that also monitored MEP and MIP were consistent with the present study but were predominantly conducted over an 8–10-week period. Ten weeks of hydrotherapy increased MEP by 3.9 cm H_2O in 4-to-18-year-olds with neuromuscular disorders (including MD) (Huguet-Rodríguez et al., 2020), and maintained (had no change in) MEP in a 12-year-old male with Duchenne MD (Silva et al., 2012). The 8.6 cm H_2O decrease in MIP found in Huguet-Rodríguez et al. (2020) was consistent with Participant 1 but not Participant 2, while the 5.0 cm H_2O increase in MIP found in Silva yet al. (2012) was consistent with Participant 2 but not Participant 1. Additionally, eight weeks of hydrotherapy was found to maintain and/or improve inspiratory capacity and peak flow in 5–13-year-olds with Duchenne MD (Adams et al., 2017) and 12 weeks of hydrotherapy had small, statistically non-significant improvements in forced vital capacity and functional capacities in Duchenne MD (Abo-zaid et al., 2021). This further supports the contribution of hydrotherapy in maintaining respiratory function, which can be attributed to water properties maintaining vital capacity and diminishing the respiratory frequency (Silva et al., 2012). It is unknown whether these changes in respiratory function over 8 to 12 weeks would reflect our results at week 40, although they are consistent with similar time points in the present study (week 8-10). Thus, this highlights the need

for further long-term research into the contribution of hydrotherapy for delaying declines in respiratory function in MD.

Inconsistencies between individuals and studies could be due to the different ages of participants who completed hydrotherapy. According to Huguet-Rodríguez et al. (2020), children under 11 did not have a "mature respiratory system that is responsive to physical therapy treatment" and were not able to optimally perform hydrotherapy exercises or use the "inspirometer with correct mouthpiece sealing". Thus, those under 11 may have a different response to hydrotherapy and data collection may have been less reliable, compared to those who are older. This was shown in our study where there was difficulty with MIP collections, as the younger participants struggled with having to breath in while keeping a seal with their lips around the mouthpiece tube. A failed seal means air leaks out, reducing the reliability that diminished inspiratory pressure is due to the inspiratory muscles weakening (Schoser et al., 2017). Additionally, the stages of disease progression in each individual may have affected the amount of respiratory dysfunction present (LoMauro & Aliverti, 2016; Pennati et al., 2021). Unlike Participant 2 who had increases at all time points compared to baseline measure, MIP in Participant 1 only increased at week 8-10 and MEP increased at week 8-10 and week 40. This could be attributed him being in the later stage of MD, resulting in the mechanical overload of respiratory muscles, where muscle fibres are replaced by connective and adipose tissues, chest wall contractions are reduced, and pumping air in and out of the lungs against potential higher levels of respiratory resistance is hindered (e.g., from mucus plugging in the peripheral airways) (Pennati et al., 2021). Nonetheless, the present study supports the use of MEP and MIP as "clinically relevant outcome measure[s] in chronic disease when respiratory failure is secondary to respiratory muscle weakness" (Schoser et al., 2017).

Notably, MIP and diaphragmatic strength are closely related because the diaphragm is a main muscle for inspiration to occur (Schoser et al., 2017), in which the diaphragm thickens with muscle

contractions during inspiration (Pennati et al., 2021). However, to our knowledge the present study is the first to monitor diaphragm thickness throughout hydrotherapy sessions for MD, despite its proposed use in clinical interventions from past studies (Laviola et al., 2018). Although our results from Figure 5c suggest the overall maintenance of individual diaphragm thickness after 40 weeks, caution should be taken when applying these results because of research finding that the diaphragm in individuals with Duchenne MD may be prone to pseudohypertrophy (Laviola et al., 2018). Interestingly, in our study Participant 1 had little change in diaphragm thickness, while MIP values decreased by 18.8 cm H_2O from week 8-10 to week 40. Although the pattern of change was similar, it could be expected that a decrease in diaphragm thickness may have occurred due to the greater extend that MIP was reduced by, as shown in Figure 5a and 5c. This could indicate the presence of pseudohypertrophy, due to the maintenance of diaphragmic thickness, despite the later stage of progression Participant 1 was in and the reduction in respiratory muscle strength (LoMauro & Aliverti, 2016). However, it is unknown whether improvements in diaphragm thickness were the results of another form of treatment. Therefore, future studies with a control group are required to investigate the effects of hydrotherapy on diaphragm thickness.

5.3.4 Health-Related Quality of Life

Our study found an overall 3.0-point increase in mean wellbeing scores in Participant 2 after 40 weeks of hydrotherapy, as shown in Figure 6. This is consistent with a 0.10 improvement when measuring HRQoL after six months of hydrotherapy using the Child Health Utility 9-Dimension Index in ambulant 7-16-year-old males with Duchenne MD (Hind et al., 2017). Within Hind et al. (2017), the control group only had a 0.03 increase in HRQoL, meaning improvements in the intervention group could be attributed to having received hydrotherapy; however, the control group had missing data so these findings may have been underestimated. Shorter term interventions of eight weeks were also consistent with increases in HRQoL for Participant 2 at week 40 and no change for Participant 1 and 2 at week 8-10, where HRQoL was found to increase in children aged 5-15 with

Duchenne MD (Adams et al., 2017; Atamturk & Atamturk, 2018). Hydrotherapy offers a safer environment that can contribute to a reduction in pain through buoyancy reducing the stress on joints and perceived fatigue, hydrostatic pressure triggering mechanoreceptors, and thermoneutral temperatures (34.0-35.5°C) stimulating thermo-receptor nerves to block nociceptors (Mooventhan & Nivethitha, 2014; Zamunér et al., 2019). Additionally, heat can diminish muscle spindle excitability that decreases muscle spasms and tension in trigger points, and/or can decrease viscosity of synovial fluid that increases soft tissue extensibility, which alleviates painful stiffness (El Geziry et al., 2018). This causes muscle and mental relaxation that can improve HRQoL and wellbeing in individuals, as well as provides an inclusive environment for non-ambulant individuals to also be able to participate. Thus, this supports that properties of water during hydrotherapy may contribute to the increase or maintenance of wellbeing in children and adolescents with MD.

Conversely in our study, the overall mean wellbeing score in Participant 1 decreased by 23.0 after 16 weeks and 4.0 after 40 weeks of hydrotherapy. These findings do not reflect the expected improvement in wellbeing and HRQoL that was predicted to occur due to the fun and supportive environment that hydrotherapy may provide (Lima & Cordeiro, 2020). Additionally, though not consistent with previous research or Participant 2's results, this could be attributed to the stage of progression of MD outweighing participation in hydrotherapy and any improvements in respiratory function, muscle strength and wellbeing. For example, Participant 1 was older, non-ambulant and at a later stage of progression, which have been associated with decreased scores on the Health State Utilities for HRQoL in 5-16-year-old boys with Duchenne MD (Szabo et al., 2022). This was supported by studies that found physical HRQoL scores for older boys with MD were lower than younger boys (Bendixen et al., 2012; Bray et al., 2010), Thus, making it more likely for the natural decline in physical and psychological function to occur at a greater rate than any improvements in this participant, causing his wellbeing and HRQol to reduce despite receiving hydrotherapy. Despite

this, hydrotherapy sessions in the present study included non-ambulant individuals unlike past studies, suggesting there was a benefit in socialisation and the possibility of exercises being able to be completed with their peers. Notably, the biggest decline in wellbeing for Participant 1 occurred from week 8-10 to week 16 (-23.0), before increasing by 19.0 back towards baseline scores at week 40 (as shown in Figure 6). This suggests that there were external factors that may have been present, which could have influenced wellbeing and in turn have contributed to the decrease found in Participant 1.

One external variable that may have been present in the current study was fatigue. Participant 1 reported he was tried and struggling with school, which may have stopped him from attending sessions and/or caused a greater reduction in his mental health and performance in outcome measures. This was shown at week 40 when Participant 1, who attended six fewer overall sessions, had a decline in wellbeing, compared to Participant 2 who had an increased wellbeing (67.9% < 89.3%, as shown in Table 1). This could suggest that attendance rates and wellbeing scores are related to one another. Unfortunately, due to the low sample size a correlation could not be conducted; however, this may be a point for future studies to investigate. Fatigue has been found to impact HRQoL in adults with MD (Jacques et al., 2019), and was found to be a strong predictor of poor HRQoL in children with Duchenne MD (Wei et al., 2016). Increasing age was related to declining physical function levels (based on Brooke Lower Extremity Functional Classification), which were related to increased energy expenditure and fatigue in children with Duchenne MD (Mutlu et al., 2018). However, within this study participants at the lowest functioning level were still ambulant and able to slowly able to ascend four stairs with help, which differs from one of our participants. Additionally, in adults with facioscapulohumeral and myotonic MD, increased age was significantly correlation with the higher severity of fatigue ($r = 0.17\text{-}0.19$, $p = 0.002$), as well as impaired physical function, greater pain, reduced activity, and reduced motivation (Kalkman et al., 2005). Thus, as Participant 1 was older, it

is likely that he is experiences greater levels of fatigue that Participant 2, meaning it is viable to suggest that fatigue may have contributed to his decrease in wellbeing. However, the NPC's Wellbeing Measure in the current study did not include questions regarding fatigue as a subscale, so it is unknown whether fatigue was present and hindered wellbeing in Participant 1. Therefore, future studies should consider including fatigue within the outcome measures to be monitored.

Additionally, one participant was self-conscious of their body, as highlighted in one of the data collection sessions where he did not want to lift his top. DiBiasio et al. (2015) found that despite receiving 32 weeks of hydrotherapy, physical appearance scores decreased by 0.8, which could be attributed to the participant gaining weight, which is a common feature in many forms of MD, especially as individuals begin steroid treatment (Weber et al., 2018). It is unknown whether this influenced attendance to hydrotherapy sessions in the present study, however it could have contributed to decreased wellbeing scores in participants as usual care (including steroid treatment) was continued throughout the study, meaning physical appearances could have been affected. Nonetheless, self-worth scores remained the same and overall self-perception scores improved, including cognitive competence (school and socially), athletic and job competence, romantic appeal, behaviour, and friendships (DiBiasio et al., 2015). This is supported by Atamturk and Atamturk (2018) who found that eight weeks of hydrotherapy improved relaxation, self-perception, and socialization. However, differences in outcomes measures between each study, make comparison harder, with DiBiasio et al. (2015) using Self-Perception Profile for Adolescents, Adams et al. (2017) using PedsQl and the present study using the NPC Wellbeing Measure. This highlights that overall HRQoL may not be the most appropriate to include for MD, due to the differences in subscales. Thus, individually reporting values for each subscale may provide a clearer insight into the HRQoL of individuals and monitor aspects of an individual's life that may need more assistance or support on. Alternatively, this further highlights the need for consistency of outcome measures across research into MD, in order to identify the effectiveness of intervention in delaying the progression of MD.

5.3.5 High Variability

Individuality between participants could explain the high variability between the results of Participant 2 and Participant 2, as shown by the standard deviation in Table 1, as shown in Figure 4, 5 and 6. Participant 1 was older and non-ambulant, whilst Participant 2 was younger and ambulant but began to more frequently use a wheelchair in his day-to-day life and had reported leg pain and stiffness. This suggests that Participant 2 was beginning his transitional stage to non-ambulation, indicating that participants were at different stages of progression, which would have impacted the overall results. Older, non-ambulant children and adolescents with Duchenne MD are further in stages of progression than younger children, that as investigated results in greater muscle weakness and respiratory dysfunction that decreases participation in activities of daily life with their peers and can contribute to a worsened HRQoL (Lima & Cordeiro, 2020).

Interestingly, although research implies or suggests that HRQoL would decrease with age, alongside the decreases in muscle strength, respiratory function, and motor function, this not consistent in all studies. A study by Uzark et al. (2012) found that while physical functioning decreased with age, boys aged 13-18 perceived better psychosocial QoL than boys aged 8-12 and their parents. This was supported by Bray et al. (2010) who found that the psychosocial health summary score had little-to-no difference in boys aged 13 to 17, compared to boys aged 8 to 12. The lack of correction between HRQoL and age in MD could be attributed to what is known as a response shift (Schwartz et al., 2007, as cited in Szabo et al., 2020). As explained in Szabo et al. (2020) people with chronic diseases, e.g., MD, may learn to adapt to their stage of progression and/or health state, meaning they ‘re-baseline’ their symptoms as the severity increases, and the continual worsening of their condition becomes normal to them. While this does not support the results of Participant 1, explored in *5.3.4 Health-Related Quality of Life*, likely due to him falling within the younger 8-12 category despite being non-ambulant, it does highlight how individuality can affect results of HRQoL.

Thus, making it harder to compare studies and draw conclusions on the effectiveness of interventions on HRQoL without an age-matched control group. Therefore, this should be considered by future studies.

Nonetheless, other studies support increases in age and later stages of progression being correlated with decreased motor function and ambulation (Bushby & Connor, 2011), and decreased respiratory function (Huguet-Rodríguez et al., 2020). Thus, the impact of hydrotherapy on wellbeing, muscle strength and respiratory function may be different between younger, ambulant children and older, non-ambulant children. It is important to monitor all types of MD at all stages to ensure effective treatment throughout the disease, although several previous studies have excluded non-ambulant individuals from participating, which would have affected their results and recruitment rate (Hind et al., 2017). Types of MD can be differentiated by age of onset, life expectancy, muscles affected, progression rate and comorbidities (Huml, 2015; Mercuri & Muntoni, 2013), thus future study design should consider the specific type(s) of MD they want to investigate and modify the intervention accordingly. This can be done though adapting study durations, suitable outcome measures, session duration and times, and exercises that consider the age (e.g., adapting language used or considering ability), muscles affected, severity, and comorbidities, however as highlighted this would be best informed through standardised measures and definitions of delayed progression.

5.4 Implications

Muscle strength, respiratory function and HRQoL are common characteristics of MD and are all important outcomes to monitor the progression of MD that should be preserved and maintained during interventions. The study provides a useful insight into the contribution of hydrotherapy for the maintenance of respiratory, physical, and psychological function in MD; as well as highlights further research areas to be investigated and actions to be considered. Future studies are needed with a control

group to determine the effects of long-term usual care with and without the addition of hydrotherapy in children and adolescents with MD. It is likely that participants may need to be matched on age and MD type, due to the differences between MDs and the stages of progression, and high variability between individuals.

There is a lack of consistency in many outcome measures across clinical trials and interventions for MD, that hinders the ability to compare results from different studies. This was highlighted in measures of HRQoL, muscle strength, and respiratory function within the present study. A form of standardisation or set of core outcome measure that can be generalised to children and adolescents with MD to monitor their progression in clinical interventions and daily life is required. The application of these outcomes would allow for consistency within and between research studies and everyday healthcare practice, supporting practitioners more in using evidence-based practice for the management of MD. It will also allow for a better-informed meta-analysis across future studies, that can be used to inform clinical NHS NICE guidelines for managing MD in children and adolescents. Additionally, a standardised definition of a delay in progression is needed to ensure consistency in and between clinical practice and research.

Study 2

The small clinical population in MD is further reduced during clinical trials and physical activities, due to restrictions of the disease and reduced rates of participation (Bendixen et al., 2016). For example, low levels of participation were found in general clinical trial participation across the USA in children and adolescents with MD, ranging from 3.7% to 27.3% (mean 17.9%), between 2000 and 2015 (Matthews et al., 2021). This highlights how little participation amongst individuals with MD can be. Thus, understanding the effects of hydrotherapy is important as it may be able to contribute to maintaining biomechanical, physiological, and psychological function and HRQoL in children and adolescents with MD, in turn slowing the progression of the disorder.

Chapter 5.0 highlighted the difficulty with conducting such a study, in which previous research (as explored briefly in *2.4.4 Considerations of Participation*) and current research from part one of the present thesis have found issues with recruitment and low rates of attendance and/or participation, which have become more apparent over time (Abo-zaid et al., 2021; Hind et al., 2017). There is little research on barriers and motivators that impact participation rates in those with MD (Peay et al., 2018). However, based on logistic regression, higher perceived barriers were the strongest predictor of and were significantly associated with lower interest in trial participation (-1.41(0.25), $p < 0.001$), (Peay et al., 2018). If participation and recruitment remain low, then the effects of hydrotherapy on disease progression in MD may not be known. Additionally, low participation could hinder the justification of using hydrotherapy from an NHS perspective and its implementation into NHS NICE guidelines, because it may not be economically cost-effective or resourceful to provide group sessions if individuals will not attend, despite the potential benefits. Therefore, identifying reasons why individuals with MD may not be able to or want to participate, as well as why they would like to participate, could facilitate our understanding into this area. It would also allow for a more robust study design and effective implementation of interventions (Shields &

Synnot, 2016). As a result, we found it essential to conduct a follow-up study on: *An investigation into the barriers and motivators that may affect participation in hydrotherapy for children and adolescents with MD.*

Chapters 6.0 to 8.0 aimed to provide a basis of discussion surrounding the best approach in providing hydrotherapy that will inform the completion of future research and in turn the prescription of hydrotherapy from practitioners (e.g., physiotherapists). Study 2 sought to answer the following questions:

1. What barriers prevent participation in hydrotherapy in children (5-17 years) with MD from the perspective of their carers?
2. What motivates participation in hydrotherapy in children (5-17 years) with MD from the perspective of their carers?

Chapter 6.0: Methodology

6.1 Participants

Following ethical approval from the University of Gloucestershire research committee (HENRY21-22, see Appendix E), 16 UK based parents and/or carers of children and adolescents with MD between the ages of 5-17-years-old completed an online questionnaire. The questionnaire was centred around motivators and barriers that may affect participation in hydrotherapy and explored the parents' perspective and their view of their child's perspective. The participants were recruited through various social media sites and support groups on Facebook™ and Twitter™, and through connections with various healthcare professional and charities within the UK. Some of the Twitter™ sites used included: Muscular Dystrophy UK, Rare Disease UK, Duchenne UK, Parent Project Muscular Dystrophy, Duchenne Family Support Group, Action Duchenne, Muscle Owl, Duchenne Now, and Coalition Duchenne. Some of the Facebook™ support groups used included: Muscular Dystrophy Stories, Muscular Dystrophy Coalition, Limb-Girdle Muscular Dystrophy, and Muscular Dystrophy Support, and The Chamwell Centre Charity.

Participants were from East Lothia (n = 1), Gloucestershire (n = 5), Hampshire (n = 2), Northumberland (n = 1), Renfrewshire (n = 1), Staffordshire (n = 1), Bedfordshire (n = 1), Kent (n =1) and Surrey (n = 1), although two individuals did not specify the county they lived in. Of the 16 children whose parents and/or carers completed the questionnaire, the majority were males (93.8%), aged 6-12 (43.8%) and 13-17 (43.8%), suffering from Duchenne MD (68.8%). The remaining five children were diagnosed with Becker, Congenital, Facioscapulohumeral, Limb-Girdle and Myotonic MD. Diagnosis frequently occurred between one and three years of age (50.0%), with many remaining ambulant (56.3%) and requiring physical aids (68.8%), including manual and power wheelchairs (n = 10), adapted buggies (n = 2), crutches (n = 1), splints (n = 1), orthosis (n = 1), and insoles (n = 1). Table 2 provides a full summary of children's demographics.

Prior to the completion of the questionnaire, participants were taken to an introduction page that provided a brief explanation, a participant information sheet, informed consent questions, questionnaire duration and researchers' contact details (see Appendix F). Once informed consent was gained, participants were able to access the questions. Participants were able to return to and skip questions that they were either unsure of or uncomfortable with, to accommodate for the sensitive nature of the topic of MD. All answers were voluntary, and no incentive was provided, whereby participants were able exit the questionnaire should they want to accept their right to withdraw from the study. Participants were reassured that all information provided would remain anonymous, in which no contact or major identifying details were collected.

Table 2

Demographics of Children Whose Parents Responded to the Motivators and Barriers Questionnaire

Variable	Number (*n*)	Frequency (%)
Sex		
Male	15	93.8
Female	1	6.3
Current Age (yrs)		
≤ 5	2	12.5
6 – 12	7	43.8
13 – 17	7	43.8
Area (County)		
Bedfordshire	1	6.3
East Lothia	1	6.3
Gloucestershire	5	31.3
Hampshire	2	12.5
Kent	1	6.3
Northumberland	1	6.3
Renfrewshire	1	6.3
Staffordshire	1	6.3
Surrey	1	6.3
Not Specified	2	12.5
Age of Diagnosis		
Pre-Birth	-	-
0 – 12 months	1	6.3
1 – 3 years	8	50.0
4 – 5 years	2	12.5
6 – 12 years	2	12.5
13 – 17 years	1	6.3
Not Specified	2	12.5
Form of Muscular Dystrophy		
Becker	1	6.3
Congenital	1	6.3
Distal	-	-
Duchenne	11	68.8
Emery-Dreifuss	-	-
Facioscapulohumeral	1	6.3
Limb-Girdle	1	6.3
Myotonic	1	6.3
Oculopharyngeal	-	-
Ambulant versus Non-ambulant		
Ambulant	9	56.3
Non-ambulant	6	37.5
Not Specified	1	6.3
Physical Aids		
None Required	5	31.3
Required	11	68.8
Aids Used		
Wheelchair (Power and Manual)	10	62.5
Adapted Buggy	2	12.5
Crutches	1	6.3
Splints	1	6.3
Insoles	1	6.3
Orthosis	1	6.3

6.2 Study Design

The questionnaire was designed on Google Forms, consisting of an introduction page, the main contents, and a debrief page that was available once all questions were completed. Prior to gaining ethical approval, the questionnaire was reviewed by research supervisors and sent off for peer review to ensure the questions asked were relevant and appropriate. The researchers developed the questionnaire, which consisted of both closed- and open-ended questions that differed slightly depending on answers given to key questions, as outlined in Figure 7. Parents who:

- Had a child who **has taken part and are currently motivated** to take part in hydrotherapy received a total of 25 questions (17 closed and 8 open).
- Had a child who **has taken part but are not currently motivated** to take part in hydrotherapy received a total of 23 questions (17 closed and 6 open).
- Had a child who **has never taken part** in hydrotherapy received a total of 23 questions (15 closed and 8 open).

