Clinics in Developmental Medicine | Mac Keith Press

Neuromuscular Disorders in Children

A Multidisciplinary Approach to Management

Edited by **Nicolas Deconinck and Nathalie Goemans**

Neuromuscular Disorders in Children:
A Multidisciplinary Approach to
Management

Clinics in Developmental Medicine

Neuromuscular Disorders in Children: A Multidisciplinary Approach to Management

Edited by

NICOLAS DECONINCK
Department of Pediatric Neurology and Neuromuscular Reference Centre, HUDERF, Université Libre de Bruxelles, Brussels, Belgium and Department of Pediatric Neurology and Neuromuscular Reference Centre, UZ Gent, Ghent, Belgium

NATHALIE GOEMANS
Department of Pediatric Neurology, Neuromuscular Reference Center for Children, University Hospitals Leuven, University of Leuven, Leuven, Belgium

2019
Mac Keith Press

Managing Director: Ann-Marie Halligan
Project Management: Riverside Publishing Solutions Ltd

First published in this edition in 2019 by Mac Keith Press
2nd Floor, Rankin Building, 139–143 Bermondsey Street, London, SE1 3UW

British Library Cataloguing-in-Publication data
A catalogue record for this book is available from the British Library

Cover designer: Marten Sealby

ISBN: 978-1-911612-08-7

Typeset by Riverside Publishing Solutions Ltd

Printed by Jellyfish Solutions Ltd

CONTENTS

SECTION 3: OVERVIEW OF THE MOST FREQUENT NEUROMUSCULAR CONDITIONS IN CHILDREN AND DISEASE SPECIFIC MEDICAL MANAGEMENT

SECTION 8: PSYCHOSOCIAL ASPECTS

AUTHOR APPOINTMENTS

Boglárka Bánsági	Centre for Metabolic Diseases, University Hospital Leuven, Leuven, Belgium
Sandra Coppens	Neuromuscular Reference Center, Université Libre de Bruxelles, Brussels, Belgium
Stacy Cossette	Congenital Muscle Disease Tissue Repository Manager, Medical College of Wisconsin, WI, USA
Rudy van Coster	Pediatric Neurology, Ghent University, Belgium
Basil T Darras	Joseph J. Volpe Professor of Neurology, Harvard Medical School; Associate Neurologist-in-Chief, Division of Clinical Neurology, Boston Children's Hospital, Boston, MA, USA
Nicolas Deconinck	Department of Pediatric Neurology and Neuromuscular Reference Center, HUDERF, Université Libre de Bruxelles, Brussels, Belgium
Imelda de Groot	Associate Professor, Consultant pediatric Rehabilitation, Department of Rehabilitation, Radboud University Medical Centre, Nijmegen, The Netherlands
Liesbeth De Waele	Department of Paediatric Neurology, University Hospitals Leuven, Leuven, Belguim
Tina Duong	Physical Therapist; Clinical Research Manager, Division of Neuromuscular Medicine, Stanford Health Care, Palo Alto, CA, USA
Sam Geuens	Clinical Neuropsychologist, University Hospitals Leuven, Leuven, Belgium
Nathalie Goemans	Department of Pediatric Neurology, Neuromuscular Reference Center for Children, University Hospitals Leuven, University of Leuven, Leuven, Belgium

Laurence Goffin	Department of Pediatrics HUDERF, Université Libre de Bruxelles; Department of Pediatrics, CHIREC Delta, Brussels, Belgium
Anne Lennox	Founding Parent and Chief Executive, Myotubular Trust, UK
Wendy K M Liew	Clinical Fellow in Neurology, Boston Children's Hospital and Harvard Medical School, Boston MA; Consultant Pediatrician and Neurologist, SBCC Baby & Child Clinic, Neurology Centre; Visiting Consultant, Neurology Service, Department of Pediatrics, KK Women's and Children's Hospital, Singapore
Oscar Mayer	Medical Director, Pulmonary Function Testing Laboratory, The Children's Hospital of Philadelphia; Professor of Clinical Pediatrics, Perelman School of Medicine at the University of Pennsylvania, PA, USA
Anna G Mayhew	John Walton Muscular Dystrophy Research Centre, Newcastle upon Tyne, UK
Pierre Moens	Surgeon-in-chief, Paediatric orthopaedics and spinal deformities, University Hospitals Leuven, Leuven, Belguim
Maarten van Nuffel	Assistant-Surgeon-in-chief, Hand Unit, Department of Orthopaedics, University Hospitals Leuven, Leuven, Belgium
Hasan Özen	Hacettepe University Children's Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
Lionel Paternoster	Department of Paediatric Neurology, Queen Fabiola Children's University Hospital, Université Libre de Bruxelles, Brussels, Belgium
Ros Quinlivan	Consultant in Neuromuscular Disorders, MRC Centre for Neuromuscular Diseases, National Hospital for Neurology and Neurosurgery, London, UK
Gauthier Remiche	Head of the Neuromuscular Reference Center Erasme-HUDERF, Department of Neurology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium

Kristy Rose	Paediatric Physiotherapist, Paediatric Gait Analysis Service of New South Wales, The Children's Hospital at Westmead, Sydney, Australia
Anne Rutkowski	Kaiser SCPMG, Los Angeles, CA, USA
Hemant Sawnani	Associate Professor, Department of Pediatrics, University of Cincinnati; Division of Pulmonology & Section of Sleep Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
Ann F Schrooten	Parent of a child with a congenital muscular dystrophy, founder and board member of The Willow Tree Foundation, Phoenix, AZ, USA
Thomas Sejerson	Professor, Senior Consultant, Pediatric Neurology, Department of Women's and Children's Health, Karolinska Institute, Stockholm, Sweden
Laurent Servais	Centre de Référence des Maladies Neuromusculaires, CHU de Liège, Liège, Belgium; Institute i-Motion, Hôpital Armand Trousseau, Paris, France
Banu Sundar	Assistant Professor in Neurology, University of Massachusetts Medical School, Worcester, MA, USA
Haluk Topaloglu	Hacettepe University Children's Hospital, Department of Child Neurology, Ankara, Turkey
Michel Toussaint	Head of Therapy and Research, Centre for Home Mechanical Ventilation and Neuromuscular Disorders, Department of Rehabilitation, Inkendaal Rehabilitation Hospital, Brussels, Belgium
Karim Wahbi	Cardiology Department, Cochin Hospital, Paris Descartes University, Paris, France
Peter Witters	Centre for Metabolic Diseases, University Hospitals Leuven, Leuven, Belgium

FOREWORD

Neuromuscular Disorders (NMDs) cover all diseases that affect one or more components of the "motor unit", composed of the alpha-motor neuron, spinal nerve roots, the peripheral nerves with their axons and myelin sheets, the neuromuscular junction, and last but not least, the muscle fibers. In peripheral neuropathies, sensory fibers and the spinal ganglia can also be affected. NMDs are rare diseases with an age-specific overall prevalence in children and adolescents of 60-70/100.000. Only 15% of cases are due to an acquired, mostly inflammatory aetiology, while most are due to a broad spectrum of rare inborn causes. Of those, Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA) have by far the highest incidence (18 and 12/100.000, respectively). Unfortunately, the most prevalent of these genetic syndromes exhibits a rapidly progressive course resulting in severe disability and a significantly shortened life-span.

This is probably why until only a few decades ago, general society and many physicians were hardly aware of these diseases. They were considered ominous without treatment perspectives, and the patients and their families were left alone, frequently in deep desperation, to deal with the diseases' consequences. However, as the genetic cause of these diseases was gradually deciphered, beginning in the 1980s, the scientific community's interest in their aetiology, pathophysiology, natural history, and hopefully cure, rose, and persists with increasing speed and success. In parallel and in close collaboration with growing numbers of patient and family support groups, innovative measures of symptomatic treatment to improve quality of life and psychosocial well-being are being developed.

This book addresses the progress made in diagnosis and classification, and particularly in treatment of NMDs. It has been written by an international group of experts highly experienced in their respective diagnostic and therapeutic fields. It comprises their up-to-date views and experiences from differential diagnosis, and monitoring the clinical course to the treatment, development and application of best-practice strategies and psychosocial care for patients and their families.

The book starts with a description of the burdensome and psychologically stressful situation of the patients and their families after the diagnosis of a NMD and its significance over their entire life span. This is followed by an overview of methods and results in developing best-practice guidelines and standards-of-care for many of these diseases, based on analyses of the scientific literature and formal consensual processes of clinical experts. The need for interdisciplinary and inter-professional co-operation in caring for these patients is highlighted already in this first part of the book.

In the second part, the nosological groups of NMDs are discussed chapter by chapter, covering the presenting symptoms, diagnosis, and differential diagnosis, genetic aspects, best-practice treatment and clinical course, and recent and (hopefully) future therapeutic developments. This discussion addresses not only the most frequent DMD, SMA and

Charcot-Marie-Tooth neuropathies, but also rarer entities such as congenital myopathies, myasthenic syndromes and hereditary ion-channel dysfunctions. The less frequent acquired and usually treatable diseases such as juvenile dermatomyositis, inflammatory polyneuropathies, and myasthenia gravis are also fully covered along with their recent therapy recommendations.

