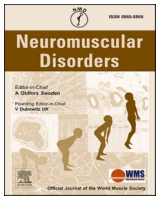
Neuromuscular Disorders 49 (2025) 105318

Contents lists available at ScienceDirect

Neuromuscular Disorders

journal homepage: www.elsevier.com/locate/nmd



281st ENMC international workshop: 2nd ENMC workshop on exercise training in muscle diseases; towards consensus-based recommendations on exercise prescription and outcome measures. Hoofddorp, The Netherlands, 4-6 October 2024

Eric Lukas Voorn [a,b,*], Alejandro Lucia [c,d], John Vissing [e], on behalf of the 281st ENMC workshop study group

[a] Amsterdam UMC location University of Amsterdam, Department of Rehabilitation Medicine, Meibergdreef 9, Amsterdam, the Netherlands
[b] Amsterdam Movement Sciences, Rehabilitation & Development, Amsterdam, the Netherlands
[c] Research Institute of Hospital "12 de Octubre" ("imas12"), Madrid, Spain
[d] Department of Sport Sciences. Faculty of Medicine, Health and Sports. Universidad Europea de Madrid, Madrid, Spain
[e] Copenhagen Neuromuscular Center, Department of Neurology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

ARTICLE INFO

Keywords:
Exercise
Muscular diseases
Neuromuscular diseases
Outcome measures
Physical activity
Healthy lifestyle

ABSTRACT

The 281st ENMC workshop on exercise in muscle diseases was held on October 4–6, 2024. The workshop study group included people with lived experience, healthcare professionals and researchers from different disciplines. To facilitate improved application of exercise in daily practice, this workshop aimed to reach a consensus on recommendations for exercise prescription and outcome measures. There were sessions on 1) scientific evidence on exercise prescription and current practice (based on international online surveys of people with muscle diseases and healthcare professionals), 2) outcome measures, and 3) long-term continuation of exercise. Based on the scientific evidence, survey results and group discussions during the workshop sessions, a strong consensus (all attendees agreed) was reached that personalized exercise is safe and beneficial for people with muscle diseases and is recommended. Recommendations were formulated for the frequency, intensity, time, and type of aerobic and resistance exercise, as well as potential outcome measures for future studies.

1. Introduction

The 281st Workshop on exercise in skeletal muscle diseases was held on October 4–6, 2024, in Hoofddorp, The Netherlands. The workshop brought together 21 international experts in the field from 9 different countries, including 2 people with lived experience, 1 patient representative (on behalf of the Dutch patient association), healthcare professionals (HCPs) and researchers from various disciplines (rehabilitation medicine, physiotherapy, neurology, exercise physiology, psychology, molecular biology, and sports medicine).

There is strong evidence that physical activity has a positive impact on physical and mental health, quality of life, and the prevention and management of many chronic diseases [1]. People with disabilities are at greater risk of physical inactivity and a sedentary lifestyle [2]. This includes people with neuromuscular diseases (NMDs), for whom staying physically active is challenging due to symptoms such as muscle weakness, fatigue, and pain [3]. Physical inactivity in NMDs leads to a reduced physical fitness (deconditioning), which in turn worsens health and physical function and may accelerate the primary disease process. When the ability to be physically active and mobile is impaired, societal participation may be restricted, and emotional well-being and health-related quality of life may be reduced. An important aim of neuromuscular rehabilitation is therefore to promote physical fitness through exercise.

There is increasing evidence for the beneficial effects of exercise in a variety of NMDs [4–6]. Two important knowledge gaps identified by recent systematic reviews are uncertainty about the prescription of Frequency, Intensity, Time (duration), and Type of exercise, also known

* Corresponding author at: Department of Rehabilitation Medicine, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands.
E-mail address: e.l.voorn@amsterdamumc.nl (E.L. Voorn).

https://doi.org/10.1016/j.nmd.2025.105318
Received 17 February 2025; Accepted 17 February 2025
Available online 18 February 2025

as the 'FITT' factors, and the lack of standardized outcome measures. This may hinder the application of exercise programs in everyday practice of people with NMDs [7].