The main contents of the questionnaire were broken down into three sections (see Appendix F for full questions and response options):

Section 1: Demographics

Parents were asked questions surrounding their child's age, biological sex, and MD diagnosis. A categorial response for biological sex ("male", "female", "other"), the type of muscular dystrophy, county living in, and ambulatory phase ("ambulant", "non-ambulant") was recorded. Open-ended responses were recorded for current age, age of diagnosis, and any physical aids used.

Section 2: Current Treatments

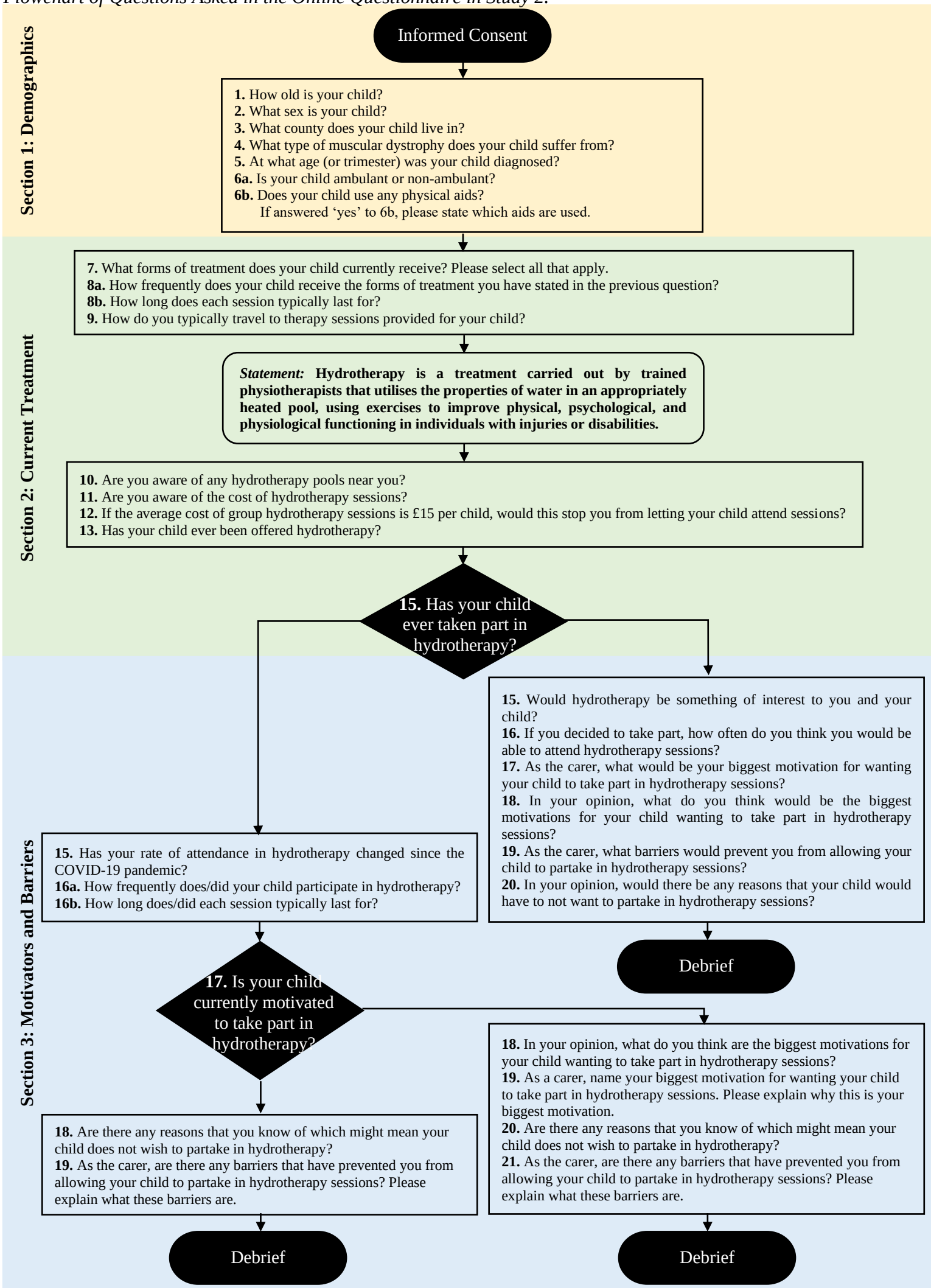
Parents were asked closed-ended questions about general forms of treatments their child currently receives. A categorial response for frequency (“less than once a month”, “once a month”, “2-3 times a month”, “1-2 times a week”, “3+ times a week”), duration (“less than 30 minutes”, “30 minutes”, “45 minutes”, “1 hour”, “more than 1 hour”), and travel to and from sessions (“walk”, “car”, “bus”, “train”, “other”) were also recorded. A definition of hydrotherapy was then provided, and parents answered ‘basic’ knowledge questions on hydrotherapy, i.e., aware of location, cost, and if their child has been offered and completed hydrotherapy, as a categorical answer (“yes”, “no”).

Section 3: Motivators and Barriers

Parents were asked open ended questions regarding motivators and barriers for current or potential participation in hydrotherapy from their perspective and their view of their child’s perspective. Those who answered “yes” to the question ‘Has your child ever taken part in hydrotherapy?’, also provided categorial answers for their rate of attendance (“attendance has increased”, “attendance has remained similar”, “attendance has decreased”, “attendance stopped completely”), frequency (“less than once a month”, “once a month”, “2-3 times a month”, “1-2 times a week”, “3+ times a week”), duration (“less than 30 minutes”, “30 minutes”, “45 minutes”, “1 hour”, “more than 1 hour”), and whether they child is currently motivated (“yes”, “no”).

Figure 7

Flowchart of Questions Asked in the Online Questionnaire in Study 2.



6.3 Data Analysis

Data from all closed-ended and open-ended questions within 'Section 1: Demographics' were quantified and summarised into Table 3. All closed-ended questions within 'Section 2: current treatment' were also quantified and reported in a table and bar graph for general treatment and hydrotherapy 'basic' knowledge, respectively. To understand motivators and barriers for participation in hydrotherapy, content analysis was conducted on the open-ended questions in 'Section 3: motivators and barriers'. The responses to each question were downloaded into an Excel spreadsheet and separated into individual responses. These were then reviewed to identify salient words to be used as codes to represent similar meaning words.

To compensate for the shorter responses, latent analysis was used, allowing us to interpret hidden and implied meaning behind the responses (Kiger & Varpio, 2020). Any words part of common grammar or not contextually specific were ignored from the responses. The frequency of parents who used these established codes within their response was calculated throughout responses to each question and presented as word (data) clouds, using https://www.wordclouds.co.uk/. Coded words were then categorised into pre-existing themes of child needs, child barriers or personal (parent) factors, or social, policy and programme, and environmental factors (based on Abid et al., 2022; Brown et al., 2022; Shields et al., 2012) to allow for further comparison, as defined by:

- (*Child Needs, Child Barriers)* Any "personal, physical or psychological factors of children".
- (Personal (Parent) Factors) Any personal, physical or psychological factors of parents.
- (*Social Factors)* Any situations or factors that involve people the parents would come in contact with.
- (*Environmental Factors)* Any factors involving "structural elements such as facilities and transport".

- (*Policy and programme Factors)* Any factors that involve the programme, organisations, and staff of hydrotherapy sessions.

To create a visual representation of themes and frequency discovered within the responses, words were colour coded and weighted, respectively. **Black** words represented **child needs, child barriers or personal (parent) factors**, **blue** represented **social factors**, **green** represented **environmental factors**, and **red** represented **policy and programmes**. Additionally, the higher the frequency of words, the larger the font used within the word clouds. To ensure the reliability of the content analysis, the coding words identified within the responses were reviewed by a different researcher on the team. To minimise researcher bias, a review of the responses and identification of coding units by each researcher was completed individually. Any disparities were discussed after each researcher's review.

Chapter 7.0: Results

7.1 Current Treatment

As presented in Table 3, physiotherapy was the most predominant form of treatment received by children and adolescents with MD (*n* = 15), followed by medication (*n* = 6) and steroid therapy (*n* =8). While creatine supplements, surgery and exon skipping trials were the least received treatment (*n* = 1). Treatments were mainly received less than once a month (*n* = 7), for a common duration of 45-mintes (*n* = 6). The majority travelled by car to these sessions (*n* = 12), compared to walking (*n* = 1) or receiving treatment at home (*n* = 1) or at school (*n* = 2).

Table 3

Background of Current Treatments for Children with Muscular Dystrophy in Study 2

Variable	Number (*n*)
Forms of treatment	
Physiotherapy	15
Occupational Therapy	6
Hydrotherapy	6
Medications	10
Steroid Therapy	8
Creatine Supplements	1
Surgery	1
Exon Skipping Trials	1
Other	1
Frequency of treatments	
Less than once a month	7
Once a month	1
2 - 3 times a month	2
1 - 2 times a week	4
3+ times a week	2
Typical duration of treatments	
Less than 30 minutes	4
30 minutes	4
45 minutes	6
1 hour	2
More than 1 hour	-
Form of travel	
Walk	1
Car	12
Bus	-
Train	-
Other	
In home	1
At school / college	2

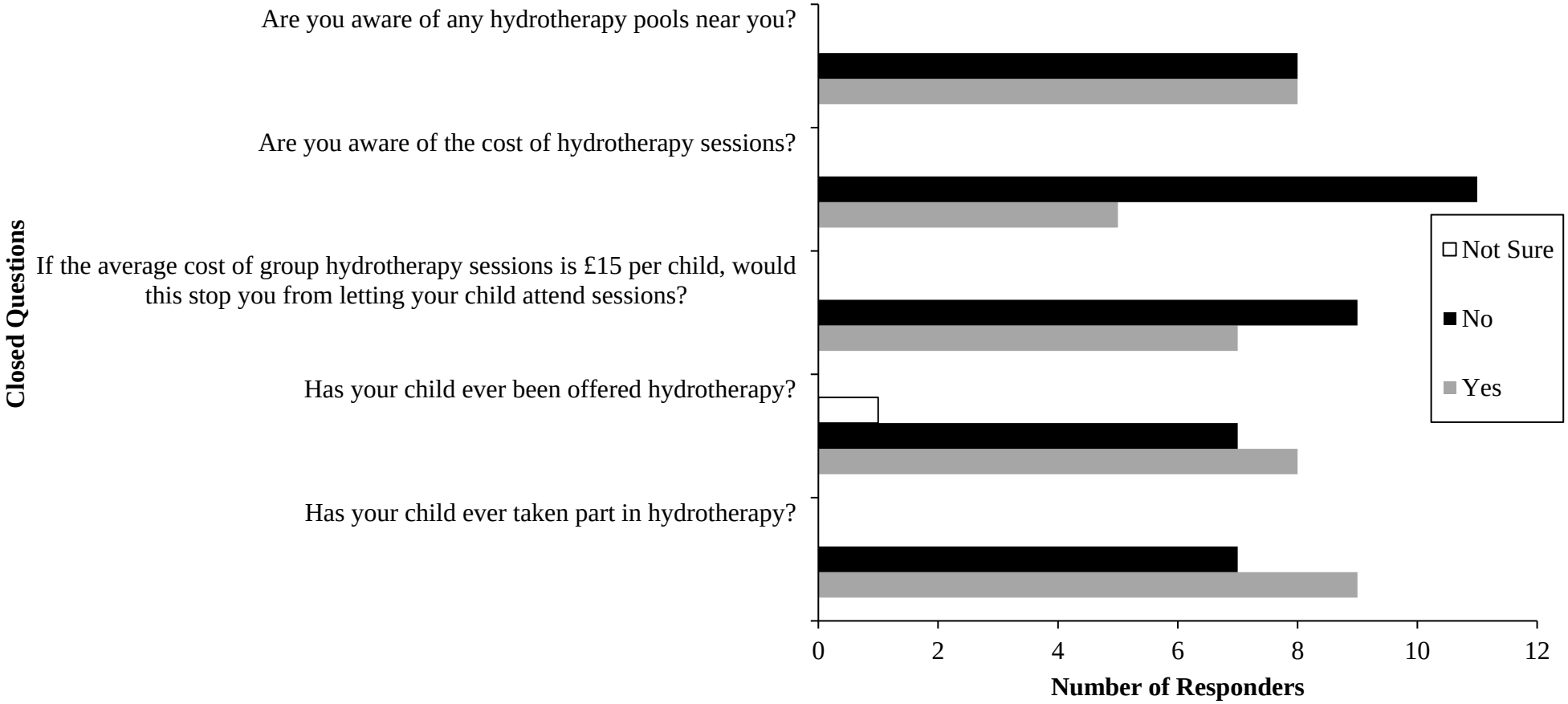
7.2 Knowledge on Hydrotherapy

As show in Figure 8, the number of parents aware of the nearest hydrotherapy pool available for their child (n = 8) was equal to the number of parents unaware of the nearest hydrotherapy pool (n = 8). The number of parents unaware of the cost of hydrotherapy (n = 11) was greater by 6 than the number of parents aware of the cost of hydrotherapy (n = 5), however the number of parents who said an average cost of £15 per hydrotherapy session would not deter them from letting their child participate in hydrotherapy (n = 9) was greater than parents who said this would deter them (n = 7).

As shown in Figure 8, the number of children who had been offered hydrotherapy (n = 8) was greater than the number of children who had never been offered hydrotherapy (n = 7). The number of children who had taken part in hydrotherapy (n = 9) was greater than the number of children who had never taken part in hydrotherapy.

Figure 8

Parents' and Carers' Knowledge on and Background in Hydrotherapy for their Child

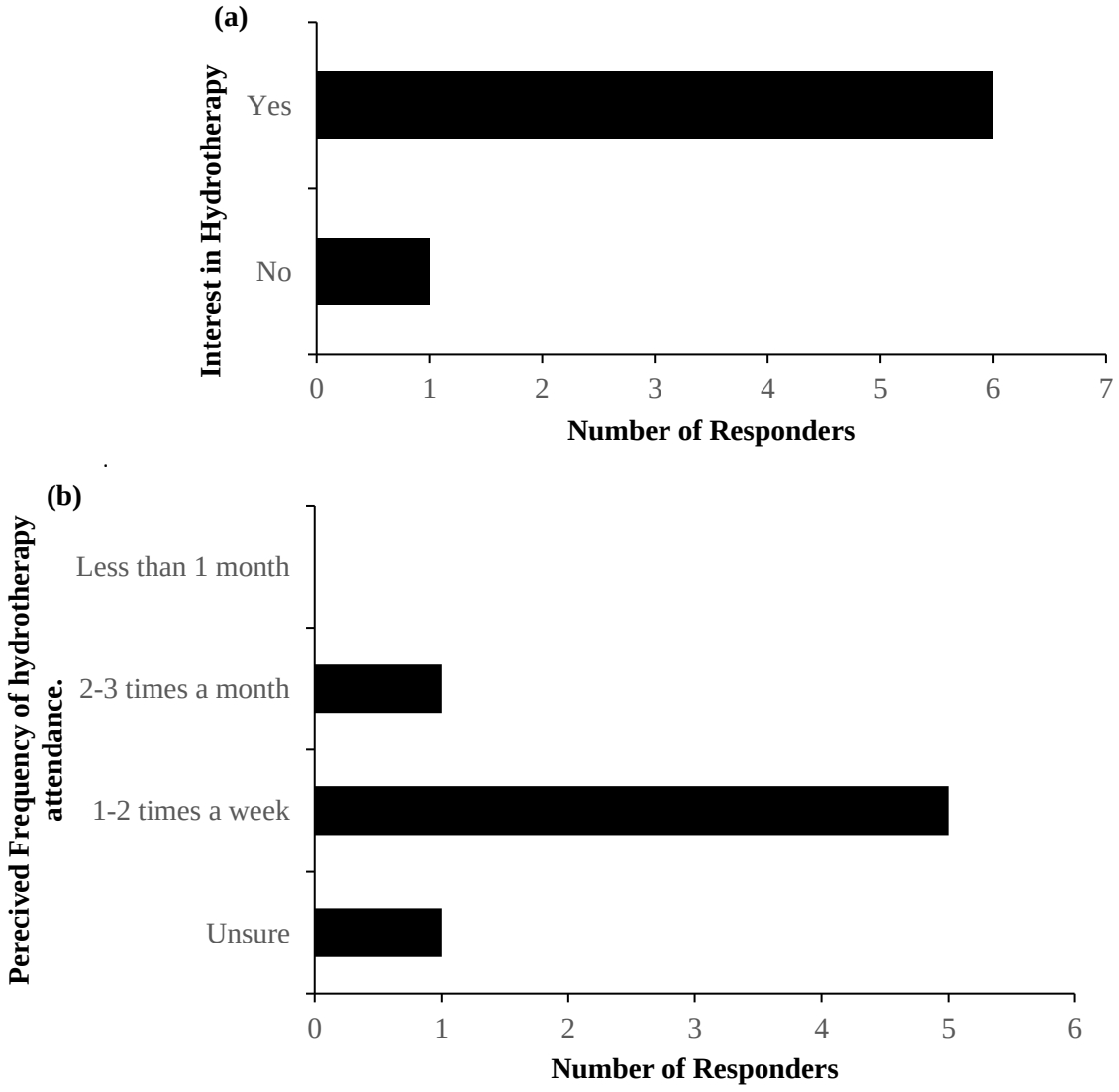


7.3 Never had Hydrotherapy

As shown in Figure 9a, the number of parents who would be interested in hydrotherapy for their child (n = 6) was greater than the number of parents uninterested in hydrotherapy (n = 1). As shown in Figure 9b, the number of parents who though their child would attend hydrotherapy sessions two-to-three times a month (n = 5), was greater than an attendance of one-to-two times a week (n = 1) and less than once a once (n = 1).

Figure 9

Responses of Parents and Carers whose Child with Muscular Dystrophy has Never Partaken in Hydrotherapy.



Note. These figures demonstrate the responses of seven parents answer the following questions: (a) Would hydrotherapy be something of interest to you and your child? and (b) How frequently would your child attend hydrotherapy sessions?

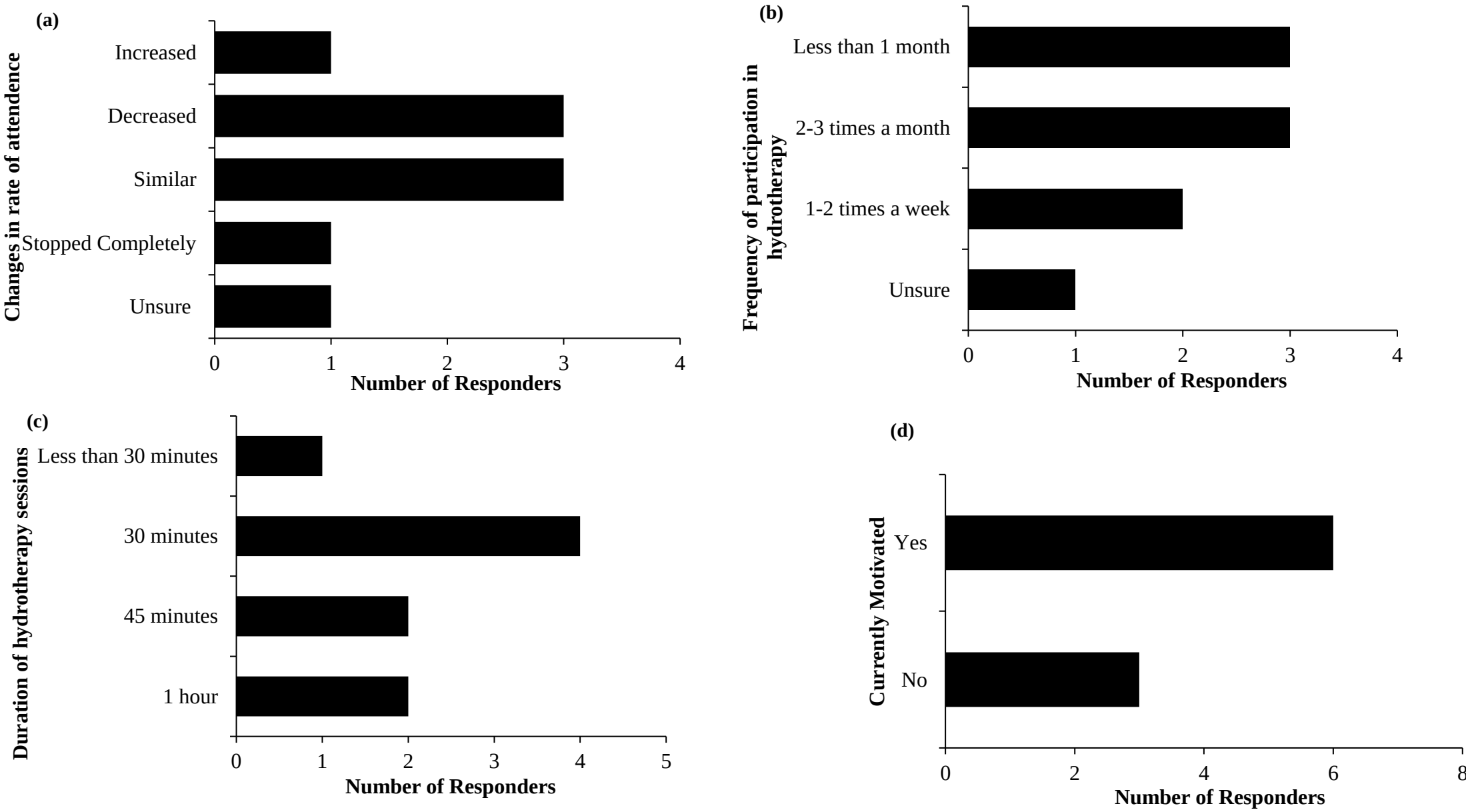
7.4 Previously had Hydrotherapy

As shown in Figure 10a, a greater number of children's attendance rate in hydrotherapy decreased (*n* = 3) or remained similar (*n* = 3) since the COVID-19 pandemic, compared to increased attendance (*n* = 1), or stopping attendance completely (*n* =1). A greater number of children attended these sessions less than once a month (*n* = 3) or two-three times a month (*n* = 3), compared to attendance once or twice a week (n = 2) (Figure 10b). A greater number of these hydrotherapy sessions lasted for a duration of 30 minutes (*n* = 4), compared to a duration of 45 minutes (*n* = 2), one hour (*n* = 2), and less than 30 minutes (*n* =1) (Figure 10c).