The third part details the monitoring of symptoms and complications as well as treatment strategies for the different groups of patients in the fields and from the perspectives of physiotherapy, occupational therapy, technical aids, orthopaedics, orthopaedic surgery, gastrointestinal, respiratory and cardiac care, and last but not least, psychosocial care.

I congratulate the editors and authors on this comprehensive and up-to-date book which is the first on NMDs in children. It is consistently patient-centred, will help readers learn about the latest classification and treatment options for these diseases, and hopefully influence their attitudes and decisions when caring for patients with neuromuscular disorders. With broad distribution this book will help to improve the fate and quality of life of many patients suffering from NMDs, as well as their families.

Rudolf Korinthenberg, M.D.
Professor Emeritus of Neuropaediatrics and Muscular Disorders,
Center of Paediatrics and Adolescent Medicine,
University Medical Centre Freiburg, Germany

PREFACE

Neuromuscular disorders are rare but often devastating for patients and their families. Their effects on the life-course trajectories of young people can be profound and long lasting. They are very often associated with dysfunction of a number of physiological systems, leading to complex symptoms and needs, e.g. impairments that require orthopaedic services, cause pain, respiratory, cardiac, and psychological distress. This increases the burden for patients, impacting participation and quality of life, and calls for complex and multidisciplinary management.

Over the last 20 years, the outlook has started to change drastically, both as a result of societal changes with respect to disability and advances in molecular genetics and histopathological technology. The latter have enabled the recognition and understanding of the underlying molecular mechanisms of many different neuromuscular conditions, highlighting therapeutic targets for the future or emerging applications, thus opening an era for new specific, sometimes gene tailored, treatment approaches.

Nowadays, clinicians undertaking training and a career in the neuromuscular disorders field very often have to "pick" their knowledge from informal contacts with more senior experts in their respective hospitals. Moreover, the knowledge and expertise in the management of some ultra rare neuromuscular disorders is often limited to a very few specialized centres that are scattered across the world and not always accessible for every student.

With this collaborative work on the management of neuromuscular disorders we aim to gather for the first time in one place the knowledge from recognized experts from various backgrounds, including clinicians, surgeons, geneticists, physiotherapists, psychologists, and parents.

On completing this writing odyssey, we are reminded of our first face-to-face meeting with Ann-Marie Halligan and Udoka Ohuonu from Mac Keith Press, at the congress of the World Muscle Society in Brighton. Ann-Marie and Udoka showed confidence in the merits of our approach for this project. Moreover it could not have become a reality without the benevolent support of Bernard Dan who helped us to structure its first steps.

An important milestone was also the decision to work together as editors, combining our personal experience and expertise in the field of neuromuscular disorders; each of us motivating the other to bring to its term a fantastic but very intensive project. We were very satisfied to build a common view on what should be the unifying idea of this work, and then to enlist contributors to build a book we hope will be new, appreciated, and useful in the field of neuromuscular disorders.

Important for us was to re-position "clinical evaluation" as key in this exciting era of high-level medicine. Thus, we included a description of the clinical features of neuromuscular disorders. The care and management of neuromuscular diseases start with a correct diagnosis. The recognition of clinical signs and symptoms will raise suspicion and prompt

an early diagnosis. Modern genetics has drastically improved the diagnostic journey for neuromuscular disorders. However, a thorough insight in clinical features has become even more important, for example in clarifying the genotype-phenotype correlation when applying whole sequencing techniques in rare diseases.

As highlighted by Rudolf Korinthenberg in the foreword, this work has been driven by our conviction that a coordinated multidisciplinary approach of management is essential to improve the quality of life of children with neuromuscular diseases and their families. This should be based as much as possible on the application of guidelines throughout all stages of the disease. We hope that this work will contribute to this end.

We live in exciting times, with promising therapeutic strategies, in development or even yet approved by the regulatory authorities, that could impact on disease progression. Throughout the book, we aimed to provide the reader with the most recent update on therapeutic advances, both in preclinical and clinical development. In addition, we highlighted the importance of validated and harmonized outcome measures for the evaluation of disease progression and the impact of interventions.

This book is the result of an intensive collaborative process. We would like to thank all the contributors, all of whom are noted experts in their fields, who enthusiastically embarked on this project, and responded to our editorial requests. We are very grateful for their commitment to produce high quality information, which reflects our longstanding collaboration in sharing expertise in this domain.

The book could not have been completed without the support and energy of Ann-Marie Halligan, Udoka Ohuonu, Lucy White, Sally Wilkinson, Rosie Outred, Duncan Potter, Tiffany Bertrand and Elke De Vos.

Finally, we would like to express our gratitude to all the patients and families, whose lives and experiences were an inspiration for the writing of this book, but more generally, have long inspired our work in the neuromuscular field.

Nicolas Deconinck and Nathalie Goemans

Section 1
Introduction

1
PARENT PERSPECTIVES ON NEUROMUSCULAR DISORDERS: FROM DIAGNOSIS, TO PARENTING AND LIVING WITH, TO ADVANCE CARE PLANNING AND PREPARING FOR DEATH

Anne Rutkowski, Stacy Cossette, Anne Lennox and Ann F Schrooten

Introduction

When a neuromuscular disease diagnosis is made, parents may leave the clinic or hospital in shock. They may not have heard or processed any information relayed by the medical professional after receiving the diagnosis. Time may seem to stand still. There are extended family members waiting to hear the news, who must be called, messaged, or seen.

Acceptance can be difficult, and soon the parents realize that nothing will be the same again. The unknowns that lie ahead may feel overwhelming. There will be a steep learning curve to understand both the disease and how their lives will change. Most parents and extended family members will have no prior knowledge about genetics and be even less familiar with the specific neuromuscular disorder that now affects their family.

Perceptions about the disorder will evolve. Parents will need to learn by trial and error how to provide the required care, master sophisticated in-home medical equipment, and navigate both the social and medical environments to ensure optimal care and quality of life. The parent's and child's health and emotional well-being will impact quality of life. The ability to cope will matter more than disease severity.

This chapter will evaluate four milestones when parenting a child with a neuromuscular disorder: 1) obtaining a genetic diagnosis, 2) living with the chronic neuromuscular disorder, 3) advance care planning and 4) preparing for death. These milestones may occur in parallel or sequentially. While significant advances have been made in genetic testing technologies, access to testing, engagement of palliative and psychological support, and discussions regarding advance care are often lacking. Support through community and advocacy forums and the world wide web provide additional resources that are complementary to medical counsel.

Diagnosis

Genetic testing can have a demonstrable impact on families and affected individuals (Smith et al. 2004). Testing may provide individual benefits, such as family planning, the end of a diagnostic odyssey and additional testing, the ability to connect with others similarly affected, and tailored medical management. The possible drawbacks of genetic testing may include the persistence of anxiety and depression in some individuals with positive or negative test results, and health discrimination (Vansenne et al. 2009; Kang 2011). Societal benefits of genetic testing include an improved understanding of a particular disease presentation, genotype to phenotype correlations, and overall disease prevalence.

While it is generally accepted that genetic testing provides potential individual and society benefits, not all clinicians endorse genetic testing in neuromuscular conditions without clinical trials or therapeutic intervention. This lack of endorsement can be a significant barrier as clinicians are the gatekeepers (Toiviainen et al. 2003).

Several studies have interrogated clinician attitudes towards presymptomatic or susceptibility testing. Clinicians report concerns that laypeople's attitudes towards genetic testing lead to high expectations with limited disease knowledge (Toiviainen et al. 2003; Hall et al. 2015). However, there are no studies that evaluate clinician attitudes and barriers to ordering genetic testing in symptomatic patients, including children and adults with presumed neuromuscular disorders.

Clinician barriers may include a bias against genetic testing, uncertainty about which genetic test to order, how to interpret genetic test results, and how to provide appropriate counseling once test results are obtained. A recent study of neurologists and psychiatrists showed that 49% of neurologists did not have a genetic professional to refer patients to and thought testing could harm the patient (Salm et al. 2014). Having access to a genetic counselor increased the likelihood that the neurologist would order genetic testing.

Additional barriers to genetic testing include lack of access to commercial or research-based testing, lack of financial ability to pay for testing, and lack of access to clinicians with neuromuscular expertise. A recent report on care of Duchenne muscular dystrophy patients in Mexico highlights the challenges in obtaining adequate care, starting with a delay in noticing first symptoms. Mean age at death in this cohort is 18.94 ± 6.73 years with a clear acknowledgement of the reduced life span of their cohort compared to developed countries (López-Hernández et al. 2014). The late diagnosis and low percentage of genetically confirmed cases may further impede proactive medical management and relate directly to lower survival. However, there are no randomized control trials to evaluate whether genetic testing has improved health outcomes or is cost effective.