To facilitate improved application of exercise in daily practice, this workshop aimed to reach a consensus on recommendations for exercise prescription and outcome measures in NMDs. Given the many types of NMDs, the focus of this workshop was on adults with muscle diseases, with a possible future perspective of a follow-up workshop focusing on other NMDs (motor neuron diseases, peripheral neuropathies, and neuromuscular junction diseases) and pediatric NMDs. The aims of the workshop were:

- To provide a scientific overview on exercise in muscle diseases.
- To reach consensus on recommendations for exercise prescription, specified in terms of the FITT factors.
- To reach consensus on recommendations for a core set of outcome measures to be used in future studies of exercise in muscle diseases.
- To define areas in the field of exercise in muscle diseases that need more research.

2. Exercise in muscle diseases: prescription and current application

The first workshop session was dedicated to reaching consensus on recommendations for exercise prescription in muscle diseases. It included presentations about a position stand outline based on scientific literature and the results of surveys on the application of exercise among HCPs and people with muscle disease, followed by a group discussion. The session concluded with presentations on exercise studies in mouse models and human-induced pluripotent stem cell (hiPSC)-derived 3D skeletal muscles.

2.1. Presentation of position stand on exercise prescription in muscle diseases

In preparation for the workshop, **Eric Voorn, John Vissing** and **Alejandro Lucia** drafted the outline of a position stand. The draft was also sent to all participants before the workshop. The position stand, inspired by the American College of Sports Medicine's position stand on exercise guidance for healthy adults [8], aims to provide practical guidance for prescribing personalized exercise to people with muscle diseases. The main target group audience is HCPs, such as physicians, physiotherapists and exercise physiologists. Eric Voorn presented the process of developing the position stand outline, from a complete overview of the scientific literature to a summary of information for individual diseases, to recommendations for aerobic and resistance exercise, specified in terms of the FITT factors. The position stand outline included the following sections: summary of the scientific evidence, diseases requiring special attention, other recommendations related to exercise prescription (i.e., pre-exercise assessment, baseline intensity assessment, supervision, monitoring and outcome assessment), potential long-term risks and continuation of exercise.

2.2. The application of exercise in muscle diseases across countries

After sharing their personal experiences of exercise, **Madelon Kroneman** and **Ingrid de Groot** (people with lived experience) presented the results of an international online survey on the application of exercise among people with NMDs that they had conducted in preparation for the workshop. The survey was prepared by Ingrid, Madelon and Charlotte (patient representative) together with the organizers. It included a definition of exercise (i.e., '*a subset of physical activity that is planned, structured, and repetitive, carried out with the objective to improve or maintain physical fitness*' [9]), followed by questions about personal experiences of exercise and barriers to and benefits of exercise. The survey was available in 5 different languages (English, Dutch, French, German and Norwegian) and was distributed through patient organisations and social media channels (e.g., LinkedIn and Facebook). There were 2074 respondents, most from The Netherlands (58 %), United States of America (12 %) and Norway (7 %). The majority of respondents were over 50 years old (73 %) and had a muscle disease (54 %); the remaining respondents had a motor neuron disease, peripheral neuropathy, or neuromuscular junction disease. The commonest muscle diseases were facioscapulohumeral muscular dystrophy (FSHD, 24 %), limb girdle muscular dystrophy (LGMD, 6 %), inclusion body myositis (IBM) and myotonic dystrophy (both 5 %).

The survey results showed that most respondents (77 %) exercised regularly, mostly under the direct supervision of a physiotherapist (39 %) or at home (37 %). A third of respondents designed their own exercise program, and the FITT factors of their exercise programs varied widely. Habitual non-exercisers experienced more barriers to and fewer benefits of exercise than respondents who exercised. The most important perceived benefits of exercise were that it was good for health and that it improved mobility, fitness and quality of life. The main barriers reported were that daily life took up most of their energy, they were too fatigued, or they were afraid of overexertion (due to too strenuous exercise). Recommendations given by respondents to facilitate exercise participation included involving a knowledgeable HCP (to design and guide the exercise program), choosing a type of exercise that is enjoyable, incorporating exercise into daily routines and exercising at home or with others (group exercise).