As shown in Figure 10d, the number of children motivated to participate in hydrotherapy (*n* = 6), was greater than the number of children unmotivated (*n* = 3).

Figure 10

Responses of Parents and Carers whose Child with Muscular Dystrophy has Previously Partaken or are Currently Participating in Hydrotherapy.



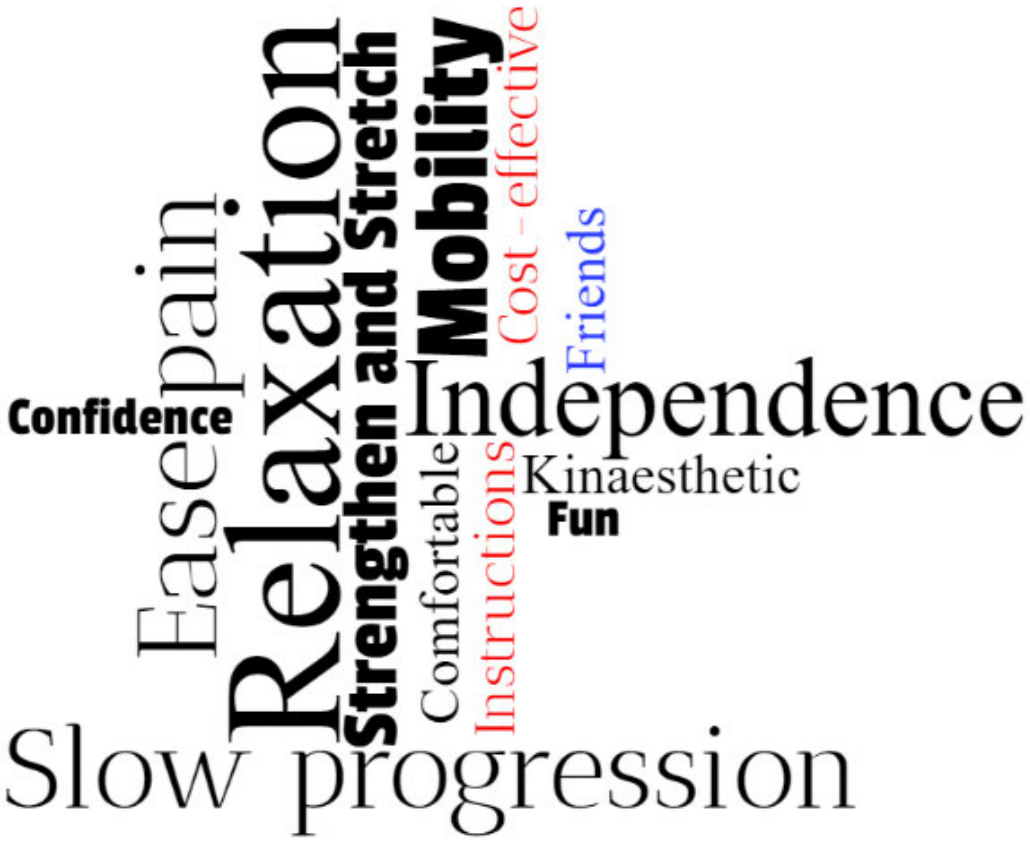
Note. These figures demonstrate the responses of seven parents answer the following questions: (a) Has your rate of attendance in hydrotherapy changed since the Covid-19 pandemic? (b) How frequently does/did your child participate in hydrotherapy? (c) How long does/did each session typically last for? (d) Is your child currently motivated to take part in hydrotherapy?

7.5 Motivators to Participation

The online questionnaire asked parents and/or carers on their perspectives of motivators for participation in hydrotherapy (Figure 11). Hydrotherapy pools encouraging relaxation and physical benefits (i.e., increase mobility, strength, and slow progression) were the most frequently reported motivator for parents and carers.

Figure 11

Parents' Perspective on Motivators for Participation in Hydrotherapy.



Note. A word cloud demonstrating responses to motivation to participate questions (a total of 12 out of 13 responses were found: Relaxation (3), Strengthen and Stretch (3), Ease Pain (2), Independence (2), Mobility, (2), Slow Progression (2), Comfortable (1), Confidence (1), Cost-effective (1), Friends (1), Fun (1), Instructions (1), and Kinaesthetic (1)). Words written in black represent child needs, blue represents social motivators, and red represents policy and programme motivators.

Parents were also asked for their views on motivators for participation in hydrotherapy that their child would report (Figure 12). Hydrotherapy pools reducing pain and promoting comfort, fun, independence, and relaxation were the most frequently reported motivators of children from their parents' view. The number of personal and social motivators were similar for children and parents from the parents' perspectives (17 versus 18, and 1 versus 1, respectively). However, reported environmental motivators were greater for children than parents (4 > 0), while policy and programme factors were greater for parents than children (2 > 0), when based on parents' perspectives.

Figure 12

Parents' view on their child's perspective on motivators for participation in hydrotherapy.

Note. A word cloud demonstrating responses to motivation to participate questions (a total of 12 out of 13 responses were found: Comfortable (3), Ease Pain (3), Fun (3), Independence (3), Relaxation (3), Accessibility (2), Slow Progression (2), Warmth (2), and Friends (1)). Words written in black represents child needs, blue represents social motivators, and green represents environmental motivators.

7.6 Barriers to Participation

Parents and/or carers were also asked on their perspectives of barriers to participation in hydrotherapy (Figure 13). Issues with distance and time management were the most frequently reported barrier for parents and carers.

Figure 13

Parents' perspective on barriers to participation in hydrotherapy.

Note. A word cloud demonstrating responses to barriers to participate questions (a total of 13 out of 16 responses were found: Distance (4), Time (4), Illness (2), Other Children (2), Covid Shielding (1), Facilities (1), Fatigue (1), and Surgery (1)). Words written in black represents personal/child barriers, blue represents social barriers, and green represents environmental barriers.

Parents were also asked for their views on barriers to participation in hydrotherapy that their child would report (Figure 14). Issues with self-esteem, fatigue, and time were the most frequently reported barrier in children from the parents' perspective. The number of personal barriers reported by parents were greater when they considered their children's views than their own (14 > 4). However, compared to their view of their child's perspective, parents' own views reported a greater number of social barriers (7 > 3) and environmental barriers (5 > 1).

Figure 14

Parents' view on their child's perspective on barriers to participation in hydrotherapy.

Note. A word cloud demonstrating responses to barriers to participate questions (a total of 13 out of 16 responses were found: Self-Esteem (5), Fatigue (3), Time (3), Boredom (2), Illness (2), Access (1), Co-morbidities (1), and Pain (1)). Words written in black represent child barriers and green represents environmental barriers.

Chapter 8.0: Discussion

The purpose of Study 2 was to investigate the motivators and barriers to hydrotherapy participation in children (5-17 years old) with MD, from the perspective of their parent and/or carer. The main findings of the study were that 1) slowing MD progression was parents' main motivation for wanting their child to participate in hydrotherapy, 2) decreasing pain and increasing comfort, fun, independence, and relaxation were parents' view of their children's main motivation to participation, 3) distance and distributing time to attend hydrotherapy was parents' main barrier to participation, and 4) decreased self-esteem was parents' view of their children's main barrier to participation.

Understanding barriers and motivators is important for the design and implementation of future studies, interventions, and therapies (Bendixen et al., 2016; Shields & Synnot, 2016). Several studies have investigated participation in clinical trials and physical activity for neuromuscular diseases, such as cerebral palsy (Abid et al., 2022; Shields & Synnot, 2016), however to our knowledge we were the first study to investigate barriers and motivators to participation in hydrotherapy for children and adolescents with MD.

8.1 Demographics

Most children whose parents responded to the online questionnaire were males (93.8%) with Duchenne MD (68.8%). This is consistent with the wider MD population, because Duchenne MD is the most common form of childhood MD that is predominantly inherited by males (Osorio et al., 2019). This further explains why the present study found 50.0% of these children were diagnosed between one and three years old, aligning with the presentation of symptoms in Duchenne MD becoming more apparent from ages two to three (Duan et al., 2021). However, only one case of Becker MD was found amongst the responses, which was unexpected due to it occurring in childhood, although less frequently and less severe in presentation than Duchenne MD (Andrews & Wahl, 2018).

Nonetheless it could be suggested that our sample was somewhat representative of the wider population.

8.2 Parent-Reported versus 'Child-Reported'

In the present study, parents reported barriers and motivators from their own perspective and their child's perspective. This was appropriate because it accounted for the wide age range within the study and potential cognitive impairments associated with MD, that might have affected children's ability to understand the questionnaire (Ferrero & Rossi, 2022). Parents' perspectives were essential in developing our understanding of barriers and motivators, because they were found to have a significant influence on facilitating their child's ability to participate, such as through finances, transportation, or encouragement, especially in those who were younger or had a higher severity of disease (Brown et al., 2022; Conchar et al., 2016; Shields & Synnot, 2016). However, it is uncertain whether parents had discussed their answers for 'child perspective' questions with their child prior to completing the questionnaire, which may have impacted the results if this was inconsistent amongst parents in the present study. Therefore, although the present study was able to capture elements of children's perspective, it should be stressed that the responses in the present study were reported by the parents. This means that while children may have expressed their views to their parent, caution must be used when interpreting 'children's perspectives' in Study 2 since it was still predominantly phrasing and views from the parents. Further research is needed to confirm the 'child-reported' motivators and barriers within participation amongst those with MD in this study.

As Study 2 gained children's perspectives via parent reports, it suggests that there are different motivators and/or barriers that may have been overlooked by parents, due to the slight difference in perspectives, where parents had higher expectations in benefits (Peay et al., 2014). For example, a study found that MD parents often underestimated their child's HRQoL, with only moderate positive correlations in physical health ($r = 0.67$, $p < 0.05$) and psychosocial health ($r = 0.44$, $p < 0.05$) between

parent-reports and child-reports (Lim et al., 2014). This suggests that parents may give similar results to their child, but they cannot provide a definite response, as other extraneous variables and experiences may influence their child's views, perspectives, and responses. Therefore, this further expresses the need for research to gain the perspectives of children and adolescents with MD for motivators and barriers to hydrotherapy participation. This will allow for further studies to compare and understand differences in views for the best way to optimise future study designs, recruitment, and attendance.

8.3 Motivators and Barriers to Participation

Overall, most motivators for participation in hydrotherapy in the present study considered child needs. This is consistent with previous research that for parent-reports defined child needs as motivators that "address the child's motor skill and psychological needs" (Brown et al., 2022) and for child-reports were personal motivators relating to the child themselves (Shields et al., 2012). Interestingly, only parents' perspectives reported any programme and policy motivators, while only children (via parents) reported any environmental motivators, likely due the child physically using the facilities compared to parents, which was also consistent with Shields et al. (2012).

Regarding barriers within the present study, children's perspectives (based on parents' views) focused more on personal factors to themselves, whereas parents' own perspectives focused more on social and environmental factors. This is consistent with previous research, where parents predominantly focused on "social, policy and programme barriers or on their own involvement" and children predominately focused on "personal, peer-related and environmental barriers" (Shields et al., 2012).

It has been acknowledged that focusing on barriers and motivators separately has previously been recommended, where barriers can "isolate and address the diverse challenges encountered by

individuals who may otherwise be willing and able to participate" and motivators can explore approaches to allow for the greater capacity for and interest in participation" (Peay et al., 2018). However, due to the nature of responses, these were presented together to gain and understand the weight of each perspective because some factors had the same base idea but opposing views. This highlights the complexity of barriers and motivators in MD, as well as the individuality of each response.

8.3.1 Addressing Child's Needs

8.3.1.1 Delaying Muscular Dystrophy Progression

The use or expectation of hydrotherapy for slowing down MD progression in their child through stretching, strengthening muscles, and improving mobility was the most frequent parent-reported motivator to participation in Study 2. Two children (via their parents) did report similar motivations, however, were less specific, only stating they wanted to take part to "help slow down problems caused by Duchenne". Similarly, 12-to-18-year-olds with cerebral palsy reported that improvements to muscle strength, agility, mobility, weight, and prolonged life via reducing heart disease, facilitated their choice to partake in physical activity (Conchar et al., 2016).

These findings could be attributed to parents and children (with childhood-onset disabilities) being more likely to participate in clinical trials, interventions, and physical activity, if there was evidence of or potential health improvements for their child (Mckenzie et al., 2021). A potential to improve health means that parents have hope for their child. Whilst hope and optimism can be beneficial, parents must be careful not to misestimate the benefits or risks (Peay et al., 2014). Additionally, caution must be used when comparing previous studies with barriers and motivators for MD because the majority of clinical populations investigated are cerebral palsy. Although similar to MD regarding muscle weakness and having no cure, cerebral palsy is non-progressive (Hendriksen et al., 2016) and MD is progressive (Cardamone et al., 2008), making it harder to determine the

maintenance of function. This was reinforced in Study 1 (*5.3.1 Defining a delay in progression*), where small decreases in function indicated maintenance (Silva et al., 2012) but no set definition of a delay in progression was available. Therefore, this means that managing expectations of parents and children with MD is important, since misinformation or hope could hinder individuals' willingness to participate in clinical trials if children constantly do not appear to be improving (Peay et al., 2014).

Additionally, this suggests that if there are no guarantee of benefits then parents may be hesitant or unwilling to join intervention studies, as seen in a study by Peay et al. (2018) who found that 97.1% of parents considered dropping out if the child with Duchenne or Becker MD was placed into a placebo group. Additionally, any doubts about the importance and/or effects of physical activity was found to hinder participation (Sandström et al., 2009). Since the use of hydrotherapy for MD has not been widely investigated, there is limited evidence and no NHS NICE guidelines available to justify its use for the maintenance of health in children with MD (Lombardo et al., 2021), making it harder to recruit for studies until further research on the use of hydrotherapy for MD is published. Thus, reaffirming the importance of Study 1 for future studies. To enhance recruitment in future MD studies, ensuring clinicians are transparent about current guidelines and the current position of research, and relay all appropriate information is required.

Interestingly, Participant 2 in Study 1 reported that how he "liked helping other people", suggesting his and his parents may have participated in the study to help raise awareness of the use of hydrotherapy for other children with MD. Altruism has commonly been used to explain motivation throughout multiple studies although recent literature suggests more parents focus on the benefits to their child instead of the whole clinical population (Engster et al., 2016; Peay et al., 2014). Notably, Peay et al. (2018) stated that social desirability bias, due to the study using ranking questionnaires, could influence them to mention altruism as a factor to not look bad. This could mean that participants

in this study were not true in their rankings. However, altruism was not reflected within the responses in Study 2, which is surprising due the close community of parents with children suffering from MD.

8.3.1.2 Relaxation and Pain-Relief

Perceptions of improved relaxation, pain, and comfort within hydrotherapy, motivated participation in the present study. These factors were more frequently reported when parents considered their child's perspective compared to their own perspective (9 reports > 6 reports, as shown in Figure 11 and 12). Only two studies investigating barriers and motivators, and one study investigating barriers only for aquatic therapy or exercise were found. Of these two, adults in one study reported pain-relief as a benefit and motivator to participation (Fisken et al., 2012). Additionally, the feeling of water against muscles and joints (kinaesthetic) reported by one parent in the present study, and warmth of the water reported by children (via parents) were motivators for hydrotherapy participation, that further contribute to that of pain-relief, comfort, and relaxation. Given that warm water allows the core temperature to increase, reducing gamma fibre and muscle spindle activity, it allowed muscle to relax and reduce high tone and spasticity in children with cerebral palsy (Adar et al., 2017). Buoyancy provides a safer environment that reduces load and thus susceptibility to injuries, promoting relaxation and reducing stiffness and pain (Mooventhan & Nivethitha, 2014; Wratten et al., 2019). Additionally, the belief that land-based exercise can promote relaxation in children and adolescents with cerebral palsy was found as a motivator for participation in interventions (Verschuren et al., 2012). This can be attributed to a release of physical tension or a distraction from stressors that may be causing frustration and anger (Conchar et al., 2016).

However, other land-based studies found that participation was reduced after the perception or experiences of physical activities and interventions being dangerous, uncomfortable, painful, and causing significant tiredness that can be exacerbated with the use of assistive devices (e.g., orthoses) (Conchar et al., 2016; Lauruschkus et al., 2015; Mckenzie et al., 2021). This was supported by Engster

et al. (2019) who found concerns about discomfort for their child prevented 52.0% of parents from participating. Understandably, research on Duchenne and Becker MD found that 98.1% of parents would not allow participation to occur if the risks of participation outweighed the benefits (Peay et al., 2018). This affects how individuals, who have never experienced hydrotherapy, may perceive a new therapy, therefore future studies should provide awareness and further research should be developed to support the use of hydrotherapy as a mediator for preventing pain experienced on land, which could be a first step into increasing participation.

8.3.2 Enjoyment versus Boredom

Enjoyment and fun are key to retaining on-going attendance and participation in physical activity for young people (Wright et al., 2018). When considering their child's perspective, three parents' responses in the present study highlighted that hydrotherapy sessions that were fun and enjoyable, maintained or encouraged participation (Figure 12). Previous research supports our findings, where children aged 8-11 years old found fun sessions kept them engaged in activities (Lauruschkus et al., 2015) and provided a sense of competence or success (Shields & Synnot, 2016). Unlike physical activity, attending clinical interventions or therapy sessions, such as physiotherapist-led hydrotherapy, can often be perceived as if children are obligated to attend sessions. To combat this, research suggests that finding out what children and adolescents want to do, adapting them to their current skill or ability, and using sessions to build "confidence, competence, sense of achievement and capacity", will encourage interventions to be fun and successful (Rosenbaum & Gorter, 2012).

In the present study, 75.0% of children with MD were interested in and/or currently motivated to participate in hydrotherapy, as reported by their parents (Figure 9a and 10d). This was similar to 94.3% of children wanting to participate, being a motivator for their parents to bring them to sessions (Peay et al., 2018). Motivation was found to be complex, being influenced by peer groups, body

perceptions, and what individuals believed were fun (Cleary et al., 2019). For example, competitive fun may be enjoyable for some children (Shimmell et al., 2013) but may diminish if skills and function continue to worsen, especially compared to children with lower degrees of severity or healthy peers (Lauruschkus et al., 2015). This may reduce the willingness to be competitive (Conchar et al., 2016), because it would cause a sense of frustration or loss of confidence, and thus contribute to being unmotivated to participate (Papadopoulos et al., 2020). Often as children age, their priorities change, so something they may have once found fun may become boring (Mckenzie et al., 2021; Shields & Synnot, 2016; Wright et al., 2018). It is unlikely that hydrotherapy sessions provided by physiotherapists are competitive, however providing a solution to incorporate an aspect of competition may accommodate to more children. Therefore, practitioners within future studies would have to get to know the children within the group to be able to provide engaging interventions for them.

8.3.3 The Presence of Friends

Fun sessions were attributed to friends, friendly people, supervisors with knowledge on their condition and a supportive social network amongst young people with disability, aged 3-17 years, and their parents (Greenberg et al., 2018; Wright et al., 2018). The presence of friends or peers, and feeling of acceptance, in individuals with neuromuscular diseases when partaking in physical activities (Fisken et al., 2012; Lauruschkus et al., 2015; Verschuren et al., 2012) or intervention programs (Teo et al., 2022) facilitates participation. This increased motivation to participation can be attributed to the supportive atmosphere that comes with a sense of belonging or connection with a group (Conchar et al., 2016). Interestingly, this was less reported in the present study with only one child with MD (reported through their parent) stating that the company of friends in hydrotherapy group sessions facilitated their participation; and one parent reporting that the opportunity for their child to form lasting close bonds with other children with MD facilitated participation in

hydrotherapy. This suggests that other barriers and motivators play more of an influence than the influence of friends do for the children with MD represented within the study.