Delay in genetic diagnosis

There are multiple reports of documented delays in obtaining a genetic diagnosis in children and adults with neuromuscular disorders (Table 1.1). Diagnostic delays can lead to additional affected children within a family and extended and costly diagnostic workups. The length of delay may vary by severity with an urgency afforded to the more severe phenotypes (Table 1.1).

TABLE 1.1
Delay in genetic diagnosis

Neuromuscular disorder	*Adult/child population*	*Average time from symptoms to diagnosis (Country)*	*Reference*
Duchenne muscular dystrophy	Child	2.5 years (United States)	Ciafaloni 2009
Duchenne muscular dystrophy	Child	1.6 years (Europe)	Van Ruiten 2014
Myotonic dystrophy (DM2)	Adult	14 years	Hilbert 2013
Spinal muscular atrophy (SMA)	Child/ Adult	3.6 months (SMA1), 14.3 months (SMA2) and 43.6 months (SMA3)	Lin 2015
Genetically confirmed muscular dystrophy	Adult	4.3 years	Spuler 2011

Family coping once a genetic diagnosis is made

The majority of studies evaluating short and long-term psychological effects of genetic testing have been performed in presymptomatic individuals. A survey of presymptomatic individuals at risk for dominant neuromuscular disorders demonstrates a high acceptance of genetic testing, regardless of the results (Smith et al. 2004).

Genetic testing may lead to a range of feelings including, blame, guilt, and isolation for some individuals, while others report an improved quality of life. Anxiety and depression may persist in some presymptomatic individuals with positive or negative results. In a retrospective review, presymptomatic and symptomatic individuals differed in their perception of their health and levels of anxiety and depression before genetic testing, with no long-term psychological impairment in either group after testing (Vansenne et al. 2009).

Advances in genetic testing and physician education

Advances in genetic testing technology, including the use of next generation and whole exome sequencing, have improved the yield of a genetic diagnosis in presumed neuromuscular patients to as high as 40% (Savarese et al. 2016; Ghaoui et al. 2015). The use of these technologies may lead to a larger number of patients identified as having a variant of unknown significance with results that are difficult to interpret. Interpretation of variants can be challenging due to overlapping phenotypes, variability in disease transmission, and lack of inclusion of phenotypic patient data on commercial order forms. It can take years to reclassify a variant of unknown significance and there can be a significant burden to recontact patients and inform them of reclassification of their variant status (Pyeritz 2011; Hunter et al. 2001).

Lay people can have difficulty in understanding the difference between a pathologic mutation and a variant of unknown significance test result in the context of susceptibility testing (Hall et al. 2015; Lindor et al. 2013). It is unclear whether parents and affected individuals understand the difference in genetic technologies, the low yield of definitive testing for new phenotypes, and whether this knowledge is important in providing informed consent. It is recommended that neurologists and pediatricians work together with geneticists and genetic counselors to improve diagnostic yield and communicate diagnostic testing

results. It is important to provide the family with realistic turnaround times for genetic testing, especially research-based testing, and a mechanism for the family to contact the testing laboratory.

When a diagnosis is not made, families may turn to direct-to-consumer commercial genetic testing. The lack of consultation with a clinician may preclude a lay person's understanding of the type of testing offered, the clinical validity of the test, and a thorough interpretation of positive and negative results in the context of their presumed diagnosis. While geneticists are reluctant to recommend direct to consumer testing for these reasons, there appears to be an increased interest by the lay public with an assumption that clinicians will help interpret results (Howard and Borry 2013; McGuire et al. 2009).

Access to preimplantation genetic diagnosis has improved. Parents of a child with a neuromuscular disorder may choose to undergo preimplantation genetic diagnosis to ensure additional unaffected children. Many neurologists and psychiatrists, however, do not feel comfortable discussing preimplantation genetic diagnosis with parents of an affected child (Klitzman et al. 2014).

Parents of children with neuromuscular disorders strongly support newborn screening, with 95.9% of parents of children with Duchenne muscular dystrophy, Becker muscular dystrophy, or spinal muscular atrophy and 92.6% among expectant parents supporting a screening program (Wood et al. 2014; Chung et al. 2016). No negative psychosocial impacts of newborn screening were identified among those families who received a diagnosis through newborn screening. However, ethical questions persist and include risks and benefits, whether it should require informed consent, be limited to boys, what is the ideal timing for screening (prenatal, newborn, or later in infancy), and what factors influence this determination.

Given the advances in genetic testing technology, preimplantation genetic testing, direct-to-consumer genetic testing, and newborn screening, these topics should be included as part of the medical school curriculum with a more in-depth evaluation of discrepancies between physician and lay person attitudes and knowledge gaps, including physician understanding of lay person priorities. A recent study demonstrated a significant improvement in medical student knowledge, attitudes, intended behavior, and self-efficacy related to genetic testing after completing a curriculum on genetic testing (Metcalf et al. 2010).

Quality of life and the lived experience

Most neuromuscular disorders are life-long, life-limiting, disabling conditions. Quality of life for those with neuromuscular disorders and their parents is lower than normative controls, but not always as low as one might predict due to the influence of coping strategies (Bach et al. 1991; Bann et al. 2015). Internal coping strategies, such as adjusting life goals and self-confidence, are critical to positive adjustment. External coping mechanisms, such as respite care and accessible transportation, lead to better adjustment. Standardized scales have identified individual, family, and community domains that may be impacted in neuromuscular disorders (Bann et al. 2015; Abresch et al. 2002) (Table 1.2).

Disease severity does not necessarily have a negative impact on an affected person's perception of quality of life (Bach et al. 1991). This is termed the disability paradox. While

TABLE 1.2
Factors affecting quality of life for those with neuromuscular disease

Individual level	*Family level*	*Community level*
Age	Socio-economic status	Accessibility
Sex	Caregiver respite	NMD-related resources
Education level	NMD-related beliefs	Inclusion precepts
Health knowledge	Values	Attitudes
Employment opportunities	Expectations	
Income		
Confidence		
Affordable health insurance		

NMD: neuromuscular disease.

functional impairment has an admittedly negative impact on muscle strength, independence level, and activity level, an affected person's satisfaction with the frequency and quality of care given, alternate values, adjusted expectations, and acceptance of one's current condition may explain the paradox (Graham et al. 2014; Kohler et al. 2005; Chen and Clark 2007). The most severe neuromuscular disorders are also the most apparent and, therefore, difficulties experienced may be better appreciated by observers who may be more sympathetic towards the affected child and parents. The severely affected child and the family may have less difficulty obtaining needed accommodations, health aids, healthcare services, and financial assistance. Conversely, those mild-to-moderately affected can experience a relatively negative perception of quality of life. (Houwen-van Opstal et al. 2014). The expectations placed upon those mild-to-moderately affected may be unreasonably high, they might not qualify for assistance or services, and they may not identify with the abled members of their community, nor the disabled members, leading to loneliness and isolation.

A lower quality of life correlates significantly with loss of function and the rate at which function is lost. Those with congenital-onset disorders along the spectrum from mild-to-severe often do not perceive a dramatic loss in function and independence, therefore, they may have higher quality of life perceptions (Narayanaswami et al. 2000). However, some of those with late-onset disorders may experience significant losses as their condition worsens. Interestingly, there may be a loss-of-function effect that can result in positive feelings in those children who have a devoted caregiver and healthy home environment. As the ability to stand or transfer positions decreases, or if arm function reduces, boys with Duchenne muscular dystrophy have been found to perceive more understanding and love from parents and "feel happier at home" (Houwen-van Opstal et al. 2014).

Children with chronic disorders have up to a three-fold increase in psychosocial complications when compared to their healthy peers (Thompson et al. 1992). Depression, anxiety, and psychological maladjustment are some of the most common issues identified in children and adolescents with chronic conditions (Perrin et al. 2012). One study found that 59% of those with slowly progressive neuromuscular disorders had high depression scores and 90%

had high anxiety scores (Ozer et al. 2010). The unpredictable nature of a neuromuscular disorder often leads to anxiety for many (Ozer et al. 2010; Rose et al. 2012).

There sometimes can be a mismatch between how parents rate their child's physical and mental health and how the child would rate it. In one study, 22% of parents rated their son's physical and mental health lower than their sons did (Lim et al. 2014). Social acceptance of the child with Duchenne muscular dystrophy was viewed as higher when rated by the affected boys, but lower when rated by the parent. The parents may have a broader perspective of what acceptance means, and may be more aware of the ways their children are not being accepted that go unnoticed by the boys themselves. The mood of the boys with Duchenne muscular dystrophy was more likely to be viewed as happy by the affected children, while reported as less happy by the parent (Houwen-van Opstal et al. 2014). These discrepancies may be related to parents using their own values to interpret limitations experienced by their children.