To assess the current application of exercise in neuromuscular care, **Sander Oorschot, Asunción Bustos** and **Nanna Scharff Poulsen** (Early Career Researchers, ECRs) conducted an international online survey of HCPs before the workshop. The survey was prepared by the ECRs together with the workshop organizers and the outline was based on a previous study on the application of aerobic exercise in NMDs [7]. There were questions on various topics including the profile of the respondents, the application of exercise, barriers to prescribing exercise and the need for support. The survey was sent to all HCPs of the European reference network EURO—NMD and to other HCPs within the network of the organisers and ECRs. Preliminary results were presented during the workshop. There were 57 respondents, most of them from Europe (74 %). Most respondents were physicians (60 %) or physiotherapists (35 %).

The results showed that almost all respondents (93 %) prescribed exercise, while 19 % of this group did not prescribe resistance exercise. The prescription of aerobic and resistance exercise programs varied widely among HCPs in terms of the FITT factors. The main barriers perceived by HCPs to prescribing exercise for people with NMDs were safety concerns (including cardiac status and fear of overexertion) and patient characteristics (including patient physical capacity and comorbidities). The majority of respondents (79 %) said they needed support to improve the application of exercise, most commonly about exercise dosing (60 %) and preferably through the development of guidelines (82 %).

2.3. Consensus meeting on exercise prescription in muscle diseases

After presentation of the survey results, **John Vissing** and **Eric Voorn** led a group discussion to reach consensus on recommendations for exercise prescription, based on the position stand draft. There was strong consensus (i.e., all attendees agreed) that the key message should be to *encourage exercise for people with muscle diseases*. Aspects that were discussed included the FITT factors for aerobic and resistance exercise (with some refinements suggested to the position stand), the pre-exercise assessment (including personal goals), monitoring (both physiological and subjective markers, such as ratings of perceived exertion and recovery) and compliance to long-term exercise (integration in the design of exercise programs and patient preferences). Specific recommendations are described in Section 6.

2.4. Lessons to be learned from exercise studies in mouse models of muscle disease and hiPSC-derived 3D skeletal muscle

The group discussion was followed by presentations on what can be learned from exercise studies in mouse models of muscle diseases and hiPSC-derived 3D skeletal muscles.

Thomas Krag explained that exercise studies in mouse models of muscle disease are generally not designed to determine the effects of exercise itself but instead are used to characterize disease models and to assess cardiovascular, metabolic and muscle function, including factors such as voluntary activity, contractile function, fatigue resistance, and susceptibility to mechanical stress. Exercise in mouse models may also be used to test for improvement of muscle function in therapy development studies, where functional testing is essential for preclinical evaluation of treatments. Mouse models provide reproducible conditions with controlled variables (i.e., genetic background, environment, and the interaction between these two) that are difficult to achieve in human studies. Disease models can be expensive and time consuming to develop. A knock-in model with a founder mutation is often a good choice for replicating human conditions, while knock-out models are commonly used to study disease mechanisms. Two main types of exercise studies are commonly used in live mice: voluntary and involuntary. Levels of voluntary activity, as well as patterns of movement, are assessed using activity wheels or cages [10]. Involuntary exercise that induces exhaustion, such as treadmill running, is valuable for metabolic analyses, as it can be combined with calorimetric measurements. This has been used in the functional analysis of mouse models of glycogen storage diseases 0b, III and V [11–13]. Standardization of treadmill protocols would improve the consistency of functional comparisons among disease models and inclusion in the TREAT-NMD repository could be considered.

Ex vivo electrophysiology, including analysis of the extensor digitorum longus and soleus muscles in organ baths, is a widely used for evaluating fundamental muscle properties such as maximal contractile force, resistance to fatigue, and force drop after eccentric contractions [14]. This technique is valuable in preclinical treatment studies and can also identify potential mechanical weakness in disease models that should be considered when prescribing exercise to people with muscle diseases. Understanding the limitations of disease models is critical, particularly for translational research.

Pim Pijnappel's laboratory focuses on lysosomal storage diseases, in particular Pompe disease, which is caused by variants in the acid alpha glucosidase (*GAA*) gene, leading to GAA enzyme deficiency and glycogen accumulation in (and also outside) the lysosomes. This results in progressive skeletal muscle pathology. Although enzyme replacement therapy is available and effective, it does not necessarily stop the progression of the disease. Healthy skeletal muscle has a high regenerative capacity mediated by muscle stem cells called satellite cells. A fundamental question is why satellite cells seem unable to prevent disease progression in Pompe disease. Pijnappel and his colleagues have shown that in Pompe disease, satellite cells are either insensitive to the pathology or actively blocked, as they are inactive while the disease progresses. However, artificial activation of satellite cells in Pompe disease mice can regenerate muscle tissue [15], suggesting that promoting satellite cell activation could delay disease progression.