Since hydrotherapy could potentially be done alongside their peers, it is interesting that few respondents mentioned the presence of friends. Although this could be due to sessions prescribed by physiotherapists not allowing friends and family to join alongside them, or the reduced sample in Study 2 when compared to previous research. Conversely, a lack of support from friends and family was found as an equally frequent barrier between adults with neuromuscular diseases (including MD) and healthy controls (Phillips et al., 2009). If a child struggles to make friends or does not know anyone in the group, they may feel as if they do not fit in and may be unmotivated to attend hydrotherapy sessions. Additionally, older children preferred to spend their free time with their friends and were more reluctant to participate for this reason (Greenberg et al., 2018). This was seen in Study 1 where one participant rejected participation in hydrotherapy due to fear of being a lot older than the other children, meaning he may have been discouraged by his higher severity of Duchenne MD. His increase in age likely meant he had reduced function, abilities, and skill levels than those younger with Duchenne MD (Mckenzie et al., 2021; Shields & Synnot, 2016), whereby as an older non-ambulant child, he may not have wanted to participate alongside younger ambulant children (Guzmán et al., 2012). Therefore, ensuring there is an opportunity to make friends of similar ages and abilities may help to facilitate recruitment to and attendance in hydrotherapy sessions. A consideration for future studies would be to have smaller age-related groups if there is a wide age range and ensure information sheets reflect this so that participants are aware. This may reassure children that they are likely to be placed with other children they may relate to more, which in MD may be important for older children. Future studies should also assess the feasibility of including friends and/or family in hydrotherapy sessions, as this may be a useful incentive to increase participation amongst children with MD.

8.3.4 Self-Esteem

Five parents in Study 2 stated that their child expressed a reluctance to participate in hydrotherapy, due to reasons associated with reduced self-esteem, such as body image and co-morbidities (like autism and anxiety) hindering their confidence, as supported by Teleman et al. (2021). This is consistent with children and young people predominately identifying self-restrictions as a barrier, including low self-esteem and a lack of motivation (Wright et al., 2018). Although in healthy young adults, body image was found to directly affect sports participation (effect value 0.124) (Ouyang et al., 2020). However, one reason children with MD may have low self-esteem and confidence could be due to physical effects associated with medications for and progressions of disease. For example, steroid medications may contribute to weight gain (Birnkrant et al., 2018b), scoliosis may affect body shape (Archer et al., 2016) and scars may be present from surgeries (Birnkrant et al., 2018a). This may contribute to a lack of body positivity and hinder the child's willingness to participate. A similar scenario was found during Study 1 of this thesis when there was difficulty with collecting data from a measure, as the child did not feel comfortable with removing his shirt. A solution to this may be to allow children to wear tops in the pool, however this can also have an adverse effect by drawing attention to them, equally stopping participation. For rare populations that face numerous barriers, gaining confidence to overcome those barriers (barriers self-efficacy) is important for maintaining participation (Mailey et al., 2016). This suggests that self-esteem is a reoccurring factor of everyday life that may hinder participation, especially in males with Duchenne MD during hydrotherapy. Therefore, future studies should aim to educate children with MD about the natural progression of their disease and encourage confidence through group sessions, such as hydrotherapy, to create that base of support so they have friends, family and clinicians helping them to overcome their personal barriers.

8.3.5 Illness, Surgery and Covid-Shielding

The explanations of missed hydrotherapy sessions amongst parents of participants in Study 1, including their child recovering from recent surgery, their child or themselves being ill and/or their family isolating from COVID-19, is consistent with findings of the parent-reports in Study 2 (see Figure 10a). Given that individuals with MD are more susceptible to illness, infections, such as pneumonia (Carannante et al., 2021), and may require more surgeries, due to fluctuating health (Cleary et al., 2019), these findings are important to consider when recruiting and designing for studies. Previous studies rarely reported illness and surgery as a barrier, however the resulting medical appointments that may be required and/or recovery period after surgery have been found to prevent participation (Cleary et al., 2019). Therefore, future studies should overestimate the sample size required to account for dropouts, not expect full attendance, and consider offering multiple sessions a week to give parents a greater choice of available sessions.

Additionally, recent circumstances also proved to be a barrier to participation. During the COVID-19 pandemic, many hydrotherapy pools across the UK were temporarily closed during lockdown in from 2020 to 2021, however many of the NHS pools remained closed for a longer period of time, despite the potential of pool chemicals eliminating the virus (Chartered Society of Physiotherapy, 2022). This mean many individuals who benefit from and require hydrotherapy were unable to receive it, decreasing participation and potentially causing a loss in motor function and skills that may make it so that children find it harder to begin participation in sessions again, due to decreased self-esteem. This is supported by 44.4% of children stopping or decreasing attendance to hydrotherapy sessions since the pandemic in the present study. Further research into attendance post-pandemic may be required, as understanding reasons why, i.e., is there a fear of returning, and finding ways to reassure families post-pandemic may be of importance.

8.3.6 Time Constraints, Fatigue and Familial Responsibilities

Parents themselves were a huge influence in facilitating and/or hindering their child's ability to participate in physical activities and therapeutic interventions. For example, the parents' willingness and ability to invest time, energy, and resources were found to influence attendance and participation (Conchar et al., 2016). An issue is that parents often become too busy and are put under pressure to balance "the competing priorities and commitments" between the parent who may be working and looking after their other children, and the children who may require assistance with daily tasks and getting to pre-existing therapy, appointments, or other activities (Wright et al., 2018). Therefore, fatigue and a lack of time are factors that may affect parents and prevent their children from attending sessions, such as hydrotherapy.

The present study found four parents (25.0%) reported that a lack of time hindered hydrotherapy session attendance in children with MD, due to school and other therapies for their child, family events, and family responsibilities (e.g., having other children to look after). This was consistent with research on organised physical activity, where 22.0% of parents, with children suffering from neurodevelopment, physical and medical conditions, had limited time to attend sessions (Papadopulous et al., 2020), likely due to difficulty fitting physical activity into the family schedule (Shields & Synnot, 2016; Shimmell et al., 2013). However, within clinical research for paediatric health, including those with Duchenne and Becker MD, a greater percentage of parents, between 39.0% (Engster et al., 2019) and 49.3% (Peay et al., 2018), reported that participation would take too much time. This suggests a difference in participation rates between clinical trials and physical activity groups. Interventions as part of clinical trials may be viewed as interrupting parents' and children's everyday routines, as supported by Peay et al. (2018) who found this would hinder participation by 95.2%. When combined with a long-term time commitment, no promise of treatment after, and the general logistics of their child participating, this further reduces parents' willingness to participate (Peay et al., 2014), especially in MD where fluctuations in their child's health may occur.

Although, commitment is needed for physical activity and therapy sessions, it is more likely individuals would participate if they were going to received something proven to be beneficial in some way.

For parents with multiple children, having to fit sessions into the family schedules and not having personal time off, can prevent children's participation and add to the feeling of exhaustion and fatigue of the parent (Shields & Synnot, 2016). This supports the present study where two parents reported feeling fatigued. This may also explain why some sessions is Study 1 were missed, as busy schedules of the parents were apparent in which they all had multiple children and often didn't want their child to miss out on important family events. This suggests that more flexibility in sessions or multiple sessions need to be offered.

8.3.7 Costings

Financial constraints are important barriers that parents and carers must consider, which subsequently hinder a child's ability to participate in physical activities and exercise (Shields et al., 2012; Shields & Synnot, 2016). In the present study, 68.8% of parents were unaware of the cost of hydrotherapy, however 56.3% of parents stated that an average price of £15 for a 30-45-minute session would not prevent them from taking their child to hydrotherapy sessions. This differs from a study of adults who stated that £14.55 (US $18) per session was too expensive for them and may be why the uptake of hydrotherapy was lower (Fisken et al., 2012). Differences in these studies may be due to parents getting hydrotherapy for their child in order to delay their MD progression, compared to healthy adults using it just as a form of exercise. However, it is often a combination of costs, such as requiring equipment and transport for hydrotherapy sessions, and paying for activities for other children, that often creates barriers to participation (Pourghane, 2017). This is supported by previous literature stating that it "comes down to affordability", where parents have to consider the additional expense of caring for a child with disability, parental income, attention for their child, and other

children (Shields & Synnot, 2016). This suggests that costs of intervention sessions and additional expenses for some families may be too expensive, which may deter parents from letting their child access hydrotherapy.

Interestingly, parents were aware that hydrotherapy sessions for children in Study 1 were funded, yet attendance rates still greatly varied from .25.0% to 89.3%. This is inconsistent with the perceived facilitator of participation, where 93.3% of parents with children with Duchenne and Becker MD stated they would take part in sessions if they were free (Peay et al., 2018). This suggests that while cost is an important consideration, other barriers may play more of a significant factor in preventing participation. Therefore, practitioners in therapeutic interventions should consider making sessions subsidised or have a flexible payment schemed. This gives the sessions a sense of worth and makes them more affordable, encouraging commitment while having a form of consequence if they do not turn up without given notice, as supported by Shields and Synnot (2016).

8.3.8 Accessibility, Independence, and Facilities

In previous studies, accessibility and facilities were found to be motivators and barriers to participation. For example, research into hydrotherapy for elderly ladies found that the limited number of appropriate pools available for hydrotherapy, alongside difficulty with entering the pool, was found as a barrier to hydrotherapy (Pourghane, 2017). A lack of facilities was reported by one parent in Study 2, which could be attributed to 50.0% of parents not being aware of hydrotherapy pools near them in the same study (see Figure 8). Combined with the limited facilities available, the distance needing to travel to sessions also prevents participation and hinders recruitment (Shields & Synnot, 2016; Shimmer et al., 2013). Four parents in the present study reported distance as a barrier to taking their child to hydrotherapy sessions. This is support by 93.3% of parents in Peay et al. (2018) only willing to drive a maximum of one hour to activities for their child with MD. Thus, the nearest hydrotherapy pools should be readily available for communities and families to find online, however

the lack of guidelines for the use of hydrotherapy in specific clinical populations like MD may be why the centres are currently difficult to find.

Previously, children reported that not being able to be independent and having to rely on others, although not always getting the help they need, deterred them from wanting to participate in activities (Lauruschkus et al., 2015). Hydrotherapy pools allowed non-ambulant individuals to participate in sessions. Since physical aids were required by 68.8% of children with MD in our study, with most using a wheelchair (62.5%) of which 43.7% were non-ambulant, having an environment that is inclusive of their condition would not prevent them from attending these sessions. When considering their child's perspective, parents reported that independence, achieved from not requiring a wheelchair in the hydrotherapy pool was a motivator, as in parents' word children felt that they could freely move in the water with limited assistance. This can be attributed to the buoyancy of the water in hydrotherapy proving support that non-ambulant individuals would not have on land, as a result of Archimedes's Principle, whereby at rest in pool of water, apparent weight loss is equal to the weight of the displaced fluid (Wratten et al., 2019). This reduces pressure off the joints, bones, and muscles giving the feeling of moving freely (Mooventhan & Nivethitha, 2014). Therefore, along with Study 1, this further encourages the use of hydrotherapy for increasing participation amongst children with MD.

8.3.9 Information and Education Surrounding Hydrotherapy

Receiving proper instructions on the structure of sessions was also found to facilitate participation for one parent. Seven people had not been offered hydrotherapy before, so it can be suggested that they were not given sufficient information regarding instructions on how sessions work or the purpose of hydrotherapy. This may decrease the willingness of parents allowing their child to participate. This is supported by recent research in elderly women finding that insufficient knowledge on the advantages of and doubting the effectiveness of hydrotherapy was a barrier to participation

(Pourghane, 2017). However, 89.0% of parents found that overabundance and complexity of information made it difficult to understand and deterred them from agreeing for their child to participate in interventions (Bendixen et al., 2016). Thus, balancing the amount of information for interventions and physical therapies is important. This is a consideration for future studies. Notably, in Study 2, one parent reported that they would prefer their child to take part in hydrotherapy sessions rather than private swimming lessons because £15 would be more cost-effective and beneficial. Swimming lessons and hydrotherapy sessions provide very different things, highlighting the need for further education of the purpose of hydrotherapy. Further research is needed to educate parents and their children on the effects of hydrotherapy for the maintenance, not improvement, of progression in children and adolescents with MD.

8.4 Limitations

Previous research suggested the importance of separating motivators and barriers of participation for better and clearer explorations of approach to motivators and solutions to challenges (Peay et al., 2018). However, a statement involving a motivator often had the opposite opinion as a barrier and vice versa. Additionally, factors were shown to be complex in nature as seen through the interaction and overlap of child needs (personal factors to the child), personal (parent) needs, social, environmental, and policy and programme factors, as supported by Abid et al. (2022), Brown et al. (2022) and Shimmell et al. (2013). This is consistent with the SCT, whereby a combination of these factors impacts participation (Brown et al., 2022). Therefore, finding a balance between inhibiting and enabling factors for participation is important (Mckenzie et al. 2021) to optimise recruitment and participation in hydrotherapy for MD.

Several open-ended responses to questions within the questionnaire in Study 2 did not provide a great depth or insight into barriers and motivators for hydrotherapy participation. This could be attributed to a lack of time, as reported by parents as a barrier to participation. Parents often are busy

with other familial responsibilities and jobs they undertake daily (Shields & Synnot, 2016; Shimmell et al., 2013), thus may be tired and fatigued by the end of the day. Based on this, it could be suggested that a lack of time contributed to parents not being able to complete the questionnaire and/or open-ended questions, meaning a full perception may not have been achieved. Additionally, it is likely that respondents to the questionnaire in Study 2 are already more motivated to participate in research and management interventions compared to other parents who may be less willing or unable to participate. Recent research found that questionnaires are more commonly completed by parents who are more active within research and the MD community (Bendixen et al., 2016). This suggests that barriers and maybe some motivators to participation for hydrotherapy may have been overlooked. This can further be seen in the difference in number of coded words (shown in Figures 11-14) compared to the number of findings from other studies (Shields et al., 2012). A follow-up interview should have been completed to gain further insight, however due to time restrictions of this being a follow-up study, we were unable to complete this. Future studies should consider combining a questionnaire and follow-up interview to gain the deepest amount of insight.

Notably, Study 2 had difficulty with recruitment for and participation in the online questionnaire, with only 16 responses even though the study was advertised on social media and MD support groups for approximately three months. There is difficulty with recruiting samples from small populations (Bendixen et al., 2016), including MD, making it difficult for the evaluation of effectiveness of studies and generalisation of results. Based on results from Carey et al. (2021), in 2019 children aged 19-years-old and under only made up 0.07% of the UK population. Therefore, whilst the sample size is relatively small, it is more reasonable for a limited population, compared to a study using a healthy population to which a larger sample can be drawn.

8.5 Implications

Findings within Study 1 established that the overall recruitment and attendance rates of children and adolescents with MD was poor. The results from the present study suggest that there are an abundance of motivators and barriers and therefore several possible solutions that could be addressed and/or implemented into future study designs to increase participation in children and adolescents with MD. Given that Study 2 investigated parents' perspectives due to their significant influence on their child's participation (Conchar et al., 2016; Shields & Synnot, 2016), older children's perspectives may deviate more and so further research into barrier and motivators specifically in children need to be investigated. Along with parents' perspectives of their child's views, we know that involving family and friends, and giving children with MD more say in their therapy interventions, could increase their interest in participating in therapeutic interventions. Additionally, the study agrees that barriers and motivators have significant implications of the wider community, by providing information to improve research designs, we can facilitate the production of appropriate resources and provide support to families who have a child with MD (Shields & Synnot, 2016; Mckenzie et al., 2021)

Collectively, findings of a lack of time, fatigue, misinterpretation, accessibility, lack of knowledge and family responsibilities indicate that parents are constantly under a lot of pressure to balance their everyday lives with their child's. Implementing strategies to reduce some of this pressure may show parents that it is possible for their child to join long-term hydrotherapy studies. Future studies should seek to (1) provide further education on the realistic expectations of hydrotherapy for the maintenance of MD, (2) determine the feasibility of involving family and friends in therapy, (3) assess participation amongst MD post-pandemic, and (4) use barriers and motivators identified in Study 2 to improve the design of a studies similar to Study 1 that must further investigate the longitudinal effects of hydrotherapy on respiratory, biomechanical, and psychological function.

Chapter 9.0: Conclusion

This thesis was comprised of two studies, that provided useful insight into 1) respiratory function, muscle strength and wellbeing prior to hydrotherapy, and 2) potential barriers and motivators to participation. Except for mean biceps muscle strength, our data suggests that MIP, MEP, diaphragm thickness, quadriceps strength, and wellbeing investigated in Study 1 were maintained and/or improved in two children with Duchenne MD after 40 weeks of hydrotherapy. However, due to case study design and the lack of control group, there is hesitation with attributing these findings to hydrotherapy and generalising results to children and adolescents with MD in the wider population. Given that death can occur with more severe types of MD, usually from respiratory failure resulting from muscle weakness, these findings are important as could indicate that hydrotherapy may contribute to a delay in the progression of MD. However, this cannot be firmly concluded due to the lack of control group, in which caution must be used with our results in Study 1 as any changes in data over time could not be compared to no intervention. We were the first study to objectively monitor the effects of 40 weeks of hydrotherapy on respiratory function, muscle strength and wellbeing within a single study. Thus, future research is required to develop this study and define a delay in progression, which in turn should aim to inform NHS NICE guidelines for the use of hydrotherapy for halting the progression of MD.

Study 1 gave brief explanations for the reduced attendance and missed sessions amongst participants, including illness (COVID-19), fatigue, family events, recovering post-surgery, and recurrent injury. Using this information and the results in Study 1, Study 2 was able to further explore the barriers and motivators that may have contributed to the poor recruitment rates and attendance. We were the first study to investigate barriers and motivators to participation in hydrotherapy for children and adolescents with MD. It was stressed that all ‘child’ and parent responses in Study 2 were reported from the parents’ perspectives only. Thus, further research is needed to confirm the

'child-reported' motivators and barriers, due to potential oversights that may have occurred. Once children with MD's perspectives are gaining, this should be combined with parent perspectives to best optimise future study designs, recruitment, and attendance.

A combination of environmental, social, and personal/child needs factors were found to impact participation, consistent with the SCT, however factors were shown to be complex in nature due to their ability to overlap and interaction with one another. Parents reported wanting to slow MD progression as their main motivator for hydrotherapy, yet an inability to distribute their time and cover distances were their main barrier to participation. When considering their child's view parents reported fun and independence as the main motivator but low self-esteem as their main barrier. While solutions on how to address barriers and reinforce motivators were discussed, the starting solution is to construct and apply a better designed study to improve the uptake of participation in hydrotherapy, that can then be used to determine its effects on respiratory function, muscle strength, and overall wellbeing in children and adolescents with MD. We suggest this could be achieved through future studies offering subsidised hydrotherapy sessions for children with MD to reduce the barrier of cost, multiple interventions sessions at different times throughout the week to reduce the pressure on parents and give them more flexibility, and sessions for smaller age ranges to increase children's comfort and confidence when in a group. Long-term solutions should consider creating a way for parents to easily locate and access hydrotherapy pools near to them, however this would be dependent on whether hydrotherapy is found to contribute to the delay in MD progression.

Although strategies to increase attendance and participation must be implemented in future designs, studies should account for dropouts and not except full attendance during the study, due to flare ups in symptoms, susceptibility to illness and injury, and increased fatigue. Thus, multiple data collections sessions over a few days should also be offered to optimise future study designs to account for these. We recommend that future studies also monitor the effects of fatigue through a standardised

outcome measure, as it was found as a factor that may have impacted performance, participation, and HRQoL in both Study 1 and 2. Additionally, Study 1 and Study 2 both highlighted the need for better standardisations of methods and procedures across research studies, to better inform meta-analysis in further research and better reflect usual care in everyday healthcare practice. To achieve this is it of upmost importance that a definition of a delay in MD progression is investigated. Despite the flaws that have been acknowledged, this thesis highlights the potential contribution that long-term hydrotherapy may have for managing MD in children and adolescents and provides direction for future study designs.