Transitions from childhood to teenage years may be accompanied by changes in quality of life perceptions (Perrin et al. 2012; Rose et al. 2012). The teenage years bring concerns with individuation, rebellion against status quo, and socialization which includes fitting-in and mating-up (Perrin et al. 2012). When teens were asked what it is like to live with their neuromuscular disorder, responses were that it takes a lot of extra effort every day, and that it is restraining, painful, and worrisome (Woodgate 1998). The themes adolescents bring up consistently when asked about living with a chronic condition include: developing/maintaining friendships, having a normal life, family importance, attitude about treatment, school experiences, encounters with clinicians, and the future (Perrin et al. 2012; Taylor et al. 2008).

With better technological advancements and medical care, young people with chronic, life-threatening conditions are more often living into adulthood. Most teens with neuromuscular disorders have grown-up with limited duties and responsibilities, but as legal adults, they may now be expected to take charge of their own care. This phase can be overwhelming for young adults, and adherence to healthy practices and/or treatment may waver at this time. The complexities of managing their level of care are best learned gradually over years of time, so it is recommended to start early and to be patient with the learning process. The adult medical care system may be different from the pediatric system in ways that do not support the best interests of someone with a neuromuscular disease. Medical supplies and equipment will be designed for large adult bodies, for example, which may be inappropriate for an adult with a neuromuscular disorder. Also, adult care practitioners are often not trained in pediatric-onset conditions like these and they may not know how to best treat the adult patient. Parents are usually accustomed to acting as advocates for their child, a role that may benefit the young adult patient throughout the transition to adult care, and whenever there is a change in the type or level of care required. Achieving a balance between the young adult's need for independence, and the parent's need to have adequate information to support their child's best interests during the transition, prepares all parties for success and a greater likelihood of satisfaction. (DH/Child Health and Maternity Services Branch et al. 2006).

For adults with neuromuscular disorders, the loss or lack of ever achieving independence, along with increasing dependence upon others and technical aids, can be discouraging

(Nätterlund et al. 2000). A scientist with muscular dystrophy recounts his personal loss of ability: "It is falling, broken bones, struggling to breathe, watching one ability after another vanish" (Munn 2010). He describes falling in a snow bank in the darkness with only the hope that a kind, able person would come along soon to help him up. He summarizes his appraisal of his diminishing quality of life by saying, "What they and I need is hope that this whole horrible thing can be reversed" (Munn 2010).

Coping skills are a stronger predictor of emotional health outcomes for affected persons when compared to the disease perceptions they have (Dempster et al. 2015). Effective coping skills (i.e. acceptance, venting, doing something about it) were found to be the most important factor in quality of life for participants across many studies. The level of self-confidence was also predictive of how well someone copes with a neuromuscular disorder (Rose et al. 2012; Dempster et al. 2015; Davis 1993; Thomas et al. 2014).

Personal values and expectations play a significant role in perceptions of quality of life. Individuals that perceive misalignment between their aspirations and their actual abilities, especially as the disease progresses, experience a greater negative impact on quality of life (Bann et al. 2015).

Parental quality of life and lived experience

When a family receives a neuromuscular diagnosis, it can be overwhelming. There will be many unpredictable challenges along the way and unfortunate circumstances that the entire family must adapt to in order to thrive. It can be a devastating blow for parents to realize there is little they can do, which may leave them feeling inadequate and hopeless (Davis 1993).

Parents are profoundly affected by their child's condition. Isolation, loneliness, stress, anxiety, anger, exhaustion, and depression are reported to impact quality of life for parents of children with Duchenne muscular dystrophy or other chronic health conditions (Perrin et al. 2012; Barlow and Ellard 2006; de Moura et al. 2015; Yilmaz et al. 2010). The caregiving activities are often physically demanding and require load-lifting, bending, pushing, and pulling many times each day (de Moura et al. 2015; Yilmaz et al. 2010). Parents often have little to no personal time, neglect hobbies and interests, limit family and social outings, and their relationships may suffer (Magliano et al. 2014; Perrin et al. 2012; Davis 1993; Davey et al. 2015).

The home is oftentimes not a haven, but a busy medical center, with service providers intruding upon family life (Davey et al. 2015). The home may need renovations to meet present and future needs. Families may decide to move to a more accessible home. Some may move closer to their family of origin to have ready access to willing helpers. The financial burden on the family can be tremendous and often includes special transportation, mobility equipment, communication aids, home medical equipment, hospital bills, expensive medications, therapies, and lost wages (Perrin et al. 2012; Davis 1993; Wolff et al. 2010).

Parents worry about their child being in pain, disfigured, rejected by peers, isolated, and unhappy (Davis 1993). Each acute illness is cause for great concern, an expansion of the already numerous cares, and any possible hospitalization represents a disruption to the lives

of the entire family. Each health crisis may resurrect a fear that parents have suppressed in order to carry on.

Fathers experience psychosocial, family, and economic difficulties. Psychosocial problems include depressive and post-traumatic stress disorder symptoms upon learning of their child's diagnosis, tremendous guilt for having passed the disorder to the child, and the need to be strong for the family (Wolff et al. 2010). Family problems include marital disagreement about how to parent the child, conflicts with extended family, siblings who feel fathers are harder on them, and struggles between feeling overprotective and giving the right amount of discipline and independence. Fathers found that just knowing someone else was in it with them, such as a spouse, made them feel better, as did having help from extended family. For some fathers, access to public assistance helped them to cope better. One father interviewed had developed fortitude from his child's determination (Wolff et al. 2010).

Mothers in particular tend to leave the workforce in order to care for their child with a neuromuscular disorder. While this is often necessary for the level of care required, giving up a rewarding job or career can have negative consequences for the mother who no longer has this outlet as a means for boosting self-esteem, feeling independent, having status, expressing creativity/interest, companionship, or being productive in her community. These losses are even more detrimental when considering that they are many of the very activities and feelings that could help a parent to cope with the daily stressors, thereby further decreasing their ability to cope with the difficulties of caring for a child with a chronic condition (Davis 1993).

Spousal relationships suffer when there is a child with a neuromuscular disorder. This is often related to fewer needs being met in the relationship, having little time for each other, and no ability to get away as a couple. Increased stress, disagreement about how to parent the child, different coping styles, lack of communication, no child care options or respite, and the brunt of the responsibilities falling onto one parent all impact the relationship. The one parent who is doing most of the caregiving work may feel resentment, while the partner doing little of the work may feel neglected. Spouses sometimes blame the other for the heritable neuromuscular disorder (Davis 1993).

Disease severity negatively impacts quality of life for parent caregivers. Families with children that have more severe conditions requiring home medical equipment may experience a greater level of stress. Quality of life for parents of children with Duchenne muscular dystrophy is lower than normative controls. However, lower burden scores were noted in parents of ambulatory children that had higher levels of social support, as would be expected. The size and developmental stage of the child also impacts the caregiver's quality of life perceptions. For example, bowel dysfunction may be very manageable in a two-year-old, but difficult when the child becomes a teenager and adult (Perrin et al. 2012).

There is upheaval for siblings that often results in behavioral and psychological problems and resentment. Siblings may experience depression, anxiety, lower activity levels, fewer social opportunities, and effects on their cognitive development. They may become irritable, jealous, anxious, and socially withdrawn. Their academic performance may decline and they may miss out on opportunities due to a shifting of most resources to the child with

a neuromuscular disorder. These factors can lead to lower self-esteem in siblings and guilt for feeling the way they do (Perrin et al. 2012).

Friendships may be lost because the parent can no longer find the time to maintain them or the friend was uncomfortable maintaining the friendship. Oftentimes the friends no longer have enough in common to continue a relationship. However, those friends could be replaced in virtual relationships via social media with other parents facing similar life circumstances. Social support is crucial to parents. It can provide practical help, diversion, and it positively impacts parental self-esteem (Davis 1993).

Fatal neuromuscular disorders bring greater amounts of psychological distress to parents and siblings (Davis 1993). True effects of the disorder on all family members are often masked by denial-like coping strategies when surveys and interviews are done. Clinicians must use observations and gather input from those outside the situation in order to obtain a more accurate evaluation of the psychological impact (Barlow and Ellard 2006).

Coping

Even though the family experiences considerable stress, some members may adapt well, while other members collapse. Coping styles that avoid social support and involve catastrophizing are associated with worse outcomes (Davis 1993; Perrin et al. 2012). Coping ability affects disease course, willingness to explore treatment options, and how effective treatment can be (Davis 1993). When affected children and family members can reset their goals and expectations, they may experience a better perception of quality of life (Rose et al. 2012).

Parental perceptions are the foundation for how the family will function and cope. Accordingly, parents are the ones to focus attention on in treatment settings (Davis 1993; Thomas et al. 2014). Most people do not want to admit psychological difficulties because they assume it reflects badly upon them. Framing the need as that of the entire family who can benefit from counseling helps encourage parents and children to productively engage in counseling. Knowing this, practitioners are best advised to include all family members in counseling efforts (Davis 1993).