To evaluate the effects of exercise, Pijnappel's laboratory has developed a technology to generate highly contractile muscle tissues in 3D from skin biopsies of healthy and Pompe disease individuals, via the generation of iPSCs and myogenic progenitors. The myogenic progenitors can be expanded over 100 billion times, allowing quantitative assessment of muscle function in both 2D and 3D models [16–18]. In collaboration with Optics11 Life and Leiden University Medical Center (The Netherlands), the Cuore system was developed, which uses optical fiber sensing to measure contractile force in real time [19]. This technology allows the non-invasive evaluation of exercise programs on 3D human muscles in vitro. Preliminary results have shown that these models can recapitulate aspects of human muscle function, including the response to overtraining (which causes muscle wasting) or muscle fiber hypertrophy in response to mild exercise with sufficient resting intervals. Future efforts will focus on evaluating different exercise programs for their potential to benefit or worsen disease progression in Pompe disease and other muscle diseases.

3. Towards a core set of outcome measures in exercise studies in muscle diseases

The next workshop session was dedicated to reaching consensus on recommendations for a core set of outcome measures to be used in future studies of exercise in muscle diseases. It included combined presentations by 2 speakers on aerobic capacity measures, muscle function measures, functional measures and scales and questionnaires, followed by group discussions and a consensus meeting.

3.1. Overview of outcome measures in exercise studies in muscle diseases

3.1.1. Aerobic capacity measures

Tanja Taivassalo and **Alejandro Lucia** focused on aerobic capacity outcome measures. Cardiopulmonary exercise testing (CPET) has been the gold standard for measuring peak oxygen uptake (VO_{2peak}) in both healthy and clinical populations for over 100 years [20]. VO_{2peak}, which reflects the ability to deliver oxygen to the exercising muscles and to extract it from the blood, is the product of cardiac output (oxygen delivery) and arteriovenous oxygen difference (oxygen extraction). In muscle diseases, measurement of VO_{2peak} provides valuable insights, including the quantification of exercise intolerance, identification of physiological limitations, determination of exercise prescription parameters, and assessment of therapeutic efficacy. First applied to metabolic myopathies four decades ago, CPET has since shown that individuals with muscle diseases, regardless of subtype, typically have reduced VO_{2peak}, with values ranging from 16 to 21 mL/kg/min (compared to an average of ~25–40 mL/kg/min in healthy adults) [21]. VO_{2peak} is responsive mainly to exercise training or detraining, but also to some pharmacological interventions mimicking exercise [22], and should be considered a primary outcome measure in therapeutic trials. Valid assessment of VO_{2peak} by CPET has shown to be feasible in most muscle diseases [23], but requires specialized equipment (e.g., ergometers, metabolic carts) and expertise.

If CPET is not possible, submaximal parameters can be assessed, preferably during exercise testing on an ergometer. These include time to exhaustion, heart rate, or blood lactate, all of which have been used to show performance improvements in response to exercise or pharmacological treatment [22]. In people with severe muscle weakness, motor-assisted cycling (no or constant load) with measurement of distance, heart rate, and blood lactate may be informative [24]. Emerging technologies, such as smartphone-based algorithms and wearable devices, offer the potential for estimating VO_{2peak} through submaximal exercise, although further technological advances are needed to reduce error. Other submaximal measures, such as the oxygen uptake efficiency slope, ventilatory threshold, or recovery heart rate, may also provide valuable insights. Continued research is necessary to establish the repeatability of VO_{2peak} and other exercise parameters in people with muscle diseases with varying disease severities [25].

3.1.2. Muscle function measures

Elise Duchesne presented on myotonic dystrophy type 1 (DM1), where patients' muscle strength is known to decline over time, with reductions ranging from 24 % to 56 % over 9 years [26]. Muscle weakness in DM1 is associated with physical limitations and reduced participation in daily activities [27]. Measurement of muscle function is therefore essential to assess disease progression and evaluate treatment efficacy. Importantly, resistance exercise programs are increasingly being prescribed in muscle diseases, mostly with maximal isometric

muscle strength (MIMS) as the primary outcome. However, standardized guidelines for MIMS assessment are needed to ensure consistency in clinical care and research. Elise's research team has developed a standardized MIMS protocol using a push-pull handheld dynamometer (MEDup™) to assess 17 muscle groups in the upper and lower limbs, showing good to excellent intra- and inter-reliability in healthy adults [28]. This protocol has also showed excellent concurrent validity and intra-rater reliability for the assessment of knee-extensor muscles in DM1 [29]. The protocol is available in both French and English and MIMS reference values are currently being established for healthy adults (18–70 years), with existing reference values for children and adolescents [30].