References

Abid, M., Cherni, Y., Batcho, C. S., Traverse, E., Lavoie, M. D., & Mercier, C. (2022). Facilitators and barriers to participation in physical activities in children and adolescents living with cerebral palsy: a scoping review. *Disability and Rehabilitation,* 1-16. https://doi.org/10.1080/09638288.2022.2150327

Abo-zaid, N. A., Khalifa, H. A., Ali, F., Abdelsamee, M. A. A., & Heneidy, W. E. (2021). Effect of Aquatic Therapy on Ventilatory Functions in patient with Duchenne Muscular Dystrophy: A randomized Controlled Trial. *Fizjoterapia Polska*, *21*(1), 206-214. https://fizjoterapiapolska.pl/hr/article/wplyw-terapii-wodnej-na-funkcje-oddechowe-u-pacjentow-z-dystrofia-miesniowa-duchennea-randomizowane-badanie-kontrolowane/

Adams, S., Hutton, S., Janszen, A., Rawson, R., Sisk, C., Stenger, S., & Ennis, B. (2017). Effects of an 8-week individualized aquatic therapy program on respiratory muscle function and quality of life in adolescents with Muscular Dystrophy. *The Journal of Aquatic Physical Therapy, 25*(2), 35-42. https://journals.lww.com/japt/Abstract/2017/25020/Effects_of_an_8_Week_Individualized_Aquatic.7.aspx

Adar, S., Dündar, Demirdal, Ü. S., Ulaşlı, A. M., Toktaş, H., & Solak, Ö. (2017). The effect of aquatic exercise on spasticity, quality of life, and motor function in cerebral palsy. *Turkish Journal of Physical Medicine and Rehabilitation, 63*(3), 239-248. https://doi.org/10.5606/tftrd.2017.280

An, J., Lee, I., & Yi, Y. (2019). The thermal effects of water immersion on health outcomes: An integrative review. International Journal of Environmental Research and Public Health, 16(7), 1280-1301. https://doi.org/10.3390/ijerph16071280

Andrews, J. G., & Wahl, R. A. (2018). Duchenne and Becker muscular dystrophy in adolescents: current perspectives. *Adolescent Health, Medicine and Therapies, 8*(9), 53-63. https://doi.org/10.2147/AHMT.S125739

Archer, J. E., Gardner, A. C., Roper, H. P., Chikermane, A. A., & Tatman, A. J. (2016). Duchenne muscular dystrophy: the management of scoliosis. *Journal of Spine Surgery, 2*(3), 185-194. https://doi.org/10.21037/jss.2016.08.05

Atamturk, H., & Atamturk, A. (2018). Therapeutic effects of aquatic exercises on a boy with Duchenne muscular dystrophy. *Journal of Exercise Rehabilitation, 14*(5), 877-882. https://doi.org/10.12965/jer.1836408.204

Bairapareddy, K. C., Augustine, A., Alaparthi, G. K., Hegazy, F., Shousha, T. M., Ali, S. A., Nagaraja, R., & Chandrasekaran, B. (2021). Maximal Respiratory Pressures and Maximum Voluntary Ventilation in Young Arabs: Association with Anthropometrics and Physical Activity. *Journal of Multidisciplinary Healthcare, 14*(1), 2923-2930. https://doi.org/10.2147/JMDH.S333710

Baldwin, C. E., Paratz, J. D., & Bersten, A. D. (2011). Diaphragm and peripheral muscle thickness on ultrasound: Intra-rater reliability and variability of a methodology using non-standard recumbent positions. *Respirology, 16*(7), 1136-1143. https://doi.org/10.1111/j.1440-1843.2011.02005.x

Ballington, S. J., & Naidoo, R. (2018). The carry-over effect of an aquatic-based intervention in children with cerebral palsy. African Journal of Disability, 7(0), 361-369. doi:10.4102/ajod.v7i0.361

Basta, M., & Pandya, A. M. (2022). *Genetics, X-Linked Inheritance*. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK557383/#_NBK557383_pubdet_

Becker, B. E. (2011). Biophysiologic Aspects of Hydrotherapy. In B. E. Becker & A. J. Cole (Eds.)., *Comprehensive Aquatic Therapy* (3rd ed.) (pp 23-61). Pullman: Washington State University Publishing.

Bendixen, R. M., Lott, D. J., Senesac, C., Mathur, S., Vandenborne, K. (2014). Participation in daily life activities and its relationship to strength and functional measures in boys with Duchenne muscular dystrophy. *Disability and Rehabilitation, 36*(22), 1918-1923. https://doi.org/10.3109/09638288.2014.883444

Bendixen, R. M., Morgenroth, L. P., & Clinard, K. L. (2016). Engaging Participants in Rare Disease Research: A Qualitative Study of Duchenne Muscular Dystrophy. *Clinical Therapeutics, 38*(6), 1474-1484. https://doi.org/10.1016/j.clinthera.2016.04.001

Bendixen, R. M., Senesac, C., Lott, D. J., & Vandenborne, K. (2012). Participation and quality of life in children with Duchenne muscular dystrophy using the International Classification of Functioning, Disability, and Health. *Health and Quality of Life Outcomes, 10*(1), 1-9. https://doi.org/10.1186/1477-7525-10-43

Bérard, C., Payan, C., Hodgkinson, I., Fermanian, J., & The MFM Collaborative Study Group. (2005). A motor function measure scale for neuromuscular diseases. Construction and validation study. *Neuromuscular Disorders*, *15*(7), 463-470. https://doi.org/10.1016/j.nmd.2005.03.004

Bertini, E., D'Amico, A., Gualandi, F., & Petrini, S. (2011). Congenital Muscular Dystrophies: A Brief Review. *Seminars in Pediatric Neurology, 18*(4), 277-288. https://doi.org/10.1016/j.spen.2011.10.010

Bieuzen, F. (2013). Water-Immersion Therapy. In C. Hausswirth & I. Mujika (Eds.), *Recovery for Performance in Sport* (pp. 191-199). Human Kinetics.

Birnkrant, D. J., Bushby, K., Bann, C. M., Alman, B. A., Apkon, S. D., Blackwell, A., Case, L. E., Cripe, L., Hadjiyannakis, S., Olson, A. K., Sheehan, D. W., Bolen, J., Weber, D. R., & Ward, L. M. (2018a). Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *The Lancet Neurology*, *17*(4), 347-361. https://doi.org/10.1016/S1474-4422(18)30025-5

Birnkrant, D. J., Bushby, K., Bann, C. M., Apkon, S. D., Blackwell, A., Brumbaugh, D., Case, L. E., Clemens, P. R., Hadjiyannakis, S., Pandya, S., Street, N., Tomezsko, J., Wagner, K. R., Ward, L. M., & Weber, D. R. (2018b). Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *The Lancet Neurology*, *17*(3), 251-267. https://doi.org/10.1016/S1474-4422(18)30024-3

Birnkrant, D. J., Bushby, K., Bann, C. M., Apkon, S. D., Blackwell, A., Colvin, M. K., Cripe, L., & Herron, A. R. (2018c). Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. *The Lancet Neurology*, *17*(5), 445-455. https://doi.org/10.1016/S1474-4422(18)30026-7

Bonne, G., Leturcq, F., & Ben Yaou, R. (2019). Emery-Dreifuss Muscular Dystrophy. *GeneReviews*. https://www.ncbi.nlm.nih.gov/books/NBK1436/

Boon, A. J., Sekiguchi, H., Harper, C. J., Strommen, J. A., Ghahfarokhi, L. S., Watson, J. C., & Sorenson, E. J. (2014). Sensitivity and specificity of diagnostic ultrasound in the diagnosis of phrenic neuropathy. *Neurology*, *83*(14), 1264-1270. https://doi.org/10.1212/WNL.0000000000000841

Bourke, J. P., Bueser, T., & Quinlivan, R. (2018). Interventions for preventing and treating cardiac complications in Duchenne and Becker muscular dystrophy and X-linked dilated cardiomyopathy. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD009068.pub3

Brandsema, J. F., & Darras, B. T. (2020). Dystrophinopathies. In R. N. Rosenberg & J. M. Pascual (Eds.), *Rosenberg's Molecular and Genetic Basis of Neurological and Psychiatric Disease* (6th ed.) Volume 2 (pp. 511-523). Academic Press. https://doi.org/10.1016/B978-0-12-813866-3.00024-2

Bray, P., Bundy, A. C., Ryan, M. M., North, K. N., & Everett, A. (2010). Health-related quality of life in boys with Duchenne Muscular Dystrophy: Agreement between parents and their sons. *Journal of Child Neurology*, *25*(10), 1188-1194. https://doi.org/10.1177/0883073809357624

Broomfield, J., Hill, M., Guglieri, M., Crowther, M., & Abrams, K. (2021). Life Expectancy in Duchenne Muscular Dystrophy: Reproduced Individual Patient Data Meta-analysis. *Neurology*, *97*(23), 2304-2314. https://doi.org/10.1212/WNL.0000000000012910

Brown, K. K., Smith, J., Bailey, T. N., Ortiz, G., Gu, X., & Tamplain, P. (2022). Parent-Reported Motivators and Barriers to Participation in a Community-Based Intervention Designed for Children with Motor Skill Difficulties: A Qualitative Program Evaluation. *Adapted Physical Activity Quarterly*, *39*(1), 109-128. https://journals.humankinetics.com/view/journals/apaq/39/1/article-p109.xml

Brussock, C. M., Haley, S. M., Munsat, T. L., & Bernhardt, D. B. (1992). Measurement of Isometric Force in Children with and without Duchenne's Muscular Dystrophy. *Physical Therapy, 72*(2), 106-114. https://doi.org/ 10.1093/ptj/72.2.105

Buffart, L. M., Westerndorp, T., van den Berg-Emons, R. J., Stam, H. J., & Roebroeck, M. E. (2009). Perceived barriers to and facilitators of physical activity in young adults with childhood-onset physical disabilities. *Journal of Rehabilitation Medicine, 41*(11), 881-885. https://doi.org/10.2340/16501977-0420

Bushby, K., & Connor, E. (2011). Clinical outcome measures for trials in Duchenne muscular dystrophy: report from International Working Group meetings. *Clinical Investigation, 1*(9), 1217-1235. https://doi.org/10.4155/cli.11.113

Bushby, K., Finkel, R., Birnkrant, D. J., Case, L. E., Clemens, P. R., Cripe, L., Kaul, A., Kinnett, K., McDonald, C., Pandya, S., Poysky, J., Shapiro, F., Tomezsko, J., & Constantin, C. (2010a). Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *The Lancet Neurology, 9*(1), 77-93. https://doi.org/10.1016/S1474-4422(09)70271-6

Bushby, K., Finkel, R., Birnkrant, D. J., Case, L. E., Clemens, P. R., Cripe, L., Kaul, A., Kinnett, K., McDonald, C., Pandya, S., Poysky, J., Shapiro, F., Tomezsko, J., & Constantin, C. (2010b). Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. *The Lancet Neurology, 9*(2), 177-189. https://doi.org/10.1016/S1474-4422(09)70272-8

Carannante, N., Annunziata, A., Coppola, A., Simioli., F., Marotta, A., Bernardo, M., Piscitelli, E., Imitazione, P., & Fiorentino, G. (2021). Diagnosis and treatment of pneumonia, a common cause of

respiratory failure in patients with neuromuscular disorders. *Acta Myologica, 40*(3), 124-131. https://doi.org/10.36185/2532-1900-053

Cardamone, M., Darras, B. T., & Ryan, M. M. (2008). Inherited Myopathies and Muscular Dystrophies. *Seminars in Neurology, 28*(2), 250-259. https://doi.org/10.1055/s-2008-1062269

Carere, A., & Orr, R. (2016). The impact of hydrotherapy on a patient's perceived well-being: a critical review of the literature. *Physical Therapy Reviews, 21*(2), 91-101. https://doi.org/10.1080/10833196.2016.1228510

Carey, I. M., Banchoff, E., Nirmalananthan, N., Harris, T., DeWilde, S., Chaudhry, U. A. R., & Cook, D. G. (2021). Prevalence and incidence of neuromuscular conditions in the UK between 2000 and 2019: A retrospective study using primary care data. *PloS ONE, 16*(12), 1-25. https://doi.org/10.1371/journal.pone.0261983

Carter, J. C., Sheehan, D. W., Prochoroff, A., & Birnkrant, D. J. (2018). Muscular Dystrophies. *Clinics in Chest Medicine, 39*(2), 377-389. https://doi.org/10.1016/j.ccm.2018.01.004

Case, L. E., Apkon, S. D., Eagle, M., Gulyas, A., Juel, L., Matthews, D., Newton, R. A., & Posselt, H. F. (2018). Rehabilitation Management of the Patient with Duchenne Muscular Dystrophy. *Pediatrics, 142*(2), 17-33. https://doi.org/10.1542/peds.2018-0333D

Chartered Society of Physiotherapy (2022, April 1). *No hydrotherapy pools? No way!* https://www.csp.org.uk/frontline/article/no-hydrotherapy-pools-no-way

Ciafaloni, E., Kumar, A., Liu, K., Pandya, S., Westfield, C., Fox, D. J., Conway, K. M. C., Cunniff, C., Matthews, K., West, N., Romitti, P. A., & McDermott, M. P. (2016). Age at onset of first signs or symptoms predicts age at loss of ambulation in Duchenne and Becker Muscular Dystrophy: Data from the MD STARnet. *Jounral of Pediatric Rehabilitation Medicine, 9*(1), 5-11. https://doi.org/10.3233/PRM-160361

Cleary, S. L., Taylor, N. F., Dodd, K. J., & Shields, N. (2019). Barriers to and facilitators of physical activity for children with cerebral palsy in special education. *Developmental Medicine and Child Neurology, 61*(12), 1408-1415. https://doi.org/10.1111/dmcn.14263

Colombo, M. G., Botto, N., Vittorini, S., Paradossi, U., & Andreassi, M. G. (2008). Clinical utility of genetic tests for inherited hypertrophic and dilated cardiomyopathies. *Cardiovascular Ultrasound, 6*(62). https://doi.org/10.1186/1476-7120-6-62

Conchar, L., Bantjes, J., Swartz, L., & Derman, W. (2016). Barriers and facilitators to participation in physical activity: The experiences of a group of South African adolescents with cerebral palsy. *Journal of Health Psychology, 21*(2), 152-163. https://doi.org/10.1177/1359105314523305

Connolly, A. M., Malkus, E. C., Mendell, J. R., Flanigan, K. M., Miller, J. P., Schierbecker, J. R., Siener, C. A., Golumbek, P. T., Zaidman, C. M., McDonald, C. M., Johnson, L., Nicorici, A., Karachunski, P. I., Day, J. W., Kelecic, J. M., Lowes, L. P., Alfano, L. N., Darras, B. T., Kang, P. B., … Florence, J. M. (2015). Outcome reliability in non ambulatory boys/men with Duchenne Muscular Dystrophy. *Muscle & Nerve, 51*(4), 522-532. https://doi.org/10.1002/mus.24346

Consolaro, A., Giancane, G., Schiappapietra, B., Davì, S., Calandra, S., Lanni, S., & Ravelli, A. (2016). Clinical outcome measures in juvenile idiopathic arthritis. *Pediatric Rheumatology*, *14*(23), 1-8. https://doi.org/10.1186/s12969-016-0085-5

Conway, K. M., Ciafaloni, E., Matthews, D., Westfield, C., James, K., Paramsothy, P., & Romitti, P. A. (2018). Application of the International Classification of Functioning, Disability and Health System to symptoms of the Duchenne and Becker muscular dystrophies. *Disability and Rehabilitation*, *40*(15), 1773-1780. https://doi.org/10.1080/09638288.2017.1312567

Curran-Everett, D., & Williams, C. L. (2015). Explorations in statistics: the analysis of change. *Advances in Physiology Education*, *39*(1), 49-54. https://doi.org/10.1152/advan.00018.2015

Darras, B. T., Menache-Starobinski, C. C., Hinton, V., & Kunkel, L. M. (2015). Dystrophinopathies. In B. T> Darras, H. Royden Jones, M. M. Ryan, & D. C. De Vivo (Eds.), *Neuromuscular Disorders of Infancy, Childhood, and Adolescence: A Clinician's Approach* (2nd ed.) (pp 551-592). Academic Press. https://doi.org/10.1016/B978-0-12-417044-5.00030-5

DiBiasio, P., Primus, K. B., Drogos, J., Husted, C., Stephens, H., & Thorpe, D. (2015). An aquatic exercise program for an adolescent with Limb Girdle Muscular Dystrophy. *The Journal of Aquatic Physical Therapy*, *23*(1), 3-13. https://web-p-ebscohost-com.glos.idm.oclc.org/ehost/pdfviewer/pdfviewer?vid=3&sid=81797749-1e7b-4ead-89f6-79f5b47d2b5e%40redis

Dimachkie, M. M., & Barohn, R. J. (2014). Distal Myopathies. *Neurologic Clinics*, *32*(3), 817-842. https://doi.org/10.1016/j.ncl.2014.04.004

Dimitriadis, Z., Kapreli, E., Konstantinidou, I., Oldham, J., & Strimpakos, N. (2011). Test/retest reliability of maximum mouth pressure measurements with the MicroRPM in healthy volunteers. *Respiratory Care, 56*(6), 776-782. https://doi.org/10.4187/respcare.00783

Duan, D., Goemans, N., Takeda, S., Mercuri, E., & Aartsma-Rus, A. (2021). Duchenne muscular dystrophy. *Nature Reviews Disease Primers, 7*(13), 1-19. https://doi.org/10.1038/s41572-021-00248-3

El Geziry, A., Toble, Y., Al Kadhi, F., Pervaiz, M., & Al Nobani, M. (2018). Non-Pharmacological Pain Management. IntechOpen. https://doi.org/10.5772/intechopen.79689

Engster, S. A., Fascetti, C., Daw, K., & Reis, E. C. (2019). Parent Perceptions of and Preferences for Participation in Child Health Research: Results from a Pediatric Practice-Based Research Network. *Journal of the American Board of Family Medicine, 32*(5), 685-694. https://doi.org/10.3122/jabfm.2019.05.190030

Elangkovan, N. & Dickson, G. (2021). Gene Therapy for Duchenne Muscular Dystrophy. *Journal of Neuromuscular Disease 8*(2), 303-316. https://doi.org/10.3233/JND-210678

Emery, A. E. H. (2000). Emery-Dreifuss muscular dystrophy – a 40 year retrospective study. *Neuromuscular Disorders, 10*(4), 228-232. https://doi.org/10.1016/S0960-8966(00)00105-X

Eser, G., & Topaloğu, H. (2022). Current Outline of Exon Skipping Trials in Duchenne Muscular Dystrophy. *Genes, 13*(7), 1241-1252. https://doi.org/10.3390/genes13071241

Falsaperla, R., Praticò, A. D., Ruggieri, M., Parano, E., Rizzo, R., Corsello, G., Vitaliti, G., & Pavone, P. (2016). Congenital muscular dystrophy: from muscle to brain. *Italian Journal of Pediatrics, 42*(78), 1-11. https://doi.org/10.1186/s13052-016-0289-9

Fan, Z. (2015). Overview of Current Treatments for Muscular Dystrophy. In R. A. Huml (Eds.), *Muscular Dystrophy: A Concise Guide* (pp. 65-72). Springer.

Fayssoil, A., Behin, A., Ogna, A., Mompoint, D., Amthor, H., Clair, B., Laforet, P., Mansart, A., Prigent, H., Orlikowsko, D., Stojkovic, T., Vinit, S., Carlier, R., Eymard, B., Lofaso, F., & Annane, D. (2018). Diaphragm: Pathophysiology and Ultrasound Imaging in Neuromuscular Disorders. *Journal of Neuromuscular Diseases, 5*(1), 1-10. https://doi.org/10.3233/JND-170276

Feder, D., Koch, M. E., Palmieri, B., Fonseca, F. L. A., & Carvalho, A. A. S. (2017). Fat embolism after fractures in Duchenne muscular dystrophy: an underdiagnosed complication? A systematic review. *Therapeutics and Clinical Risk Management, 13*(1), 1357-1361. https://doi.org/10.2147/TCRM.S143317

Ferreira, A. V. S., Goya, P. S. A., Ferrari, R., Durán, M., Franzini, R. V., Caromano, F. A., Favero, F. M., & Oliveira, A. S. B. (2015). Comparison of motor function in patients with Duchenne muscular dystrophy in physical therapy in and out of water: 2-year follow up. *Acta Fisiatrica, 22*(2), 51-54. https://doi.org/10.5935/0104-7795.20150011

Ferrero, A., & Rossi, M. (2022). Cognitive profile and neuropsychiatric disorders in Becker muscular dystrophy: A systematic review of literature. *Neuroscience and Biobehavioural Reviews, 137*(1), 1-8. https://doi.org/10.1016/j.neubiorev.2022.104648

Feingold, B., Mahle, W. T., Auerbach, S., Clemens, P., Domenighetti, A. A., Jefferies, J. L., Judge, D. P., Lal, A. K., Markham, L. W., Parks, W. J, Tsuda, T., Wang, P. J., & Yoo, S. (2017). Management of Cardiac Involvement Associated With Neuromuscular Diseases: A Scientific Statement From the American Heart Association. *Circulation, 136*(13), 200-231. https://doi.org/10.1161/CIR.0000000000000526

Fischer, R. (2010). Standardization. In N. J. Salkind (Eds.), *Encyclopedia of Research Design* (pp. 1433-1437). SAGE Publications.