Parents can develop new values, goals, and attitudes in light of the diagnosis. A positive reinterpretation of the situation and subsequent growth can lead to better adjustment (Thomas et al. 2014). Those that have hope and a positive outlook tend to experience better outcomes (Barlow and Ellard 2006). How parents construe the child now that they know about the diagnosis is directly related to how well the family will adapt and thrive (Thomas et al. 2014). It is best to see them as a child first, and then see the muscle disorder with all its consequences. When those affected and the parents realize that they are all in it together, they can learn to appreciate each other's feelings and empathize with what each is going through.

Parents and family members sometimes develop unhealthy coping strategies as they care for a child with a neuromuscular disorder. Some of the most commonly used dysfunctional coping strategies are overprotection of the child, denial of reality, and magical thinking. Protecting the child is natural, and overprotection is a gray area for some parents. For example, parents may not share distressing news with the child to spare him or her anguish, nor involve the child in communications with clinicians who often present the

prognosis as grim. They may not insist upon age-and-ability-appropriate responsibility or may avoid disciplining the child. While discipline may seem like it adds to the gross unfairness of having the neuromuscular disorder, without it, the child may end up uncooperative, self-absorbed, and unable to share or relate kindly to others. These personal qualities would make for a very unattractive friend or mate which may put such a child at an even greater disadvantage socially. Furthermore, this results in major problems within the family and can affect parental and sibling expressions of love for the affected child (Thomas et al. 2014; Buchanan et al. 1979).

Some family members may fail to differentiate the child from the disease. This is problematic because the child may end up identifying himself or herself as the disease. Such a self-conception is not compatible with therapy, treatment, or a cure and may result in the child's refusal to engage in therapies that could alleviate discomfort, mitigate limitations, and prolong a higher-quality life (Davis 1993).

Factors that mitigate the burden of neuromuscular disease include internal coping strategies as well as external resources. Because functional impairment is natural for affected individuals, some are bothered less by what they cannot do. For those individuals experiencing deterioration of their condition, a positive reappraisal of their situation can make a difference in how well they cope (Nätterlund et al. 2000). Families need access to external resources, such as respite or financial aid, and greater participation in social activities that are meaningful to them in order to experience an improved quality of life (Davey et al. 2015; Dowling and Dolan 2001; Yantzi et al. 2007).

Parents have a natural inclination to cure their child as part of their desire to protect, provide, and problem-solve. Parental confidence in the ability to provide excellent care must be supported by clinicians and can lead to better outcomes for the child (Davis 1993).

Societal challenges of living with a neuromuscular disorder

Social integration and community participation are enriching aspects of life. When a family member has a neuromuscular disorder, the entire family often is restricted in the level of community participation they can obtain. Leaving the residence may require additional assistance and added expense (Davey et al. 2015; Yilmaz et al. 2010). Community access requires curb cut-outs, ramps, elevators, lift systems, and accessible transportation. Barriers to community access can include attitudinal, communication, physical, policy, programmatic, social, and transportation (Center for Disease Control and Prevention et al. 2016). The lack of accessibility may be unanticipated, such as an elevator malfunction at the child's school, friends or relatives that cannot be visited due to steps or narrow doorways, and no accessible parking. Many vacation destinations and activities to be enjoyed while on vacation are not completely accessible to these families.

The economic burden of neuromuscular disorders is another consideration. In the United States (US), the liability over the course of the disease has been estimated at an average yearly cost for each patient (medical, non-medical, and indirect) of "$63 693 for ALS [amyotrophic lateral sclerosis], $50 952 for DMD [Duchenne muscular dystrophy], and $32 236 for DM [myotonic dystrophy]. Population-wide national costs were $1 023 million (ALS), $787 million (DMD) and $448 million (DM)" (Larkindale et al. 2014). In another

study, a total of 770 participants from Germany, Italy, the United Kingdom (UK), and the US completed questionnaires to gauge costs incurred due to the muscle disease in their respective families. The results showed that, "the total societal burden was estimated at between $80 120 and $120 910 per patient and annum, and increased markedly with disease progression. The corresponding household burden was estimated at between $58 440 and $71 900" (Landfeldt et al. 2014).

Even with the best coping skills, resources, and care, neuromuscular disorders are life-limiting conditions. End-of-life discussions with those living with neuromuscular disorders and their parents are challenging yet critical for planning and assessing the ongoing health and well-being of the family unit.

Advance care planning and preparing for death

The increasing numbers, complexities, and technology dependencies of children and young adults with neuromuscular disorders calls for advance care planning to increase quality of life and promote patient autonomy (Horridge 2015; Lotz et al. 2015). Advance care planning is an ongoing process that guides patients and their families to an understanding of the diagnosis, prognosis, decisions, and treatment options they may consider (Edwards et al. 2012). The benefits of advance care planning, as perceived by clinicians, include providing a sense of security and control, improving quality of care, and ensuring that patients' and parents' wishes are respected (Lotz et al. 2015).

Parents who are less prepared for the death of a child suffer more bereavement complications. Parental grief when a child dies is poorly understood by professionals despite universal acceptance of the overwhelming pain and distress grieving parents experience. Parents often say they want to be a part of the care team, and they want their expertise as parent caregivers to be recognized. Parents want their child and their family values to be respected and their traditions accommodated during the time of advance care planning.

The importance of making memories within this limited time, and having no regrets after the child is gone, cannot be overstated. While witnessing the death of an infant or child is naturally distressing for everyone, parents often report that no matter how harrowing the time, they treasure every moment as a memory.

Importance of advance care planning

In advance, clinician-initiated discussions about the possibility of death may help families communicate among themselves what might otherwise remain unspoken. If these discussions are avoided, patients and families may not have an opportunity to state their wishes, such as the preferred place of care and of death. Such discussions may help with the grieving process, establishment of realistic hope, and effective coping (Horridge 2015). Studies have demonstrated that parents of children with chronic conditions find that advance care planning is, or would be, beneficial to them, and they wish to know all the options, including the option to forgo interventions (Edwards et al. 2012).

Advance care planning provides a sense of security and control for both medical professionals and parents, while clarifying goals of care and providing a clear direction. Advance care planning can improve quality of care by avoiding treatments that are not in the family's

best interests and reduce unnecessary suffering. Having a written advance care directive in place can lead to a decreased number of emergency and intensive care interventions for the child and ensure that the care provided is consistent with the parent's and child's treatment goals (Lotz et al. 2015).

Ideally, discussions regarding goals of care should be initiated upon diagnosis and revisited during a period when the patient is stable (Durall et al. 2012; Hauer and Wolfe 2014). Unfortunately, the majority of clinicians find that advance care planning happens too late in the patient's clinical course (Edwards et al. 2012; Durall et al. 2012). Many of these discussions typically take place during an acute illness or deterioration and during a hospitalization, or when death is imminent (Edwards et al. 2012; Durall et al. 2012; Hauer and Wolfe 2014).

Identifying the potential barriers to advance care planning will allow the clinician to better engage families and encourage advance care planning before critical illness. The late timing of advance care planning indicates that many families are not open to discuss end-of-life issues at a time when their child is relatively stable. Therefore, clinicians should offer anticipatory guidance and proactively gauge family readiness for advance care planning discussions. Advance care planning is not a single discussion intended to elicit a particular decision. Rather, advance care planning involves ongoing discussions with an emphasis on informing the family about events that could occur, guiding them as they consider treatment options, and reassuring them that caring for their child will be the primary goal under all circumstances (Edwards et al. 2012).

Barriers to advance care planning

Although there is an increasing recognition of the benefits to advance care planning, there continue to be barriers to utilization (Hauer and Wolfe 2014). The challenges stem from both clinicians and families (Edwards et al. 2012).

Barriers reported by clinicians highlight their fear and discomfort with the topic. Clinicians are reluctant to address end-of-life issues with patients and parents because they fear taking away hope, and risk losing the trusting relationship with the family (Lotz et al. 2015). However, studies do not support these concerns. Greater information disclosure may actually support hope, even when the child's prognosis is poor. Higher levels of parental optimism were associated with increased likelihood of parental enactment of an order for limited intervention. On the other hand, withholding information may promote false hope, leading to feelings of betrayal, anger, and mistrust (Durall et al. 2012).

Clinician uncertainty about the patient's prognosis and not knowing how, or the right time, to address the issue of advance care planning creates barriers to advance care discussions (Horridge 2015; Lotz et al. 2015; Edwards et al. 2012; Durall et al. 2012; Hauer and Wolfe 2014). Clinicians' avoidance of raising sensitive, difficult issues with families and projecting their own lack of readiness to discuss these issues onto families also inhibit advance care planning. Clinicians may also be unable or unwilling to accept their patient's fate, and may make conscious and unconscious attempts to impose their own values on the family (Edwards et al. 2012).