Alfredo Santalla's presentation focused on people with glycogen storage disease type V (GSDV). He explained how virtually any exercise task can cause pain and contractures (at least in the most unfit people), and that to prevent this and muscle rhabdomyolysis, strength training and testing should involve low-repetition sets (3 for testing, 6 for training) with relatively long (2–3) minutes of rest between sets. The low number of repetitions allows the use of muscle phosphocreatine as the main energy substrate to fuel contraction with no major reliance on muscle glycogen deposits. In turn, the 'long' rest periods between each set of repetitions and exercises allows muscle phosphocreatine to be resynthesized in a given muscle before this muscle is utilized again. A pre-exercise glucose drink is recommended to enhance safety [31]. To measure muscle function in GSDV, muscle power (the practical application of force) can be safely assessed using sport science instruments like linear encoders or force platforms. Increasing the load up to the decrease of the force-velocity curve allows for stopping the test before reaching the one-repetition maximum, avoiding risky contractions. Videos demonstrated examples in vertical movements (half squat, bench press) and leg press using force platforms. Data from resistance exercise interventions in people with GSDV showed positive responses when following disease specific guidelines [31]. Videos highlighted both conventional machine-based training and training using music apps to motivate patients. Additionally, Dual Energy X-Ray Absorptiometry was suggested as a complementary tool for assessing muscle mass, and strength relative to muscle mass. This non-invasive approach helps understand training adaptations [32].

3.1.3. Functional measures

Meredith James explained that exercise studies in muscle diseases should select outcome measures for the patient population of interest that inform inclusion criteria, study design, and endpoint selection. These studies must consider the impact of disease on function, the muscles affected and expected trajectory of disease progression. Patient-centered, standardized functional assessments, appropriate to age, ability, and disease stage, should be utilized. Functional outcome measures should reflect the lived experience and relevance to the population. Exercise programs should consider the potential impact of the intervention to carry over to daily life function and design and measure interventions accordingly. Potential outcomes include motor function, strength, timed tests, respiratory function, patient-reported outcomes and quality of life. These measures should align with the International Classification of Functioning, Disability and Health (ICF) framework, addressing body structures, activity, and participation, while ensuring reliability, validity, and sensitivity to change. Existing NMD exercise studies have limited use of standardized tests like the six-minute (6MWT) and 2-minute (2MWT) walk tests and Timed Up and Go (TUG) test [5,33,34]. Disease-specific tools, such as the North Star Ambulatory Assessment or Performance of Upper Limb, are underutilized. The relationship between strength and function is complex, as strength improvements do not always correlate with functional gains but can influence other elements of motor performance such as fatigue. Using standardized outcome measures helps recruit more homogenous populations and refine exercise prescriptions. Natural history data from these measures also informs expected functional changes, enhancing understanding of exercise intervention effects and informing trial design.

Helene Alexanderson discussed several functional measures to assess muscle function and activity limitations in muscle diseases. The 6MWT and 2MWT are validated across different muscle diseases, including DM1, LGMD and IBM, showing excellent test-retest reliability (intra-class correlation coefficient [ICC], 0.91 to 1.00) and small measurement errors [35]. The 2MWT is preferred for efficiency, as it correlates almost perfectly with the 6MWT [36]. Focusing on myositis, the walking tests and the TUG test have found to be relevant for assessing walking, balance, and sit-to-stand ability, particularly in people with IBM, who perform worse than healthy controls. While walking tests are important for long-term follow-up, balance impairments can affect performance on courses below the recommended 30 m. The Timed Stand Test (TST) evaluates the ability to rise from a chair several times (e.g., 5) as fast as possible, with reference values available for different age groups. The Functional Index 2 and 3 (shorter duration) measure myositis-specific impairments, showing good reliability (ICC 0.83 to 0.96) and correlating with isokinetic muscle endurance (r-coefficients 0.58 to 0.69). Both are independent of the assessor's strength and therefore preferred over manual muscle testing and hand-held dynamometry.