Fisken, A., Keogh, J. W. L., Waters, D. L., & Hing, W. A. (2012). Perceived Benefits, Motives, and Barriers to Aqua-Based Exercise Among Older Adults With and Without Osteoarthritis. *Journal of Applied Gerontology, 34*(3), 377-396. https://doi.org/10.1177/0733464812463431

Gaina, G., Budisteanu, M., Manole, E., & Ionica, E. (2019). Clinical and Molecular Diagnosis in Muscular Dystrophies. In K. Sakuma (Ed.), *Muscular Dystrophies*. IntechOpen. https://doi.org/10.5772/intechopen.85339

Gao, Q. Q., & McNally, E. M. (2015). The Dystrophin Complex: Structure, Function, and Implications for Therapy. *Comprehensive Physiology, 5*(3), 1223-1239. https://doi.org/10.1002/cphy.c140048

Goselink, R. J. M., Mul, K., van Kernebeek, C. R., Lemmers, R. J. L. F., van der Maarel, S. M., Schreuder, T. H. A, Erasmus, C. E., Padberg, G. W., Statland, J. M., Voermans, N. C., & van Engelen, B. G. M. (2019). Early onset as a marker for disease severity in facioscapulohumeral muscular dystrophy. *Neurology, 92*(4), 378-385. https://doi.org/10.1212/WNL.0000000000006819

Greenberg, R. G., Gamel, B., Bloom, D., Bradley, J., Jafri, H. S., Hinton, D., Nambiar, S., Wheeler, C., Tiernan, R., Smith, P. B., Roberts, J., & Benjamin, D. K. (2018). Parents' perceived obstacles to pediatric clinical trial participation: findings from the clinical trials transformation initiative. *Contemporary Clinical Trials Communications*, *9*(1), 33–39. https://doi.org/10.1016/j.conctc.2017.11.005

Gumerson, J. D., & Michele, D. E. (2011). The dystrophin-glycoprotein complex in the prevention of muscle damage. *Journal of Biomedicine and Biotechnology*, *2011*(8), 1-13. https://doi.org/10.1155/2011/210797

Guzmán, O. R. C., García, A. L. C., & Rodríguez-Cruz, M. (2012). Muscular Dystrophies at Different Ages: Metabolic and Endocrine Alterations. *International Journal of Endocrinology*, *2012*(2), 1-12. https://doi.org/10.1155/2012/485376

Hallemans, A., Verbeque, E. & de Walle, P. V. (2020). Motor functions. In A. Gallagher, C. Bulteau, D. Cohen, & J. L. Michaud (Eds.), *Handbook of Clinical Neurology*, *Volume 173* (pp. 157-170). Elsevier.

Harjpal, P., Kovela, R. K., Raipure, A., Dandale, C., & Qureshi, M. I. (2022). The Refinement of Home Exercise Program for Children and Adolescents With Muscular Dystrophy in the Present COVID-19 Pandemic Scenario: A Scoping Review. *Cureus*, *14*(9), 1-7. https://doi.org/10.7759/cureus.29344

Hébert, L. J, Maltais, D. B., Lepage, C., Saulnier, J., Crête, M., Perron, M. (2011). Isometric muscle strength in youth assessed by hand-held dynamometry: A feasibility, reliability, and validity study. *Pediatric Physical Therapy*, *23*(3), 289-299. https://doi.org/10.1097/PEP.0b013e318227ccff

Heller, S. A., Shih, R., Kalra, R., & Kang, P. B. (2019). Emery-Dreifuss muscular dystrophy. *Muscle and Nerve, 61*(4), 436-448. https://doi.org/10.1002/mus.26782

Hendriksen, R. G. F., Aalbers, M. W., Hendriksen, J. G. M., de Die-Smulders, C. E. M., Hoogland, G., & Vles, J. S. H. (2016). An Unusual Triad in Pediatric Neurology: A Case Report on Cerebral Palsy, Epilepsy, and Duchenne Muscular Dystrophy. *Child Neurology Open, 3*(1), 1-5. https://doi.org/10.1177/2329048X16642948

Henricson, E. K., Abresch, R. T., Cnaan, A., Hu, F., Duong, T., Arrieta, A., Han, J., Escolar, D. M., Florence, J. M., Clemens, P. R., Hoffman, E. P., & McDonald, C. M. (2013). The cooperative international neuromuscular research group Duchenne natural history study: glucocorticoid treatment preserves clinically meaningful functional milestones and reduces rate of disease progression as measured by manual muscle testing and other commonly used clinical trial outcome measures. *Muscle Nerve, 48*(1), 55-67. https://doi.org/10.1002/mus.23808

Hind, D., Parkin, J., Whitworth, V., Rex, S., Young, T., Hampson, L., Sheehan, J., Maguire, C., Cantrill, H., Scott, E., Epps, H., Main, M., Geary, M., McMurchie, H., Pallant, L., Woods, D., Freeman, J., Lee, E., Eagle, M., … & and Baxte, P. (2017). Aquatic therapy for boys with Duchenne muscular dystrophy (DMD): an external pilot randomised controlled trial. *Pilot and Feasibility Studies, 3*(1), 1-17. https://doi.org/10.1186/s40814-017-0132-0

Ho, G., Carey, K. A., Cardamone, M., Farrarm M. A. (2019). Myotonic dystrophy type 1: clinical manifestations in children and adolescents. *Archives of Disease in Childhood, 104*(1), 48-52. https://doi.org/10.1136/archdischild-2018-314837

Hoffmann, T., Bennett, S., & Del Mar, C. (2013). *Evidence-Based Practice across the health professions* (2nd ed.). Elsevier.

Honório, S., Batista, M., & Martins, J. (2013). The influence of hydrotherapy on obesity prevention in individuals with Duchenne Muscular Dystrophy. *Journal of Physical Education and Sport, 13*(2), 140-146. https://doi.org/10.7752/jpes.2013.02023

Huguet-Rodríguez, M., Arias-Buría, J. L., Huguet-Rodríguez, B., Blanco-Barrero, R., Braña-Sirgo, D., & Güeita-Rodríguez, J. (2020). Impact of aquatic exercise on respiratory outcomes and functional activities in children with neuromuscular disorders: Findings from an open-label and prospective preliminary pilot study. *Brain Sciences, 10*(7), 458-472. https://doi.org/10.3390/brainsci10070458

Hull, J., Aniapravan, R., Chan, E., Chatwin, M., Forton, J., Gallagher, J., Gibson, N., Gordon, J., Hughes, H., McCulloch, R., Russell, R R. & Simonds, A. (2012). British Thoracic Society guideline for respiratory management of children with neuromuscular weakness. *Thorax, 67*(1), 1-40. https://doi.org/10.1136/thoraxjnl-2012-201964

Huml, R. A. (2015). Muscular Dystrophy: Historical Background and Types. In R. A. Huml (Eds.), *Muscular Dystrophy: A Concise Guide* (pp. 5-8). Springer.

Huml, R. A., & Perez, D. P. (2015). FSHD: The most common type of Muscular Dystrophy? In R. A. Huml (Eds.), *Muscular Dystrophy: A Concise Guide* (pp. 9-20). Springer.

Jacques, M. F., Stockley, R. C., Onambele-Pearson, G. L., Reeves, N. D., Stebbings, G. K., Dawson, E. A., Groves, L., & Morse, C. I. (2019). Quality of life in adults with muscular dystrophy. *Health and Quality of Life Outcomes, 17*(121), 1-10. https://doi.org/10.1186/s12955-019-1177-y

Jones, P., & Comfort, P. (2020). Strength and conditioning: Scientific aspects including principles of rehabilitation. In S. Porter, & J. Wilson (Eds.), *A Comprehensive Guide to Sports Physiology and Injury Management: An Interdisciplinary Approach* (pp. 25-45). Elsevier.

Kalkman, J. S., Schillings, M. L., van der Werf, S. P., Padberg, G. W., Zwarts, M. J., van Engelen, B. G. M., & Bleijenberg, G. (2005). Experienced fatigue in facioscapulohumeral dystrophy, myotonic dystrophy, and HMSN-1. *Journal of Neurology, Neurosurgery & Psychiatry, 76*(10), 1406-1409. http://dx.doi.org/10.1136/jnnp.2004.050005

Kang, H. (2013). The prevention and handling of the missing data. *Korean Journal of Anesthesiology, 64*(5), 402-406. https://doi.org/10.4097/kjae.2013.64.5.402

Katz, S., Arish, N., Rokach, A., Zaltzman, Y., & Marcus, E. (2018). The effect of body position on pulmonary function: a systematic review. *BMC Pulmonary Medicine, 18*(1), 159-175 https://doi.org/10.1186/s12890-018-0723-4

Kennedy, R. A., Carroll, K., McGinley. J. L., & Paterson, K. L. (2020). Walking and weakness in children: a narrative review of gait and functional ambulation in paediatric neuromuscular disease. *Journal of Foot and Ankle Research, 13*(10), 1-15. https://doi.org/10.1186/s13047-020-0378-2

Kiger, M. E., & Varpio, L. (2020). Thematic analysis of qualitative data: AMEE Guide No. 131. *Medical Teacher, 42*(8), 846-854. https://doi.org/10.1080/0142159X.2020.1755030

Kinane, T. B., Mayer, O. H., Duda, P. W., Lowes, L. P., Moody, S. L., & Mendell, J. R. (2018). Long-Term Pulmonary Function in Duchenne Muscular Dystrophy: Comparison of Eteplirsen-Treated

Patients to Natural History. *Journal of Neuromuscular Diseases, 5*(1), 47-58. https://doi.org/10.3233/JND-170272

Koessler, W., Wanke, T., Winklet, G., Nader, A., Toifl, K., Kurz, H., & Zwick, H. (2001). 2 Years' experience with inspiratory muscle training in patients with neuromuscular disorders. *Chest, 120*(3), 765-769. https://doi.org/10.1378/chest.120.3.765

Kornegay, J. N., Childers, M. K., Bogan, D. J., Bogan, J. R., Nghiem, P., Wang, J., Fan, Z., Howard, J. F., Schatzberg, S. J., Dow, J. L., Grange, R. W., Styner, M. A., Hoffman, E. P., & Wagner, K. R. (2012). The Paradox of Muscle Hypertrophy in Muscular Dystrophy. *Physical Medicine and Rehabilitation Clinics of North America, 23*(1), https://doi.org/10.1016/j.pmr.2011.11.014

Kostanjsek, N. (2011). Use of The International Classification of Functioning, Disability and Health (ICF) as a conceptual framework and common language for disability statistics and health information systems. *BMC Public Health, 11*(4). https://doi.org/10.1186/1471-2458-11-S4-S3

Kovalchuk, T., Yakovleva, E., Fetisova, S., Vershinina, T., Lebedeva, V., Lyubimtseva, T., Lebedev, D., Mitrofanova, L., Ryzhkov, A., Sokolnikova, P., Fomicheva, Y., Kozyreva, A., Zhuk, S., Smolina, N., Zlotina, A., Pervunina, T., Kostareva, A., & Vasichkina, E. (2021). Case Reports: Emery-Dreifuss Muscular Dystrophy presenting as a heart rhythm disorders in children. *Frontiers in Cardiovascular Medicine, 8*(1), 1-11. https://doi.org/10.3389/fcvm.2021.668231

Lauruschkus, K., Nordmark, E., & Hallström, I. (2015). "It's fun, but …" Children with cerebral palsy and their experiences of participation in physical activities. *Disability and Rehabilitation An International, Multidisciplinary Journal, 37*(4), 283-289. https://doi.org/10.3109/09638288.2014.915348

Laviola, M., Priori, R., D'Angelo, M. G., & Aliverti, A. (2018). Assessment of diaphragmatic thickness by ultrasonography in Duchenne muscular dystrophy (DMD) patients. *PloS ONE 13*(7), 1-13. https://doi.org/10.1371/journal.pone.0200582

Liao, Q., Zhang, Y., He, J., & Huang, K. (2022). Global Prevalence of Myotonic Dystrophy: An Updated Systematic Review and Meta-Analysis. *Neuroepidemiology, 56*(3), 163-173. https://doi.org/10.1159/000524734

Lim, Y., Velozo, C., & Bendixen, R. M. (2014). The level of agreement between child self-reports and parent proxy-reports of health-related quality of life in boys with Duchenne muscular dystrophy. *Quality of life research, 23*(7), 1945-1952. https:/doi.org/10.1007/s11136-014-0642-7

Lima, A. A. R., & Cordeiro, L. (2020). Aquatic physical therapy in individuals with muscular dystrophy: systematic scoping review. *Fisioterapia e Pesquisa, 27*(1), 100-111. https://doi.org/10.1590/1809-2950/18031327012020

LoMauro, A., & Aliverti, A. (2016). Physiology of respiratory disturbances in muscular dystrophies. *Breathe, 12*(4), 318-327. https://doi.org/10.1183/20734735.012716

LoMauro, A., D'Angelo, M. G., & Aliverti, A. (2015). Assessment and management of respiratory function pateints with Duchenne muscular dystrophy: current and emerging options. *Therapeutics and Clinical Risk Management, 11*(1), 1475-1488. https://doi.org/10.2147/TCRM.S55889

Lombardo, M. E., Carraro, E., Sancricca, C., Armando, M., Catteruccia, M., Mazzone, E., Ricci, G., Salamino, F., Santorelli, F. M., & Filosto, M. (2021). Management of motor rehabilitation in

individuals with muscular dystrophies. 1st Consensus Conference report from UILDM – Italian Muscular Dystrophy Association (Rome, January 25-25, 2019). *Acta Myologica, 40*(2), 72-87. https://doi.org/10.36185/2532-1900-046

Longman, C. (2006). Myotonic dystrophy. *The Journal of the Royal College of Physicians of Edinburgh, 36*(1), 51-55. https://www.rcpe.ac.uk/sites/default/files/n_myotonic_dystrophy.pdf

Lott, D. J., Taivassalo, T., Cooke, K. D., Park, H., Moslemi, Z., Batra, A., Forbes, S. C., Byrne, B. J., Walter, G. A., & Vandenborne, K. (2021). Safety, feasibility, and efficacy of strengthening exercise in Duchenne muscular dystrophy. *Muscle & Nerve, 63*(3), 320-326. https://doi.org/10.1002/mus.27137

Lovering, R. M., Porter, N. C., & Bloch, R. J. (2005). The Muscular Dystrophies: From Genes to Therapies. *Physical Therapy and Rehabilitation Journal, 85*(12), 1372-1388. https://doi.org/10.1093/ptj/85.12.1372

Lu, Y., & Lue, Y. (2012). Strength and Functional Measurement for Patients with Muscular Dystrophy. In M. Hegde, & A. Ankala (Eds.), *Muscular Dystrophy* (pp 321-330). InTech.

Luz, L. E. S., Nascimento, R. C. R., Jacob, M. M., Bento-Torres, N. V. O. (2021). Aquatic Physical therapy in a patient with Limb-Girdle Muscular Dystrophy, type 2b: a case report. *Journal of Physiotherapy Research, 11*(3), 583-592. http://dx.doi.org/10.17267/2238-2704rpf.v11i3.3718

Madej-Pilarczyk, A. (2018). Clinical aspects of Emery-Dreifuss muscular dystrophy. *Nucleus, 9*(1), 314-320. https://doi.org/10.1080/19491034.2018.1462635

Mah, J. K. (2015a). An overview of the Other Muscular Dystrophies: Underlying Genetic and Molecular Mechanisms. In R. A. Huml (Eds.), *Muscular Dystrophy: A Concise Guide* (37-54). Springer.

Mah, J. K. (2015b). Duchenne and Becker Muscular Dystrophies: Underlying Genetic and Molecular Mechanisms. In R. A. Huml (Eds.), *Muscular Dystrophy: A Concise Guide* (21-36). Springer.

Mailey, E. L., Phillips, S. M., Dlugonski, D., & Conroy, D. E. (2016). Overcoming barriers to exercise among parents: a social cognitive theory perspective. *Journal of Behavioural Medicine, 39*(4), 599-609. https://doi.org/10.1007/s10865-016-9744-8

Manzur, A. Y., & Muntoni, F. (2009). Diagnosis and new treatments in muscular dystrophies. *Journal of Neurology, Neurosurgery and Psychiatry, 80*(7), 706-714. https://doi.org/10.1136/jnnp.2008.158329

Matthews, K. D., Conway, K. M., Gedlinske, A. M., Johnson, N., Street, N., Butterfield, R. J., Hung, M., Ciafaloni, E., & Romitti, P. A. (2021). Characteristics of Clinical Trial Participants with Duchenne Muscular Dystrophy: Data from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STAR*net*). *Children, 8*(10), 835-847. https://doi.org/10.3390/children8100835

Mazzone, E. S., Vasco, G., Palermo, C., Bianco, F., Galluccio, C., Ricotti, V., Castronovo, A., Mauro, M. S. D., Pane, M., Mayhew, A., & Mercuri, E. (2012). A critical review of functional assessment tools for upper limbs in Duchenne muscular dystrophy. *Developmental Medicine & Child Neurology*, *54*(10), 879-885. https://doi.org/10.1111/j.1469-8749.2012.04345.x

McDonald, D. G. M., Kinali, M., Gallagher, A. C., Mercuri, E., Muntoni, F., Roper, H., Jardine, P., Jones, D. H., & Pike, M. G. (2002). Fracture prevalence in Duchenne muscular dystrophy. *Developmental Medicine & Child Neurology*, *44*(10), 695-698. https://doi.org/10.1017/s0012162201002778

McIntyre, D. (2017). Aquatic Therapy and Pain in the Rehabilitation Patient. In A. Carayannopoulos (Eds.), *Comprehensive Pain Management in the Rehabilitation Patient* (pp. 347-355). Springer.

Mckenzie, G., & Willis, C., & Shields, N. (2021). Barriers and facilitators of physical activity participation for young people and adults with childhood-onset physical disability: a mixed methods systematic review. *Developmental Medicine and Child Neurology, 63*(8), 914-924. https://doi.org/10.1111/dmcn.14830

Meola, G., & Cardani, R. (2015a). Myotonic dystrophies: An update on clinical aspects, genetic, pathology, and molecular pathomechanisms. *Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease, 1852*(4), 594-606. https://doi.org/10.1016/j.bbadis.2014.05.019

Meola, G., & Cardani, R. (2015b). Myotonic Dystrophy Type 2: An Update on Clinical Aspects, Genetic and Pathomolecular Mechanism. *Journal of Neuromuscular Diseases, 2*(2), 59-71. https://doi.org/10.3233/JND-150088

Mercuri, E., & Muntoni, F. (2013). Muscular dystrophies. *The Lancet, 381*(9869), 845-860. https://doi.org/10.1016/S0140-6736(12)61897-2

Messina, S., Bruno, C., Moroni, I., Pegoraro, E., D'Amico, A., Biancheri, R., Berardinelli, A., Boffi, P., Cassandrini, D., Farina, L., Minetti, C., Moggio, M., Mongini, T., Mottarelli, E., Pane, M.,

Pantaleoni, C., Pichiecchio, A., Pini, A., Ricci, E., … Mercuri, E. (2010). Congenital muscular dystrophies with cognitive impairment: A population study. *Neurology, 75*(10), 898-903. https://doi.org/10.1212/WNL.0b013e3181f11dd5

Mooventhan, A., & Nivethitha, L. (2014). Scientific evidence-based effect of hydrotherapy on various systems of the body. *North American Journal of Medical Sciences, 6*(5), 199-209. https://doi.org/10.4103/1947-2714.132935

Morales, A., & Mahajan, K. (2021). *Dystrophinopathies*. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK534245/

Mul, K., Lassche, S., Voermans, N. C., Padberg, G. W., Horlings, C. G. C., & van Engelen, B. G. M. (2016). What's in a name? The clinical features of facioscapulohumeral muscular dystrophy. *Practical Neurology, 16*(3), 201-207. https://doi.org/10.1136/practneurol-2015-001353

Muñoz-Blanco, E., Merino-Andrés, J., Aguilar-Soto, B., García, Y. C., Puente-Villalba, M., Pérez-Corrales, J., & Güeita-Rodríquez, J. (2020). Influence of Aquatic Therapy in Children and Youth with Cerebral Palsy: A Qualitative Case Study in a Special Education School. *International Journal of Environmental Research and Public Health, 17*(10), 3690-3706. https://doi.org/10.3390/ijerph17103690

Murad, M. H., Asi, N., Alsawas, M., & Alahdab, F. (2016). New evidence pyramid. *BMJ Evidence Based Medicine, 21*(4), 125-127. http://dx.doi.org/10.1136/ebmed-2016-110401

Murphy, A. P., & Straub, V. (2015). The classification, natural history and treatment of the Limb Girdle Muscular Dystrophies. *Journal of Neuromuscular Diseases*, *2*(2), 7-19. https://doi.org/10.3233/JND-150105

Mutlu, A., Alkan, H., Fırat, T., Karaduman, A. A., & Yılmaz, Ö. T. (2018). How do physical capacity, fatigue and performance differ in children with Duchenne muscular dystrophy compared with their healthy peers? *NeuroSciences*, *23*(1), 39-45. https://doi.org/10.17712/nsj.2018.1.20170242

National Health Service (2021, July 20). *Treatment: Muscular Dystrophy.* https://www.nhs.uk/conditions/muscular-dystrophy/treatment/

National Institute of Neurological Disorders and Stroke (2013, August). *Muscular Dystrophy: Hope Through Research.* https://www.ninds.nih.gov/health-information/patient-caregiver-education/hope-through-research/muscular-dystrophy-hope-through-research

Nozoe, K. T., Akamine, R. T., Mazzotti, D. R., Polesel, D. N., Grossklauss, L. F., Tufik, S., Andersen, M. L., & Moreira, G. A. (2016). Phenotypic contracts of Duchenne Muscular Dystrophy in women: Two case reports. *Sleep Science*, *9*(3), 129-133. http://dx.doi.org/10.1016/j.slsci.2016.07.004

Nunes, M. F., Hukuda, M. E., Favero, F. M., Oliveira, A. B., Voos, M. C., & Caromano, F. A. (2016). Relationship between muscle strength and motor function in Duchenne muscular dystrophy. *Arquivos de Neuro-psiquiatria*, *74*(7), 530-535. https://doi.org/10.1590/0004-282X20160085