The majority of clinicians view advance care planning as a multi-professional process that should include all relevant healthcare providers in the community. However,

insufficient information sharing between clinicians and the lack of a continuous contact person are reported as barriers to the cooperation deemed indispensable for advance care planning (Lotz et al. 2015). Other reported factors limiting the implementation of advance care planning include shortage of time and lack of funds.

Clinicians perceive parental prognostic understanding and attitudes as the most common barriers to advance care planning (Durall et al. 2012). The top three parental barriers were reported to be unrealistic expectations, differences between clinician and patient/parent understanding of prognosis, and lack of parent readiness to have the discussion (Horridge 2015; Durall et al. 2012; Hauer and Wolfe 2014).

A study involving children on long-term assisted ventilation with life-limiting conditions recognized that a family may have an idealistic outlook on the child's prognosis because the child has survived a previous critical illness. In addition, the development of a mutually dependent relationship between the child and family members who have devoted so much energy to the child's care gives rise to parental resistance to end-of-life discussions (Edwards et al. 2012).

The burden of responsibility felt by parents when signing an advance care directive for their child is a factor of their resistance (Lotz et al. 2015). This can be especially difficult when the child suffers from a communication impairment and is unable to express his or her wishes.

Inadequate communication is often the source of barriers to advance care discussions. Patients and family members may be waiting for the clinical team to initiate the discussion, or may not be aware of the need for such discussions. The clinical team may assume the family is not ready for the discussion because they have not yet introduced the subject.

To better prepare clinicians for advance care discussions, physician trainee and continuing education programs should include topics on communication skills, managing prognostic uncertainty, and how to make decisions to forgo life-sustaining therapy (Durall et al. 2012).

Death of a child

For those parents whose infant is never well enough to leave the hospital, the hospital environment is the sole place they will parent their child. Medical professionals involved in the infant's care need to acknowledge that the family will experience their entire relationship with their child in a hospital environment which is a public place and a working environment. In this public environment, parents sometimes need help to feel comfortable with providing a natural, loving relationship (Meyer et al. 2006; McGraw et al. 2012).

Parents need to be parents even in the hospital. They should be respected as competent to carry out as much of their child's care as they wish. Parents want meaningful roles in providing love, comfort, and care for their child (McGraw et al. 2012).

> We … didn't know how to comfort him. He was sedated. You know, the thing I remember the most was the one nurse who said that, "He likes to have his head rubbed". That was really important to us (McGraw et al. 2012).

Parents report a deep need for privacy and security for the whole family with more control over their child's environment. This includes limiting interruptions, the timing of routine observations, and having more quiet time (McGraw et al. 2012). Time spent as a family is

very important (Tan et al. 2012). Every moment with their child is precious; therefore, asking parents to leave their child for lower priority reasons, such as meetings with clinicians, should be carefully considered (McGraw et al. 2012).

> And when the intensivist wanted to talk to us about what we were going to do next, we were always asked to go into this consult room. And so the whole time I was afraid we weren't going to be in the room with her. … If I had known then I would have said, "No. Can't we just talk about this right here? I want to talk about this right here," if I'd been a little more forceful. But I didn't know I was going to feel like this (McGraw 2012).

Parents want to be physically close to their dying child and will express regret about times they were not able to do this. Parents appreciate guidance to find ways they can be close to their child in a medical environment (McGraw et al. 2012).

> And I think she knew she was going to die because she said, "Will you get in the bed with me?" I couldn't do that with [pause] [crying] all the nurses …. Everybody in and out, you can't have those private moments. And I just wished I had got in bed with her one time and gave her that last hug before she became incoherent. I never got that chance because it's so damn busy in there (McGraw 2012).

Parents want to know that they pursued all reasonable treatment options and did everything possible for their child in the time they had (Caeymaex et al. 2011). They want to evaluate treatment options, not just the availability of those options, but in terms of their individual goals for their child. Clinicians should note that parents are generally able to distinguish between hope and wishful thinking (Xafis et al. 2015). Kindness, respect, and sympathy increase parental trust in clinicians' positive intentions (Caeymaex et al. 2011). After the death of a child, parents benefit from a continuation of kindness and respect, such as the gentle, unrushed handling of their child's body (Higgs et al. 2016).

Later-life loss

Advances in medical care, especially respiratory care, allow many children with neuromuscular disorders to live longer into their late teens and young adulthood. Death is a risk associated with any form of neuromuscular disorder, a fact that is sometimes lost to those that experience longer periods of relative stability. An acute episode, such as sudden illness or infection, can result in what parents perceive as an unexpected death of the child and not a foreseen outcome of the progression of their child's disorder (Edwards et al. 2012).

A parent whose child has a progressive neuromuscular disorder is often experienced with a hospital environment and particularly knowledgeable about the child's disorder. Many parents, however, report finding it difficult to advocate for their child, as their experience and knowledge is underestimated (McGraw et al. 2012). Clinicians should bear in mind that these parents may have had to prepare for their child's death on several occasions already.

A majority of parents spend a considerable amount of time trying to keep their children with a neuromuscular disorder stable at home to avoid hospital admissions. Keeping their child at home to die, and after death for a period of time, is a natural extension of this desire.

Eighty-nine percent of families who had time to make an advance plan about where their child would die chose home (Heath et al. 2010). Evidence that children and young people with a neuromuscular disorder would rather die at home than at a hospital setting has been extrapolated from work with adults and cancer patients (Bluebond-Langner et al. 2013). After a preferred location for the child's death is chosen, there should be continued flexibility as circumstances may change (Hauer and Wolfe 2014; Vickers et al. 2007). Some parents are very passionate about their child being cared for at home while also wanting the place of death to be elsewhere, such as a hospice (Vickers et al. 2007). It may be that the opportunity to plan where their child might die is more important to parents than the actual location it happens in the end.

Particularly in a short life, every single moment and interaction may take on special meaning:

> It sounds so strange but it was one of the most peaceful, beautiful things I've ever seen and ever been a part of. That sounds weird because it's your child. But that's how it started out. It was daddy and I and [my child]. That's how it started. And that's how it ended, with the three of us in a room together. There was something beautiful about that … I was able to get right in that bed with her (McGraw 2012).

A lack of privacy and autonomy in deciding how to be with their dying child is often reported as a source of deep and lasting regret for bereaved parents. Providing love and comfort, even in the most distressing of circumstances, becomes a memory that parents can draw on for peace during bereavement (Tan et al. 2012).

Studies show that parents who are less prepared for the death of their loved one are more prone to depression, anxiety, and complicated grief (Tan et al. 2012). Therefore, anything that can be done to support parents' plans for preparation of their child's death has a positive impact.

Hospice movement in the United Kingdom

A children's hospice is a publicly or charitably funded care home specifically designed to help children who are not expected to reach adulthood with the emotional and physical challenges they face, and also to provide respite care for their families. Until the 1980s, there was no provision anywhere in the world for respite and end-of-life care specifically for children with life-shortening conditions. The first hospice for children from birth to age 16, called Helen House, was founded in et al. 1982. There are now about 49 children's hospices around the world. Douglas House was opened in et al. 2004, the world's first specialist hospice for young adults aged 16 to 35 years (Helen & Douglas House et al. 2018). There are over 200 hospices in the UK supported by the national charity for hospice care, Hospice UK (Hospice UK, 2018).

Hospices should be respectful of individual family needs and customs, religious or secular. They can provide specialist doctors, nurses, and services such as family support and bereavement services for the entire family. Hospices generally offer short medically-supported breaks, as well as pain and symptom management, and end-of-life care. The family can stay on-site to enjoy being a parent and not a full-time carer; or they can leave their child in the experienced hands of medical care teams while they spend time as a couple or

with their other children. Hospice care can be provided in the hospice, or sometimes services can be offered in the home (Together for short lives 2018).

Role of the clinician

Advances in genetic testing technology have improved the yield of a genetic diagnosis in presumed neuromuscular patients. Delays in obtaining a genetic diagnosis have been shown to impede medical management and lower survival. As the gatekeepers, it is imperative that clinicians endorse early and universal genetic testing for neuromuscular disorders. Genetic testing should be mandatory for all pediatric and adult neuromuscular disorders; and universal access to genetic testing, even for rare neuromuscular disorders, a priority. Genetic counselors are integral to implementation of universal genetic testing and should be part of every neuromuscular clinic. While families and affected individuals may have a limited grasp of genetic testing technology, disease knowledge, and interpretation of their own genetic testing results, this should not preclude offering genetic testing and counseling.

Living with a neuromuscular disorder impacts the quality of life of both the affected individual and their family. Parental quality of life perception forms the foundation of how the family will cope. Therefore, the clinician needs to give attention to parents in the treatment setting. Encouraging internal coping strategies and supporting access to external resources can mitigate the burden on affected individuals and their families, leading to better adjustment and an improved perception of quality of life.