3.1.4. Scales and questionnaires

Nicole Voet and **Kristin Ørstavik** discussed the use of the Egen Klassifikation Scale and the Activities-Specific Balance Confidence Scale to measure the benefits of physical activity in muscle diseases. These measures aim to capture meaningful changes in patients' abilities, especially for those with severe disabilities. Patient-Reported Outcome Measures (PROMs) are essential for assessing health and quality of life, as they provide insight into the patient's subjective experience, including physical functioning and overall well-being. PROMs can be disease-specific, like the Amyotrophic Lateral Sclerosis (ALS) Functional Rating Scale, or generic, like the 36-Item Short Form Health Survey (SF-36), which is used across various muscle diseases. It is crucial to choose PROMs that are valid, reliable, and responsive to the needs of the specific patient population. A scoping review identified 190 PROMs used in muscle diseases research, with physical functioning as the most commonly assessed domain [37]. However, few PROMs have been thoroughly evaluated for their validity and responsiveness in measuring social functioning, activity [38,39] or long-term treatment outcomes, highlighting the need for further research . In this process, it is important to collaborate with patient representatives from the beginning.

Two psychological concepts, the *disability paradox,* and *response shift*, are important for interpreting PROMs [40]. The *disability paradox* refers to the phenomenon where individuals with major physical impairments report high quality of life, challenging the assumption that disabilities *always* lead to lower well-being. *Response shift* describes how patients' perceptions of their quality of life may change as they adapt to disability. Both concepts are important for understanding how patients cope with their conditions and how their assessments of health may change over time. Individualized outcome measures, such as the Canadian Occupational Performance Measure (COPM) and Goal Attainment Scaling (GAS), allow for patient-centered assessment, aligning outcomes with personal goals [41]. Using appropriate PROMs and understanding psychological and physical barriers can help HCPs better support people with muscle diseases and improve their quality of life [42].

3.2. Consensus meeting on a core set of outcome measures in exercise studies in muscle diseases

Following the duo presentations, **Helene Alexanderson** led a group discussion to reach consensus on recommendations for a core set of outcomes to be used in future studies of exercise in muscle disease. The group was first divided into four groups, and aspects that were discussed in each group included the outcome measures that should be included in

a core set (e.g., differences between clinical practice and research, and between ambulatory and non-ambulatory people), disease-specific outcomes, and how to incorporate patient priorities in the selection of outcomes (e.g., inclusion of patient partners). This was followed by a presentation of each group's findings and then a consensus meeting with the whole group. Specific recommendations are described in Section 6.

4. Exercise continuation

The next session was dedicated to maintaining a physically active lifestyle and continuing exercise in the long term, and it included 6 presentations from different perspectives.

Charlotte van Esch presented as a patient representative on behalf of '*Spierziekten Nederland*', a non-governmental patient organization for NMDs in The Netherlands. She discussed the results of 2 recent surveys and a focus group. In 2023, *Spierziekten Nederland* surveyed >1000 members to understand their priorities in quality-of-life research. The most common problems experienced in daily life reported by respondents were fatigue (61 %), reduced mobility (52 %), and pain (34 %). Respondents emphasized that quality of life research should focus on exercise. '*Gehandicaptensport Nederland*' (Dutch disabled sports association) conducted a survey to investigate the perceived motivators and barriers to exercise for people with NMDs. Adults reported health benefits (86 %) and improved fitness (63 %) as the main motivating factors, while children were mainly motivated because exercise is fun (69 %). The main barriers to exercise were physical, including pain and fatigue. In September 2024, *Spierziekten Nederland* organized a focus group, where participants emphasized on the importance of making exercise fun, with local sports facilities being crucial to increasing participation. They also highlighted the need for more awareness, guidance on how to exercise, and recommendations on how to get started. To promote social change, the group recommended organizing local multi-sport events to try out different activities and educating sports clubs, trainers, and coaches to adapt their provision to the needs of people with NMDs. Patients and HCPs also need guidance on how to prescribe exercise based on the FITT factors.