Ogonowska-Slodownik, A., de Lima, A. A. R., Cordeiro, L., Morgulec-Adamowicz, N., Alonso-Fraile, M., & Güeita-Rodríguez, J. (2022). Aquatic Therapy for Persons with Neuromuscular

Diseases – A Scoping Review. *Journal of Neuromuscular Disease*, *9*(2), 237-256. https://doi.org/10.3233/JND-210749

Ohlendieck, K., & Swandulla, D. (2021). Complexity of skeletal muscle degeneration: multi-systems pathophysiology and organ crosstalk in dystrophinopathy. *Pflügers Archiv – European Journal of Physiology*, *473*(1), 1813-1839. https://doi.org/10.1007/s00424-021-02623-1

Okubo, M., Noguchi, S., Hayashi, S., Nakamura, H., Komaki, H., Matsuo, M., & Nishino, I. (2020). Exon skipping induced by nonsense/frameshift mutations in DMD gene results in Becker muscular dystrophy. *Human Genetics*, *139*(2), 247-255. https://doi.org/10.1007/s00439-019-02107-4

Osama, S., Osama, L., & Hamed, S. (2020). Efficacy of underwater exercises on Egyptian children with juvenile idiopathic arthritis. Life Science Journal, 17(2), 18-26. doi:10.7537/marslsj170220.04

Osorio, A. N., Cantillo, J. M., Salas, A. C., Garrido, M. M., & Padilla, J. J. V. (2019). Consensus on the diagnosis, treatment and follow-up of patients with Duchenne muscular dystrophy. *Neurología*, *34*(7), 469-481. https://doi.org/10.1016/j.nrleng.2018.01.001

Ouyang, Y., Wang, K., Zhang, T., Peng, L., Song, G., & Luo, J. (2020). The influence of sports participation on body image, self-efficacy, and self-esteem in college students. *Frontiers in Psychology*, *10*(2019), 3039–3039. https://doi.org/10.3389/fpsyg.2019.03039

Ozer, U., & Tufan, A. E. (2019). Psychiatric comorbidities in cases with Duchenne muscular dystrophy: a case series. *The Journal of Psychiatry and Neurological Sciences*, *32*(1), 359-364. https://doi.org/10.14744/DAJPNS.2019.00052

Paganoni, S., Nicholson, K., Leigh, F., Swoboda, K., Chad, D., Drake, K., Haley, K., Cudkowicz, M., & Berry, J. D. (2017). Developing multidisciplinary clinics for neuromuscular care and research. *Muscle and Nerve, 56*(5), 848-858. https://doi.org/10.1002/mus.25725

Papadopoulos, N. V., Whelan, M., Skouteris, H., Williams, K., McGinley, J., Shih, S. T. F., Emonson, C., Moss, S. A., Sivaratnam, C., Whitehouse, A. J. O., & Rinehart, N. J. (2020). An Examination of Parent-Reported Facilitators and Barriers to Organized Physical Activity Engagement for Youth With Neurodevelopmental Disorders, Physical, and Medical Conditions. *Frontiers in Psychology, 11*(2020), 1-13. https://doi.org/10.3389/fpsyg.2020.568723

Pascual-Morena, C., Cavero-Redondo, I., Reina-Gutiérrez, S., Saz-Lara, A., López-Gil, J. F., & Martínez-Vizcaíno, V. (2022). Prevalence of Neuropsychiatric Disorders in Duchenne and Becker Muscular Dystrophies: A Systematic Review and Meta-analysis. *Archives of Physical Medicine and Rehabilitation, 104*(12), 2444-2453. https://doi.org/10.1016/j.apmr.2022.05.015

Pattman, J., Wratten, S., Turner, A., Cox, S., Krouwel, O., English, V., MacSwiney, K., & Epps, H. (2021). ATACP Guidance on Aquatic Physiotherapy Practice 2021. *Aquatic Therapy Association of Chartered Physiotherapists*. https://atacp.csp.org.uk/publications/atacp-guidance-aquatic-physiotherapy-2021

Peay, H. L., Biesecker, B. B., Wilfond, B. S., Jarecki, J., Umstead, K. L., Escolar, D. M., & Tibben, A. (2018). Barriers and facilitators to clinical trial participation among parents of children with pediatric neuromuscular disorders. *Clinical Trials, 15*(2), 139-148. https://doi.org/10.1177/1740774517751118

Peay, H. L., Tibben, A., Fisher, T., Brenna, E., & Biesecker, B. B. (2014). Expectations and experiences of investigators and parents involved in a clinical trial for Duchenne/Becker muscular dystrophy. *Clinical Trials, 11*(1), 77-85. https://doi.org/10.1177/1740774513512726

Pennati, F., LoMauro, A., D'Angelo, M. G., & Aliverti, A. (2021). Non-Invasive Respiratory Assessment in Duchenne Muscular Dystrophy: From Clinical Research to Outcome Measures. *Life, 11*(9), 947-966 https://doi.org/10.3390/life11090947

Phillips, M., Flemming, N., & Tsintzas, K. (2009). An exploratory study of physical activity and perceived barriers to exercise in ambulant people with neuromuscular disease compared with unaffected controls. *Clinical Rehabilitation, 23*(8), 746–55. https://doi.org/10.1177/0269215509334838

Pourghane, P. (2017). Barriers to Participating in Hydrotherapy in Older Women: A Qualitative Study. *Journal of Nursing and Midwifery Sciences, 4*(1), 14-20. https://doi.org/10.18869/acadpub.jnms.4.1.14

Powell, P. A., & Carlton, J. (2023). A comprehensive qualitative framework for health-related quality of life in Duchenne muscular dystrophy. *Quality of Life Research, 32*(1), 225-236. https://doi.org/10.1007/s11136-022-03240-w

Prel, J. B., Hommel, G., Röhrig, B., & Blettner, M. (2009). Confidence interval or p-value? Part 4 of a series on evaluation of scientific publications. *Deutsches Arzteblatt International, 106*(19), 335-339. https://doi/org/10.3238/arztebl.2009.0335

Rahimov, F., & Kunkel, L. M. (2013). Cellular and molecular mechanisms underlying muscular dystrophy. *Journal of Cell Biology, 201*(4), 499-510. https://doi.org/10.1083/jcb.201212142

Rahmawati, P. L., Wijayanti, I. A. S., Arimbawa, I. K, Purwata, T. E., Putra, P., Sumadi, W. J., Wiratnaya, G. E., Antara, M. P. S., & Dwianingshih, E. K. (2021). Serial case report: Becker's muscular dystrophy phenotype with dilated cardiomyopathy in patients with out-of-frame deletion involving exons 38-43 of *DMD* gene. *Neurology Asia, 26*(1), 153-159. https://www.neurology-asia.org/articles/neuroasia-2021-26(1)-153.pdf

Ricotti, V., Mandy, W. P. L., Scoto, M., Pane, M., Deconinck, N., Messina, S., Mercuri, E., Skuse, D. H., & Muntoni, F. (2016). Neurodevelopmental, emotional, and behavioural problems in Duchenne muscular dystrophy in relation to underlying dystrophin gene mutations. *Developmental Medicine and Child Neurology, 58*(1), 77-84. https://doi.org/10.1111/dmcn.12922

Rocha, C. T., & Hoffman, E. P. (2010). Limb-Girdle and Congenital Muscular Dystrophies: Current Diagnostics, Management, and Emerging Technologies. *Current Neurology and Neuroscience Reports, 10*(4), 267-276. https://doi.org/10.1007/s11910-010-0119-1

Rosenbaum, P., & Gorter, J. W. (2012). The'F-words' in childhood disability: I swear this is how we should think! *Child: Care, Health and Development, 38*(4), 457-463. https://doi.org/10.1111/j.1365-2214.2011.01338.x

Sabri, F., Rotheroe, A., & Kazimirski, A. (2015). Measuring the well-being of young people with special educational needs. *NPC*. https://npproduction.wpenginepowered.com/wp-content/uploads/2018/07/Measuring-the-well-being-of-young-people-with-SEN.pdf

Sacconi, S., Salviati, L., & Desnuelle, C. (2015). Facioscapulohumeral muscular dystrophy. *Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease, 1852*(4), 607-614. https://doi.org/10.1016/j.bbadis.2014.05.021

Sanders, M. E., & Torres, L. E. (2010). Aquatic exercise for muscular dystrophy: The story of Laura Sos, Castellón, Spain. *American College of Sports Medicine's Health and Fitness Journal, 14*(6), 35-41. https://doi.org/10.1249/FIT.0b013e3181f8a332

Sandström, K., Samuelsson, K., & Öberg, B. (2009). Prerequisites for carrying out physiotherapy and physical activity – experiences from adults with cerebral palsy. *Disability and Rehabilitation, 31*(3), 161-169. https://doi.org/10.1080/09638280701850934

Santos, C. P. A., Hengles, R. C., Cyrillo, F. N., Rocco, F. M., & Braga, D. M. (2016). Aquatic physical therapy in the treatment of a child with merosin-deficient congenital muscular dystrophy: case report. *Acta Fisiatrica, 23*(2), 102-106. https://doi.org/10.5935/0104-7795.20160020

Savarese, M., Sarparanta, J., Vihola, A., Jonson, P. H., Johari, M., Rusanen, S., Hackman, P., & Udd, B. (2020). Panorama of the distal myopathies. *Acta Myologica, 39*(4), 245-265. https://doi.org/10.36185/2532-1900-028

Sayre, J. W., Toklu, H. Z., Ye, F., Mazza, J., & Yale, S. (2017). Case reports, case series – From clinical practice to evidence-based medicine in graduate medical education. *Cureus 9*(8), 1-5. https://doi.org/10.7759/cureus.1546

Schoser, B., Fong, E., Geberhiwot, T., Hughes, D., Kissel, J. T., Madathil, S. C., Orlikowski, D., Polkey, M. I., Roberts, M., Tiddens, H. A., & Young, P. (2017). Maximum inspiratory pressure as a

clinically meaningful trial endpoint for neuromuscular diseases: a comprehensive review of the literature. *Orphanet Journal of Rare Diseases, 12*(52), 1-19. https://doi.org/10.1186/s13023-017-0598-0

Shi, W., Li, H., Su, Y., Lu, K., Hou, F., & Yang, H. (2015). Reliability of hand-held dynamometry for measurement of lower limb muscle strength in children with Duchenne and Becker muscular dystrophy. *Chinese Journal of Contemporary Neurology & Neurosurgery, 15*(5), 387-392. doi:10.3969/j.issn.1672-6731.2015.05.009

Shields, N., & Synnot, A. J. (2016). Perceived barriers and facilitators to participation in physical activity for children with disability: a qualitative study. *BMC Pediatrics, 16*(9), 1-10. https://doi.org/10.1186/s12887-016-0544-7

Shields, N., Synnot, A. J., & Barr, M. (2012). Perceived barriers and facilitators to physical activity for children with disability: a systematic review. *British Journal of Sports Medicine, 46*(14), 989-997. https://doi.org/10.1136/bjsports-2011-090236

Shimmell, L. J., Gorter, J. W., Jackson, D., Wright, M., & Galuppi, B. (2013). "It's the Participation that Motivates Him": Physical Activity Experiences of Youth with Cerebral Palsy and Their Parents. *Physical and Occupational Therapy in Pediatrics, 33*(4), 405-420. https://doi.org/10.3109/01942638.2013.791916

Siciliano, G., Simoncini, C., Giannotti, S., Zampa, V., Angelini, C., & Ricci, G. (2015). Muscle exercise in limb girdle muscular dystrophies: pitfall and advantages. *Acta Myologica, 34*(1), 3-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4478773/

Silva, K. M., Braga, D. M., Hengles, R. C., Beas, A. R. V., & Rocco, F. M. (2012). The impact of aquatic therapy on the agility of a non-ambulant patient with Duchenne muscular dystrophy. *Acta Fisiatrica*, *19*(1), 42-45. https://doi.org/10.5935/0104-7795.20120009

Silva, T. H., Anequini, I. P., Fávero, F. M., Voos, M. C., Oliveira, A. S. B., Telles, J. A. R., & Caromano, F. A. (2020). Functional performance and muscular strength in symptomatic female carriers of Duchenne muscular dystrophy. *Arquivos de Neuro-Psiquiatria*, *78*(3), 143-148. https://doi.org/10.1590/0004-282X20190168

Simonds, A. K. (2002). Respiratory complications of the muscular dystrophies. *Seminars in Respiratory and Critical Care Medicine*, *23*(3), 231-238. https://doi.org/10.1055/s-2002-33031

Song, T., Lee, K., Kang, S., Cho, H., & Choi, Y. (2011) Three cases of manifesting female carriers in patients with Duchenne muscular dystrophy. *Yonsei Medical Journal*, *52*(1), 192-195. https://doi.org/10.3349/ymj.2011.52.1.192

Statland, J. M. (2020). Facioscapulohumeral muscular dystrophy. In R. N. Rosenberg & J. M. Pascual (Eds.), *Rosenberg's Molecular and Genetic Basis of Neurological and Psychiatric Disease* (6_{th} ed.) Volume 2 (pp. 511-523). Academic Press. https://doi.org/10.1016/B978-0-12-813866-3.00030-8

Statland, J. M., & Tawil, R. (2016). Facioscapulohumeral Muscular Dystrophy. *Continuum: Lifelong Learning in Neurology*, *22*(6), 1916-1931. https://doi.org/10.1212/CON.0000000000000399

Strafella, C., Campoli, G., Galota, R. M., Caputo, V., Pagliaroli, G., Carboni, S., Zampatti, S., Peconi, C., Mela, J., Sancricca, C., Primiano, G., Minozzi, G., Servidei, S., Cascella, R., & Giardina, E.

(2019). Limb-Girdle Muscular Dystrophies (LGMDs): The Clinical Application of NGS Analysis, a Family Case Report. *Frontiers in Neurology*, *10*(619), 1-8. https://doi.org/10.3389/fneur.2019.00619

Sun, C., Shen, L., Zhang, Z., & Xie, X. (2020). Therapeutic Strategies for Duchenne Muscular Dystrophy: An Update. *Genes*, *11*(8), 837-862. https://doi.org/10.3390/genes11080837

Szabo, S. M., Audhya, I. F., Malone, D. C., Feeny, D., & Gooch, K. L. (2020). Characterizing health state utilities associated with Duchenne muscular dystrophy: A systematic review. *Quality of Life Research*, *29*(3), 593-605. https://10.1007/s11136-019-02355-x

Szabo, S. M., Audhya, I. F., Rogula, B., Feeny, D., & Gooch, K. L. (2022). Factors associated with the health-related quality of life among people with Duchenne muscular dystrophy: a study using the Health Utilities Index (HUI). *Health and Quality of Life Outcomes*, *20*(93), 1-10. https://doi.org/10.1186/s12955-022-02001-0

Takahashi, T., Aoki, M., Suzuki, N., Tateyama, M., Yaginuma, C., Sato, H., Hayasaka, M., Sugawara, H., Ito, M., Abe-Kondo, E., Shimakura, N., Ibi, T., Kuru, S., Wakayama, T., Sobue, G., Fujii, N., Saito, T., Matsumura, T., Funakawa, I., … Itoyama, Y. (2013). Clinical features and a mutation with late onset of limb girdle muscular dystrophy 2B. *Journal of Neurology, Neurosurgery and Psychiatry*, *84*(4), 433-440. http://dx.doi.org/10.1136/jnnp-2011-301339

Takaso, M., Nakazawa, T., Imura, T., Okada, T., Fukushima, K., Ueno, M., Takahira, N., Takahashi, K., Yamazaki, M., Ohtori, S., Okamoto, H., Okutomi, T., Okamoto, M., Masaki, T., Uchinuma, E., & Sakagami, H. (2010). Surgical management of severe scoliosis with high risk pulmonary dysfunction in Duchenne muscular dystrophy: patient function, quality of life and satisfaction. *International Orthopaedics*, *34*(5), 695-702. https://doi.org/10.1007/s00264-010-0957-0

Takeda, S., Clemens, P. R., & Hoffman, E. P. (2021). Exon-Skipping in Duchenne Muscular Dystrophy. *Journal of Neuromuscular Diseases, 8*(2), 343-358. https://doi.org/10.3233/JND-210682

Tang, Y., Tang, R., & Gross, J. J. (2019). Promoting psychological well-being through an evidence-based mindfulness training program. *Frontiers in Human Neuroscience, 13*(237), 1-5. https://doi.org/10.3389/fnhum.2019.00237

Teleman, B., Vinblad, E., Svedberg, P., Nygren, J. M., & Larsson, I. (2021). Exploring Barriers to Participation in Pediatric Rehabilitation: Voices of Children and Young People with Disabilities, Parents, and Professionals. *International Journal of Environmental Research and Public Heath, 18*(19), 1-13. https://doi.org/10.3390/ijerph181910119

Teo, J. L., Zheng, Z., & Bird, S. R. (2022). Identifying the factors affecting 'patient engagement' in exercise rehabilitation. *BMC Sports Science, Medicine and Rehabilitation, 14*(1). https://doi.org/10.1186/s13102-022-00407-3

Thada, P. K., Bhandari, J., & Umapathi, K. K. (2022). *Becker Muscular Dystrophy*. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK556092/#_NBK556092_pubdet_

Theadom, A., Rodrigues, M., Roxburgh, R., Balalla, S., Higgins, C., Bhattacharjee, R., Jones, K., Krishnamurthi, R., & Feigin, V. (2014). Prevalence of Muscular Dystrophies: A Systematic Literature Review. *Neuroepidemiology, 43*(3-4), 259-268. https://doi.org/10.1159/000369343

Torres-Ronda, L., & Schelling I del Alcázar, X. (2014). The properties of water and their applications for training. *Journal of Human Kinetics, 44*(1), 237-248. https://doi.org/10.2478/hukin-2014-0129

Tsuda, T. (2018). Clinical Manifestations and Overall Management Strategies for Duchenne Muscular Dystrophy. In Bernardini, C. (Eds.), *Duchenne Muscular Dystrophy: Methods in Molecular Biology*, vol 1687. Humana Press. https://doi.org/10.1007/978-1-4939-7374-3_2

Udd, B. (2011). Distal muscular dystrophies. In A. A. Amato & R. C. Griggs (Eds.), *Handbook of Clinical Neurology, Volume 101* (pp. 239-262). Elsevier.

Uttley, L., Carlton, J., Woods, H. B., & Brazier, J. (2018). A review of quality of life themes in Duchenne muscular dystrophy for patients and carers. *Health and Quality of Life Outcomes, 16*(237), 1-16. https://doi.org/10.1186/s12955-018-1062-0

Uzark, K., King, E., Cripe, L., Spicer, R., Sage, J., Kinnett, K., Wong, B., Pratt, J., & Varni, J. W. (2012). Health-related quality of life in children and adolescents with Duchenne muscular dystrophy. *Pediatrics, 130*(6), 1559-1566. https://doi.org/10.1542/peds.2012-0858

van der Ploeg, H. P., van der Beek, A. J., van der Woude, L. H. V., & Mechelen, W. (2004). Physical Activity for People with a Disability: A Conceptual Model. *Sports Medicine, 34*(10), 639-649. https://doi.org/10.2165/00007256-200434100-00002

van Ruiten, H. J. A., Straub, V., Bushby, K., & Guglieri, M. (2014). Improving recognition of Duchenne muscular dystrophy: a retrospective case note review. *Archives of Disease in Childhood, 99*(12), 1074-1077. https://doi.org/10.1136/archdischild-2014-306366

Verhaert, D., Richards, K., Rafael-Fortney, J. A., & Raman, S. V. (2011). Cardiac Involvement in Patients with Muscular Dystrophies: Magnetic Resonance Imaging Phenotype and Genotypic

Considerations. *Circulation. Cardiovascular Imaging*, *4*(1), 67-76. https://doi.org/10.1161/CIRCIMAGING.110.960740

Verschuren, O., Wiart, L., Hermans, D., & Ketelaar, M. (2012). Identification of facilitators and barriers to physical activity in children and adolescents with cerebral palsy. *The Journal of Pediatrics*, *161*(3), 488–494. https://doi.org/10.1016/j.jpeds.2012.02.042

Vestergaard, P., Glerup, H., Steffensen, B. F., Rejnmark, L., Rahbek, J., & Mosekilde, L. (2001). Fracture risk in patients with muscular dystrophy and spinal muscular atrophy. *Journal of Rehabilitation Medicine*, *33*(4), 150-155. 150-155. https://www.medicaljournals.se/jrm/content/abstract/10.1080/16501970119066

Voos, M. C., Goya, P. S. A., Freitas, B. L., Pires, A. M. T., Favero, F. M., & Caromano, F. A. (2020). Timed immersion expiration measures in patients with muscular dystrophies. *Archies of Physiotherapy*, *10*(4), 1-8. https://doi.org/10.1186/s40945-020-0074-3

Wahlgren, L., Kroksmark, A., Tulinius, M., & Sofou, K. (2022). One in five patients with Duchenne muscular dystrophy dies from other causes than cardiac or respiratory failure. *European Journal of Epidemiology*, *37*(2), 147-156. https://doi.org/10.1007/s10654-021-00819-4

Walsh, L., & Potvin, M-C. (2019). Effect of verbal directions on grip strength evaluated using the handheld dynamometer. *The Open Journal of Occupational Therapy*, *7*(4), 1-5. https://doi.org/10.15453/2168-6408.1584

Walters, J. (2017). Muscle hypertrophy and pseudohypertrophy. *Practical Neurology*, *17*(5), 369-379. http://dx.doi.org/10.1136/practneurol-2017-001695

Wang, S., & Peng, D. (2019). Cardiac involvement in Emery-Dreifuss Muscular Dystrophy and related management strategies. *International Heart Journal*, *60*(1), 12-18. https://doi.org/10.1536/ihj.17-604

Watson, K., Egerton, T., Sheers, N., Retica, S., McGaw, R., Clohessy, T., Webster, P., & Berlowitz, D. J. (2022). Respiratory muscle training in neuromuscular disease: a systematic review and meta-analysis. *European Respiratory Review*, *31*(166). https://doi.org/10.1183/16000617.0065-2022

Weber, D. R., Hadjiyannakis, S., McMillan, H. J., Noritz, G., & Ward, L. M. (2018). Obesity and Endocrine Management of the Patient With Duchenne Muscular Dystrophy. *Pediatrics*, *142*(2), 43-52. https://doi.org/10.1542/peds.2018-0333F

Wei, Y., Speechley, K. N, & Campbell, C. (2015). Health-Related Quality of Life in children with Duchenne Muscular Dystrophy: A Review. *Journal of Neuromuscular Diseases*, *2*(3), 313-324. https://doi.org/10.3233/JND-150071

Wei, Y., Speechley, K. N., Zou, G., & Campbell, C. (2016). Factors associated with health-related quality of life in children with Duchenne muscular dystrophy. *Journal of Child Neurology*, *31*(1), 879-886. https://doi.org/10.1177/0883073815627879

Wenninger, S., Montagnese, F., & Schoser, B. (2018). Core clinical phenotypes in myotonic dystrophies. *Frontiers in Neurology*, *9*(303), 1-9. https://doi.org/10.3389/fneur.2018.00303

Werlauff, U., & Steffensen, B. F. (2014). The applicability of four clinical methods to evaluate arm and hand function in all stages of spinal muscular atrophy type II. *Disability and Rehabilitation, 36*(25), 2120-2126. https://doi.org/10.3109/09638288.2014.892157

Wilson, D. G. S., Tinker, A., & Iskratsch, T. (2022). The role of the dystrophin glycoprotein complex in muscle cell mechanotransduction. *Communications Biology, 5*(1022), 1-18. https://doi.org/10.1038/s42003-022-03980-y

Wratten, S., Pattman, J., & Harrison, S. (2019). *Foundation Aquatic Physiotherapy Course Handbook.* Aquatic Therapy Association of Chartered Physiotherapists.