The increased number of children living longer with neuromuscular disorders and technology dependency requires early, ongoing advance care planning discussions between the clinician, parents and, if appropriate, the affected child. The clinician should initiate discussions regarding the goals of care upon diagnosis or during a period when the child is stable, offering anticipatory guidance while gauging the family's readiness for advance care planning. Advance care planning discussions should involve a multidisciplinary team, which may include the primary care physician, palliative care, nursing, social work, and chaplaincy.

When a child nears death, it is important that the parent's role as caregiver and advocate be respected. Supporting the family's need for privacy, time and physical closeness with their dying child, and making memories is invaluable. Hospice care, if available, can provide the family with respite. In a hospital environment, interruptions to family time should be limited and asking parents to leave their child's side for lower priority reasons ought to be avoided. A parent's trust in a clinician's intentions is increased when kindness, respect, and sympathy are shown. Extending kindness and respect after the death of a child can have a positive and lasting impact on the family.

Conclusion and key points

Parenting a child with a neuromuscular disorder involves a multitude of emotions, responsibilities, and decisions from diagnosis to end of life. Obtaining a genetic diagnosis, living with a chronic neuromuscular disease, advance care planning, and preparing for death are significant milestones that parents may experience during their child's lifetime.

Diagnosis: key points

- There is a high acceptance of genetic testing by families and affected individuals regardless of the results.
- Universal access to genetic testing should be a priority regardless of whether there is a lack of treatment options.
- Genetic counselors are integral to the implementation of universal genetic testing and should be a part of every neuromuscular clinic.
- Developing either separate reports for the families or revising current language to make reports understandable to a lay person may facilitate understanding and ownership of results.
- Clinicians need to have knowledge of the diagnostic tools available and an understanding of the discrepancies between physician and lay person attitudes, including an understanding of the lay person's priorities.

Quality of life and lived experience: key points

- Quality of life for those with neuromuscular disorders and their parents is lower than normative controls, but not always as low as one may predict due to the influence of coping strategies.
- Internal coping strategies, like adjusting life goals and self-confidence, are critical to positive adjustment.
- External coping mechanisms, like respite care and accessible transportation, lead to better adjustment.
- Families need access to external resources, such as respite or financial aid, and greater participation in social activities that are meaningful to them in order to experience an improved quality of life.

Advance care planning and preparing for death: key points

- Advance care planning is ideally initiated upon diagnosis and revisited during periods of stability.
- Advance care planning is not a single discussion, but rather ongoing discussions that inform families about events that could occur, guide them as they consider treatment options, and reassure them that caring for their child is the primary goal under all circumstances.
- Parents who are less prepared for the death of their child suffer more bereavement complications.
- Parents who live with a child's life-threatening condition are used to the duality of living with hope at the same time as preparing for the possibility of their child's death.
- Parents report feeling regret for what they were not able to do for their infant or child, but no regret for the things they were able to do, however small those actions seemed at the time.
- Parents want the loss of their child as an individual to be recognized as important and devastating, not simply "expected".

Role of the clinician: key points

- Clinicians must endorse early and universal genetic testing for all pediatric and adult neuromuscular disorders, even for rare neuromuscular disorders.

- Clinicians can help mitigate the burden on affected individuals and their families by encouraging positive coping strategies and by supporting access to external resources in the form of referrals, letters of support, orders for supplies and equipment, and so forth.
- Clinicians should initiate advance care planning discussions early, have ongoing discussions during periods when the child is stable, and involve a multidisciplinary team in the advance care planning process.
- Respect for the parent's role as caregiver and advocate, as well as kindness and sympathy on the part of the clinician, before and after a child's death increases a parent's trust in the clinician, and can have a lasting and positive impact on the family.

REFERENCES

Abresch RT, Carter GT, Jensen MP, Kilmer DD (2002) Assessment of pain and health-related quality of life in slowly progressive neuromuscular disease. *Am J Hosp Palliat Care* 19: 39–48.

Bach JR, Campagnolo DI, Hoeman S (1991) Life satisfaction of individuals with Duchenne muscular dystrophy using long-term mechanical ventilatory support. *Am J Phys Med Rehabil* 70: 129–135.

Bann CM, Abresch RT, Biesecker B, Conway KC, Heatwole C, Peay H et al. (2015) Measuring quality of life in muscular dystrophy. *Neurology* 84: 1034–1042.

Barlow JH, Ellard DR (2006) The psychosocial well-being of children with chronic disease, their parents and siblings: an overview of the research evidence base. *Child Care Health Dev* 32: 19–31.

Bluebond-Langner M, Beecham E, Candy B, Langner R, Jones L (2013) Preferred place of death for children and young people with life-limiting and life-threatening conditions: a systematic review of the literature and recommendations for future inquiry and policy. *Palliat Med* 27: 705–713.

Buchanan DC, LaBarbera CJ, Roelofs R, Olson W (1979) Reactions of families to children with Duchenne muscular dystrophy. *Gen Hosp Psychiatry* 1: 262–269.

Caeymaex L, Speranza M, Vasilescu C, Danan C, Bourrat MM, Garel M et al. (2011) Living with a crucial decision: a qualitative study of parental narratives three years after the loss of their newborn in the NICU. *PLoS One* 6:e28633.

Center for Disease Control and Prevention.(2016) *Common barriers to participation experienced by people with disabilities* [online]. http://www.cdc.gov/ncbddd/disabilityandhealth/disability-barriers.html#ref (accessed on 1 May 2016).

Chen JY, Clark MJ (2007) Family function in families of children with Duchenne muscular dystrophy. *Fam Community Health* 30: 296–304.

Chung J, Smith AL, Hughes SC, Niizawa G, Abdel-Hamid HZ, Naylor EW et al. (2016) Twenty-year follow-up of newborn screening for patients with muscular dystrophy. *Muscle Nerve* 53: 570–578.

Davey H, Imms C, Fossey E (2015) "Our child's significant disability shapes our lives": experiences of family social participation. *Disabil Rehabil* 37: 2264–2271.

Davis H (1993) *Counseling Parents of Children with Chronic Illness or Disability*. Oxford: Wiley-Blackwell.

de Moura MC, Wutzki HC, Voos MC, Resende MB, Reed UC, Hasue RH (2015) Is functional dependence of Duchenne muscular dystrophy patients determinant of the quality of life and burden of their caregivers? *Arq Neuropsiquiatr* 73: 52–57.

Dempster M, Howell D, McCorry NK (2015) Illness perceptions and coping in physical health conditions: A meta-analysis. *J Psychosom Res* 79: 506–513.

DH/Child Health and Maternity Services Branch (2006) *Transition: Getting it Right for Young People. Improving the Transition of Young People with Long Term Conditions from Children's to Adult Health Services*. Waterloo Road, London: Alcuin Edwards, Child Health and Maternity Services Branch. https://webarchive.nationalarchives.gov.uk (accessed on 1 May 2016).

Dowling M, Dolan L (2001) Families with children with disabilities – inequalities and the social model. *Disabil Soc* 16: 21–35.

Durall A, Zurakowski D, Wolfe J (2012) Barriers to conducting advance care discussions for children with life-threatening conditions. *Pediatrics* 129(4): e975–982. doi.10.1542/peds.2011–2695.

Edwards JD, Kun SS, Graham RJ, Keens TG (2012) End-of-life discussions and advance care planning for children on long-term assisted ventilation with life-limiting conditions. *J Palliat Care* 28: 21–27.

Ghaoui R, Cooper ST, Lek M, Jones K, Corbett A, Reddel SW et al. (2015) Use of whole-exome sequencing for diagnosis of limb-girdle muscular dystrophy: outcomes and lessons learned. *JAMA Neurol* 72: 1424–1432.

Graham CD, Weinman J, Sadjadi R, Chalder T, Petty R, Hanna MG et al. (2014) A multicentre postal survey investigating the contribution of illness perceptions, coping and optimism to quality of life and mood in adults with muscle disease. *Clin Rehabil* 28: 508–519.

Hall MJ, Forman AD, Montgomery SV, Rainey KL, Daly MB (2015) Understanding patient and provider perceptions and expectations of genomic medicine. *J Surg Oncol* 111: 9–17.

Hauer JM, Wolfe J (2014) Supportive and palliative care of children with metabolic and neurological diseases. *Curr Opin Support Palliat Care* 8: 296–302.

Heath JA, Clarke NE, Donath SM, McCarthy M, Anderson VA, Wolfe J (2010) Symptoms and suffering at the end of life in children with cancer: an Australian perspective. *Med J Aust* 192: 71–75.

Helen & Douglas House.(2018) Helen & Douglas House: Hospice care for children. https://www.helenanddouglas.org.uk (accessed on 2 April 2018).

Higgs EJ, McClaren BJ, Sahhar MA, Ryan MM, Forbes R (2016) "A short time but a lovely little short time": bereaved parents' experiences of having a child with spinal muscular atrophy type 1. *J Paediatr Child Health* 52: 40–46.

Hill DL, Miller VA, Hexem KR, Carroll KW, Faerber JA, Kang T et al. (2015) Problems and hopes perceived by mothers, fathers and physicians of children receiving palliative care. *Health Expect* 18: 1052–1065.

Horridge KA (2015) Advance Care Planning: practicalities, legalities, complexities and controversies. *Arch Dis Child* 100: 380–385.

Hospice UK (2018) Hospice UK. https://www.hospiceuk.org (accessed on 2 April 2018).

Houwen-van Opstal SLS, Jansen M, van Alfen N, de Groot IJM (2014) Health-related quality of life and its relation to disease severity in boys with Duchenne muscular dystrophy: satisfied boys, worrying parents – a case-control study. *J Child Neurol* 29: 1486–1495.

Howard HC, Borry P (2013) Survey of European clinical geneticists on awareness, experiences and attitudes towards direct-to-consumer genetic testing. *Genome Med* 5: 45.

Hunter AG, Sharpe N, Mullen M, Meschino WS (2001) Ethical, legal, and practical concerns about recontacting patients to inform them of new information: the case in medical genetics. *Am J Med Genet* 103: 265–276.

Kang PB (2011) Presymptomatic and early symptomatic genetic testing. *Continuum (Minneap Minn)* 17(2 Neurogenetics): 343–346.

Klitzman R, Abbate KJ, Chung WK, Ottman R, Leu CS, Appelbaum PS (2014) Views of preimplantation genetic diagnosis among psychiatrists and neurologists. *J Reprod Med* 59: 385–392.

Kohler M, Clarenbach CF, Böni L, Brack T, Russi EW, Bloch KE (2005) Quality of life, physical disability, and respiratory impairment in Duchenne muscular dystrophy. *Am J Respir Crit Care Med* 172: 1032–1036.

Landfeldt E, Lindgren P, Bell CF, Schmitt C, Guglieri M, Straub V et al. (2014) The burden of Duchenne muscular dystrophy: an international, cross-sectional study. *Neurology* 83: 529–536.

Larkindale J et al. (2014) *Cost of Illness for Neuromuscular Diseases in the U.S.* Tucson, AZ: Muscular Dystrophy Association. www.mda.org/sites/default/files/Report_Summary-Cost_of_Illness_0.pdf (accessed on 1 May 2016)

Lim Y, Velozo C, Bendixen RM (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. *Qual Life Res* 23: 1945–1952.

Lindor NM, Goldgar DE, Tavtigian SV, Plon SE, Couch FJ (2013) BRCA1/2 sequence variants of uncertain significance: a primer for providers to assist in discussions and in medical management. *Oncologist* 18: 518–524.

López-Hernández LB, Gömez-Dïaz B, Escobar-Cedillo RE et al. (2014) Duchenne muscular dystrophy in a developing country: challenges in management and genetic counseling. *Genet Couns* 25(2): 129–41.

Lotz JD, Jox RJ, Borasio GD, Führer M (2015) Pediatric advance care planning from the perspective of health care professionals: a qualitative interview study. *Palliat Med* 29: 212–222.

Magliano L, D'Angelo MG, Vita G, Pane M, D'Amico A, Balottin U et al. (2014) Psychological and practical difficulties among parents and healthy siblings of children with Duchenne vs. Becker muscular dystrophy: an Italian comparative study. *Acta Myol* 33: 136–143.

McGraw SA, Truog RD, Solomon MZ, Cohen-Bearak A, Sellers DE, Meyer EC (2012) "I was able to still be her mom" parenting at end of life in the pediatric intensive care unit. *Pediatr Crit Care Med* 13:e350–e356.

McGuire AL, Diaz CM, Wang T, Hilsenbeck SG (2009) Social networkers' attitudes toward direct-to-consumer personal genome testing. *Am J Bioeth* 9: 3–10.

Metcalf MP, Tanner TB, Buchanan A (2010) Effectiveness of an online curriculum for medical students on genetics, genetic testing and counseling. *Med Educ Online* 15: 4856.

Meyer EC, Ritholz MD, Burns JP, Truog RD (2006) Improving the quality of end-of-life care in the pediatric intensive care unit: parents' priorities and recommendations. *Pediatrics* 117: 649–657.

Munn MW (2010) Living with muscular dystrophy: personal reflections. *Neuromuscul Disord* 20: 152–153.

Narayanaswami P, Bertorini TE, Pourmand R, Horner LH (2000) Long-term tracheostomy ventilation in neuromuscular diseases: patient acceptance and quality of life. *Neurorehabil Neural Repair* 14: 135–139.

Nätterlund B, Gunnarsson LG, Ahlström G (2000) Disability, coping and quality of life in individuals with muscular dystrophy: a prospective study over five years. *Disabil Rehabil* 22: 776–785.

Ozer S, Yildirim SA, Yilmaz O, Düger T, Yilmaz SA (2010) Assessment of health-related quality of life, depression, and anxiety in slowly and rapidly progressive neuromuscular disorders. *Neurosciences (Riyadh)* 15: 177–183.

Perrin JM, Gnanasekaran S, Delahaye J (2012) Psychological aspects of chronic health conditions. *Pediatr Rev* 33: 99–109.

Pyeritz RE (2011) The coming explosion in genetic testing – is there a duty to recontact? *N Engl J Med* 365: 1367–1369.

Rose MR, Sadjadi R, Weinman J, Akhtar T, Pandya S, Kissel JT et al. (2012) Role of disease severity, illness perceptions, and mood on quality of life in muscle disease. *Muscle Nerve* 46: 351–359.

Salm M, Abbate K, Appelbaum P, Ottman R, Chung W, Marder K et al. (2014) Use of genetic tests among neurologists and psychiatrists: knowledge, attitudes, behaviors, and needs for training. *J Genet Couns* 23: 156–163.

Savarese M et al. (2016) The genetic basis of undiagnosed muscular dystrophies and myopathies: results from 504 patients. *Neurology* 87: 71–76.

Smith CO, Lipe HP, Bird TD (2004) Impact of presymptomatic genetic testing for hereditary ataxia and neuromuscular disorders. Arch Neurol 61: 875–880.

Tan JS, Docherty SL, Barfield R, Brandon DH (2012) Addressing parental bereavement support needs at the end of life for infants with complex chronic conditions. *J Palliat Med* 15: 579–584.

Taylor RM, Gibson F, Franck LS (2008) The experience of living with a chronic illness during adolescence: a critical review of the literature. *J Clin Nurs* 17: 3083–3091.

Thomas PT, Rajaram P, Nalini A (2014) Psychosocial challenges in family caregiving with children suffering from Duchenne muscular dystrophy. *Health Soc Work* 39: 144–152.

Thompson RJJ Jr, Zeman JL, Fanurik D, Sirotkin-Roses M (1992) The role of parent stress and coping and family functioning in parent and child adjustment to Duchenne muscular dystrophy. *J Clin Psychol* 48: 11–19.

Together for short lives (2018) Together for short lives. http://www.togetherforshortlives.org.uk (accessed on 2 April 2018).

Toiviainen H, Jallinoja P, Aro AR, Hemminki E (2003) Medical and lay attitudes towards genetic screening and testing in Finland. *Eur J Hum Genet* 11: 565–572.

Vansenne F, Bossuyt PM, de Borgie CA (2009) Evaluating the psychological effects of genetic testing in symptomatic patients: a systematic review. *Genet Test Mol Biomarkers* 13: 555–563.

Vickers J, Thompson A, Collins GS, Childs M, Hain R, Paediatric Oncology Nurses' Forum/United Kingdom Children's Cancer Study Group Palliative Care Working Group (2007) Place and provision of palliative care for children with progressive cancer: a study by the Paediatric Oncology Nurses' Forum/United Kingdom Children's Cancer Study Group Palliative Care Working Group. *J Clin Oncol* 25: 4472–4476.

Wolff J, Pak J, Meeske K, Worden JW, Katz E (2010) Challenges and coping styles of fathers as primary medical caretakers: a multicultural qualitative study. *J Psychosoc Oncol* 28: 202–217.

Wood MF, Hughes SC, Hache LP, Naylor EW, Abdel-Hamid HZ, Barmada MM et al. (2014) Parental attitudes toward newborn screening for Duchenne/Becker muscular dystrophy and spinal muscular atrophy. *Muscle Nerve* 49: 822–828.

Woodgate RL (1998) Adolescents' perspectives of chronic illness: "it's hard". *J Pediatr Nurs* 13: 210–223.

Xafis V, Wilkinson D, Sullivan J (2015) What information do parents need when facing end-of-life decisions for their child? A meta-synthesis of parental feedback. *BMC Palliat Care* 14: 19.

Yantzi NM, Rosenberg MW, McKeever P (2007) Getting out of the house: the challenges mothers face when their children have long-term care needs. *Health Soc Care Community* 15: 45–55.

Yilmaz O, Yildirim SA, Oksüz C, Atay S, Turan E (2010) Mothers' depression and health-related quality of life in neuromuscular diseases: role of functional independence level of the children. *Pediatr Int* 52: 648–652.