Wright, A., Roberts, R., Bownman, G., & Crettenden, A. (2018). Barriers and facilitators to physical activity participation for children with physical disability: comparing and contrasting the views of children, young people, and their clinicians, Disability and Rehabilitation. *Disability and Rehabilitation, 41*(13), 1499-1507. https://doi.org/10.1080/09638288.2018.1432702

Yamashita, S. (2021). Recent progress in oculopharyngeal muscular dystrophy. *Journal of Clinical Medicine, 10*(7), 1375-1385. https://doi.org/10.3390/jcm10071375

Yao, S., Chen, Z., Yu, Y., Zhang, N., Jiang, H., Zhang, G., Zhang, Z., & Zhang, B. (2021). Current Pharmacological Strategies for Duchenne Muscular Dystrophy. *Frontiers in Cell and Developmental Biology, 9*(1), 1-22. https://doi.org/10.3389/fcell.2021.689533

Zamunér, A. R., Andrade, C. P., Arca, E. A., & Avila, M. A. (2019). Impact of water therapy on pain management in patients with fibromyalgia: current perspectives. *Journal of Pain Research, 12*(1), 1971-2007. https://doi.org/10.2147/JPR.S161494.

Zhu, Z., Li, J., Yang, D., Gao, F., Du, L., & Yang, M. (2021). Ultrasonographic evaluation of diaphragm thickness and excursion in patients with cervical spinal cord injury. *The Journal of Spinal Cord Medicine, 44*(5), 742-747. https://doi.org/10.1080/10790268.2019.1669955

Appendices

Appendix A: Study 1 Ethical Approval

UNIVERSITY OF GLOUCESTERSHIRE

Via email

Researcher Name
[redacted]

26/09/2018

Dr Emily Ryall
Research Ethics Committee Chair
Reader in Applied Philosophy

Oxstalls Campus,
Longlevens, Gloucester, GL2 9HW

Tel: [redacted]
Email: [redacted]

Dear Nicola

Thank you for your application for ethical approval.

I am pleased to confirm ethical clearance for your research following ethical review by the University of Gloucestershire's Research Ethics Committee (REC).

Please keep a record of this letter as a confirmation of your ethical approval.

Project Title:	The effects of hydrotherapy on respiratory function, strength and wellbeing in children and adults with muscular dystrophy
Start Date:	26/09/2018
Projected Completion Date:	17/08/2020
REC Approval Code:	REC.18.85.8

If you have any questions about ethical clearance please feel free to contact me. Please use your REC Approval Code in any future correspondence regarding this study.

Good luck with your research project.

Regards,

[redacted]

Dr Emily Ryall
Chair of Research Ethics Committee

Appendix B: Study 1 Informed Consent Form

UNIVERSITY OF GLOUCESTERSHIRE
at Cheltenham and Gloucester

CONSENT FORM – PARENT/GUARDIAN

A randomised-controlled trial to investigate the effect of long-term hydrotherapy in children and adolescents with Joint Hypermobility Syndrome.

The participant's parent/legal guardian should complete the whole of this sheet him/herself

You will be given a copy of the consent form to keep.

	Please tick the appropriate box YES	NO
Have you read the Research Participant Information Sheet, and has the research participation sheet been read out and explained to you and your child?	☐	☐
Have you and your child had an opportunity to ask questions and discuss this study?	☐	☐
Have you and your child received satisfactory answers to all your questions?	☐	☐
Who have you and your child spoken to? _____		
Do you understand that your child will not be referred to by name in any report concerning the study?	☐	☐
Do you understand that your child is free to withdraw from the study:		
- at any time (until one month before the study submission)	☐	☐
- without having to give a reason for withdrawing?	☐	☐
- *(where relevant)* without affecting your child's future care?	☐	☐
Do you agree for your child to take part in this study?	☐	☐
Do you agree to your GP and/or doctor being informed for your participation in the study?	☐	☐
Do you understand that any personal data will be kept for 6 months but may be analysed in connection with the research project before that time?	☐	☐

Signature of Research Participant's Parent/Legal Guardian:

Date:

Name in capitals:

Appendix C: Study 1 Information Sheet

Chamwell Centre
Overcoming disability in Gloucestershire

Researching the effects of hydrotherapy and muscular dystrophy – Information sheet

The primary aim of management for those with muscular dystrophy is to preserve physical function, activities of daily life and quality of life. Based on limited research evidence and clinical consensus, international guidelines recommend a range of voluntary activities should be prescribed including swimming-pool based exercise. Hydrotherapy is supervised exercise in warm water. The water decreases loading of joints through buoyancy and can provide resistance to movement. It may also allow physical training that is not possible on land. The possible benefits of hydrotherapy may include: improved joint range, maintenance of muscle strength, improved feelings of wellbeing and the maintenance of respiratory function.

We would like to do a clinical assessment of your child to look at the benefits of hydrotherapy. An assessment will take place when your child starts the hydrotherapy programme, then after approximately 5 and 10 weeks of doing hydrotherapy. These measures will take place at the Chamwell Centre (where the pool is located), at a time that is convenient for you and your child. The measures will take approximately 30-40 minutes to complete and the results will be available to you after the final measurements have been made. These clinical assessments will be very important to help us understand the benefits of hydrotherapy for children with muscular dystrophy but may also allow us to access funding to run more hydrotherapy sessions in the future

.

The measures we will take are described below:

1. Breathing measures. We will ask your child to perform a series of breathing manoeuvres into a small hand-held machine. This will measure the size of your child's lungs as well as how the air moves in and out.

Chamwell Centre
Overcoming disability in Gloucestershire

2. Diaphragm thickness. The diaphragm is a muscle located under the rib cage and helps with breathing. We will measure the size of the diaphragm using ultrasound. This involves placing a small amount of ultrasound gel on the skin just below the rib cage and moving the probe across the chest.

3. Muscle strength. We will measure muscle strength in the arms and legs using a small handheld machine. The machine will be placed on your child's arm or leg and we will ask you to try and bend your arm/leg and pull or push against the resistance of the machine as much as possible.

4. Wellbeing. We will ask your child to complete a short wellbeing questionnaire to ask how they feel when performing daily activities.

We will contact you to arrange a time for you're the baseline clinical assessment to be done. However, if you would prefer your child not to have these assessments do just let us know. This will not affect their access to the Centre of hydrotherapy sessions. If you have any questions, please contact Dr Nicola Theis [redacted].

Appendix D: Muscle Strength, Respiratory and Wellbeing Variables Throughout the 40-Week Study Duration

Participant 1 and Participant 2's Muscle Strength, Respiratory and Wellbeing Measures Throughout the 40-Week Study Duration (Mean ± SD)

						% Change				
		Week 0	**Week 8-10**	**Week 16**	**Week 40**	**Week 0 versus 8-10**	**Week 0 versus 16**	**Week 0 versus 40**	**Week 8-10 versus 16**	**Week 16 versus 40**
Muscle Strength (N)										
Biceps	Participant 1	63.5±10.0	35.0±2.2	57.1±7.3	23.4±0.4	-44.9%	-10.1%	-63.1%	63.1%	-59.0%
	Participant 2	79.3±1.3	89.4±3.6	69.1±5.2	47.3±8.5	12.7%	-12.9%	-40.4%	-22.7%	-31.5%
Quadriceps	Participant 1	27.2±7.4	65.7±7.6	56.6±1.9	60.2±8.4	141.5%	108.1%	121.3%	-13.9%	6.4%
	Participant 2	87.0±6.4	106.6±10.3	112.6±9.2	135.6±12.1	22.5%	29.4%	55.9%	5.6%	20.4%
Respiratory Function										
MIP (cm H_20)	Participant 1	14.0±1.0	28.3±2.1	25.3±7.4	9.5±0.7	102.1%	80.7%	-32.1%	-10.6%	-62.5%
	Participant 2	12.0±1.4	13.0±5.0	13.3±2.1	18.3±3.5	8.3%	10.8%	52.5%	2.3%	37.6%
MEP (cm H_20)	Participant 1	33.3±7.2	51.7±2.1	39.7±2.1	33.7±3.2	55.3%	19.2%	1.2%	-23.2%	-15.1%
	Participant 2	14.0±2.0	25.0±5.0	26.7±8.0	32.0±4.6	78.6%	90.7%	128.6%	6.8%	19.9%
Diaphragm Thickness (cm)	Participant 1	0.38±0.11	0.49±0.01	0.49±0.02	0.37±0.08	28.9%	28.9%	-2.6%	0.0%	-24.5%
	Participant 2	0.26±0.01	0.30±0.01	0.27±0.04	0.36±0.04	15.4%	3.8%	34.6%	-10.0%	33.3%
HRQoL										
NPC's Wellbeing Measure	Participant 1	56.0	56.0	33.0	52.0	0.0%	-41.1%	-7.1%	-41.1%	57.6%
	Participant 2	58.0	58.0	57.0	61.0	0.0%	-1.7%	5.2%	-1.7%	7.0%

Notes. HRQoL = health-related quality of life; MEP = maximal expiratory pressure; MIP = maximal inspiratory pressure; NPC = New Philanthropy Capital. NPC's Wellbeing Measure is scored from 0 to 100, where higher scores represent better wellbeing.

Appendix E: Study 2 Ethical Approval

UNIVERSITY OF GLOUCESTERSHIRE
at CHELTENHAM and GLOUCESTER

Dear Nadine,

Thank you for your application for ethical approval.

I am pleased to confirm ethical clearance for your research following ethical review by the School of Sport and Exercise - Research Ethics Panel (SSE-REP).

Please keep a record of this letter as a confirmation of your ethical approval.

Project Title:	An investigation into barriers and motivators that may affect participation in hydrotherapy for children and adolescents with Muscular Dystrophy.
Start Date:	August 2022
Projected Completion Date:	August 2023
SSE-REP Clearance code:	HENRY21-22

If you have any questions about ethical clearance, please feel free to contact me. Please use your SSE-REP clearance code in any future correspondence regarding this study.

Best wishes

[redacted]

Stephen C. How PhD
Chair of School of Sport and Exercise - Research Ethics Panel

School of Sport and Exercise - Research Ethics Panel (SSE-REP)
University of Gloucestershire, Oxstalls Campus, Oxstalls Lane, Gloucester, GL2 9HW
Tel: [redacted]
Email: [redacted]

Appendix F: Study 2 Online Questionnaire Format (Full)

UNIVERSITY OF GLOUCESTERSHIRE
at Cheltenham and Gloucester

Online Questionnaire Format

Carers' perspectives into barriers and motivators that may affect participation in hydrotherapy amongst children and adolescents with Muscular Dystrophy.

Information Sheet

You are being invited to participate in a research study that will investigate barriers and motivators for participation in hydrotherapy for Muscular Dystrophy. Specifically, we are trying to find out carers' perspectives into why you think your child (aged 5-17-years-old) may or may not want to participate in hydrotherapy and why you may or may not allow your child to partake in hydrotherapy. We would also like to see if you have ever been offered hydrotherapy.

Your participation in this study will require you to complete the following questionnaire, which should take no longer than ***15 minutes*** of your time. Your participation will be anonymous. This study involves minimal risk to you. The study consists of a few questions about your child's diagnosis and management of Muscular Dystrophy but neither you nor your child will be identifiable from any of the information you provide.

***PLEASE* NOTE: The completion of this study implies your consent to participate; consent will be asked for on page 1 of the questionnaire online.**

Why are we doing this research?

Hydrotherapy is a form of physical management that used movements and exercises to improve physical, psychological, and physiological functioning. It is performed by a trained professional in a heated pool. Research has indicated benefits of hydrotherapy for Muscular Dystrophy; however, the rate of attendance and participation is often low. Understanding why may help increase participation and/or inform professionals and researchers whether investing resources to provide hydrotherapy is worthwhile. Therefore, we want to investigate your perspective on the barriers and facilitators that may exist for hydrotherapy participation in children and adolescents with Muscular Dystrophy.

Who has reviewed the study?

All research has been approved by the University of Gloucestershire Research Ethics Committee.

Do I have to take part?

You do not have to participate in this study if you do not want to and are free to stop completing the questionnaire at any point. Upon completion you are free to withdraw your data at any point, without reason, up to one month before study submission.

For further information:

We will be happy to answer any question you have about this study at any point – if you have any questions or have a research-related problem, please contact Nadine Henry at [redacted] or Dr Simon Fryer at [redacted]. Please send all complaints to Dr Emily Ryall the Research Ethics Chair on [redacted]

Link to Questionnaire

https://docs.google.com/forms/d/e/1FAIpQLSdq5y3P8XZsBT6SZqFtcTuFk2-LdaDUHmJCkpGzHYpeOsKWTQ/viewform?usp=sf_link

Section 1: Demographics

1. **How old is your child?**

   Open ended

2. **What sex is your child?**

   Male | Female | Prefer not to say

3. **What county does your child live in?**

   Open ended

4. **What type of muscular dystrophy does your child suffer from?**

   Becker | Congenital | Distal | Duchenne | Emery-Dreifuss | Facioscapulohumeral | Limb-Girdle | Myotonic | Oculopharyngeal | Other

5. **At what age (or trimester) was your child diagnosed?**

   Open ended

6.

   a. **Is your child ambulant or non-ambulant?**

      Ambulant | Non-ambulant

   b. **Does your child use any physical aids?**

      Yes | No

      If answered 'yes' to 6b, please state which aids are used (E.g., wheelchair, crutches, orthosis, etc.).

      Open ended

Section 2: Current Treatment

7. **What forms of treatment does your child currently receive?** *Please select all that apply.*

   Physiotherapy | Occupational Therapy | Medications | Steroid Therapy | Creatine Supplements | Surgery | Exon Skipping Trials | Hydrotherapy | Other (*please explain*)

8.

   a. **How frequently does your child receive the forms of treatment you have stated in the previous question?**

      Less than once a month | Once a month | 2-3 times a month | 1-2 times a week | 3+ times a week

   b. **How long does each session typically last for?**

      Less than 30 minutes | 30 minutes | 45 minutes | 1 hour | More than 1 hour

9. **How do you typically travel to therapy sessions provided for your child?**

   Walk | Car | Bus | Train | Other

Section 2: Current Treatment (continued)

***Statement*:**

Hydrotherapy is a treatment carried out by trained physiotherapists that utilises the properties of water in an appropriately heated pool, using exercises to improve physical, psychological, and physiological functioning in individuals with injuries or disabilities.

10. **Are you aware of any hydrotherapy pools near you?**

    Yes | No

11. **Are you aware of the cost of hydrotherapy sessions?**

    Yes | No

12. **If the average cost of group hydrotherapy sessions is £15 per child, would this stop you from letting your child attend sessions?**

    Yes | No

13. **Has your child ever been offered hydrotherapy?**

    Yes | No

14. **Has your child ever taken part in hydrotherapy*?**

    Yes [*continue to ROUTE 1*]

    No [*continue to ROUTE 2*]

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at Cheltenham and Gloucester

ROUTE 1

Section 3: Motivators and Barriers (Part 1)

15. Has your rate of attendance in hydrotherapy changed since the Covid-19 pandemic?

Attendance has increased | Attendance has remained similar | Attendance has decreased | Attendance stopped completely

16.

a. **How frequently does/did your child participate in hydrotherapy?**

Less than once a month | Once a month | 2-3 times a month | 1-2 times a week | 3+ times a week

b. **How long does/did each session typically last for?**

Less than 30 minutes | 30 minutes | 45 minutes | 1 hour | More than 1 hour

17. Is your child currently motivated to take part in hydrotherapy?

Yes [*continue to ROUTE 1A*]

No [*continue to ROUTE 1B*]

ROUTE 1A

Section 3: Motivators and Barriers (Part 2)

18. In your opinion, what do you think are the biggest motivations for your child wanting to take part in hydrotherapy sessions?

Open ended

19. As a carer, name your biggest motivation for wanting your child to take part in hydrotherapy sessions. *Please explain why this is your biggest motivation.*

Open ended

20. Are there any reasons that you know of which might mean your child does not wish to partake in hydrotherapy?

Open ended

21. As the carer, are there any barriers that have prevented you from allowing your child to partake in hydrotherapy sessions? *Please explain what these barriers are.*

Open ended

[*Continue to debrief section*]

ROUTE 1B

Section 3: Motivators and Barriers (Part 2)

18. Are there any reasons that you know of which might mean your child does not wish to partake in hydrotherapy?

Open ended

19. As the carer, are there any barriers that have prevented you from allowing your child to partake in hydrotherapy sessions? *Please explain what these barriers are.*

Open ended

[Continue to debrief section]

ROUTE 2

Section 3: Motivators and Barriers ***(If you answered 'no' to Q13 or Q14).***

15. Would hydrotherapy be something of interest to you and your child?

Yes | No

16. If you decided to take part, how often do you think you would be able to attend hydrotherapy sessions?

Less than once a month | Once a month | 2-3 times a month | 1-2 times a week | 3+ times a week

17. As the carer, what would be your biggest motivation for wanting your child to take part in hydrotherapy sessions?

Open ended

18. In your opinion, what do you think would be the biggest motivations for your child wanting to take part in hydrotherapy sessions?

Open ended

19. As the carer, what barriers would prevent you from allowing your child to partake in hydrotherapy sessions?

Open ended

20. In your opinion, would there be any reasons that your child would have to not want to partake in hydrotherapy sessions?

Open ended

[Continue to debrief section]

Section 4: Debrief Letter

Dear Madam/Sir,

UNIVERSITY OF GLOUCESTERSHIRE
at Cheltenham and Gloucester

Thank you very much for participating in our study 'An investigation into barriers and motivators that may affect participation in hydrotherapy for children and adolescents with Muscular Dystrophy'. Our hope is that the data collected from you and other participants will help us to better understand the barriers that prevent and factors that motivate participation in hydrotherapy within families who have a child suffering from Muscular Dystrophy. This would assist in the prescription of treatments for those with muscular dystrophy, as well as inform us whether it is worthwhile continuing research in hydrotherapy for Muscular Dystrophy and what the best approach to maintain participation may be.

We would like to take this opportunity to reassure you that any data collected during this study will remain anonymous and confidential, where you will not be identifiable in any publications or reports resulting from this research. Data will be held for a maximum of 10 years before being destroyed. We would like to remind you that you have the right to withdraw your data, without having reason, at any point for up to one month before the study submission. If you would like to withdraw your data, please contact a member of the research team (email addresses provided at the end). The University's Privacy Notice can be found at this link: https://www.glos.ac.uk/information/knowledge-base/Research-Participants-Privacy-Notice/.

Again, thank you for your participation in this study. If you would like to see a summary of the research findings following its submission, or if you have any further questions, please don't hesitate to contact a member of the research team.

Kind regards,
Nadine Henry and Dr Simon Fryer
University of Gloucestershire

Email addresses:
[redacted]
[redacted]