Linda van den Berg introduced that the World Health Organization (WHO) recommends adults to engage in 150 to 300 mins or 75 to 150 mins per week of moderate-to-vigorous or vigorous aerobic physical activities, respectively (or in a combination thereof) along with at least two days of muscle-strengthening activities [43]. Despite the established benefits of exercise for various muscle diseases, evidence on long-term physical activity is limited. A recent study on adults with late-onset Pompe disease, examined the impact of long-term physical activity following the WHO guidelines, as well as maintaining a previous exercise program. Results showed that participants who remained physically active had significantly better endurance, muscle strength, and function compared to inactive individuals. While the group that continued the prior exercise program generally performed better than active controls who did not participate in the previous exercise program, differences were not statistically significant, possibly due to a small sample size and the integration of the exercise program components (endurance, strength, core stability) into standard clinical practice after the initial study [44]. Main reasons for quitting the exercise program included time constraints, perceived difficulty of exercises, and lack of professional support after the program [45]. This study highlighted the importance of personalized exercise programs for people with muscle diseases. These programs should maximize effectiveness within time limitations, and HCPs should actively promote and support physical activity in daily life.

Hans Knoop discussed how behavioral and psychological processes can influence the outcomes of exercise programs. Most exercise programs focus on short term gains and less time and effort is spent on how participants will continue after the program. This should receive more attention and be seen as an integral part of an exercise program. To motivate people with NMD to exercise it may be helpful to: 1) making exercise more relevant to achieving goals in everyday life that are valued by patients; 2) educating patients about the positive aspects of exercise; 3) making exercise rewarding (e.g., through positive feedback or gamification of exercise) and 4) social support. Behavioral goal setting and self-monitoring of exercise behavior are evidence-based strategies to increase motivation to exercise. Persistent physical symptoms occurring in NMDs, like fatigue, pain and apathy, can make it difficult to adhere to exercise programs. Patients may avoid exercise for fear of fatigue or pain, while exercise can reduce fatigue in chronic medical conditions. Ideally, fatigue and pain are addressed in an exercise program and patients' beliefs about the relationship between their symptoms and their ability to exercise are discussed. Research has shown that addressing fatigue in NMD can help to increase the physical activity levels in people with NMD [46].

Eric Voorn presented the results of an unpublished qualitative study to explore the perceived barriers and facilitators to behavior change towards a more active lifestyle in people with NMDs. The study described data from 19 participants (63 % female, aged 28–73 years) with 4 different NMDs who were allocated to a physical activity program as part of a randomized controlled trial [34]. The physical activity program included coaching sessions using motivational interviewing techniques. All sessions were audio-recorded, and a random selection (until data saturation: 29 audio recordings) was subjected to thematic analysis, using the International ICF as a framework [47]. There were barriers and facilitators in all the ICF domains, and it was recommended that HCPs systematically assess them as they could guide the discussion of physical activity behavior during consultations and so that they can be addressed in a personalized way during multidisciplinary neuromuscular rehabilitation treatment.

Nanna Scharff Poulsen addressed the question whether people with NMDs who are in a wheelchair and have a very low muscle mass can also benefit from exercise. She discussed one study accepted for publication and one unpublished study. The first was a systematic review of exercise in wheelchair users with NMDs [48]. After reviewing the literature, only 14 studies were found (with at least 60 % of participants being a wheelchair user), most of which were of low quality. These studies focused on Duchenne muscular dystrophy (DMD), spinal muscular atrophy (SMA), LGMD, FSHD, and ALS. Half of the studies targeted respiratory exercises, two focused on masticatory exercises, and five addressed extremity exercises (all with different interventions). Results showed that exercise could improve strength and endurance of respiratory muscles, occlusal strength and satisfaction with meals, and range of motion, strength and endurance of extremities [49–53]. The second study involved 19 wheelchair users with muscular dystrophy (DMD, BMD, LGMD, FSHD, and collagen 6 deficiency). Participants underwent a 10-week control period followed by a 10-week exercise program using a cycle ergometer adapted for wheelchair use. Assessments were done at baseline, after the control period and after the exercise program. The exercise program significantly reduced lower back pain (assessed with the lower back pain rating scale), constipation (home-made questionnaire based on the ROM-IV criteria), and fatigue (fatigue severity scale), and improved quality of life (quality of life for genetic NMDs) and glycemic control (glycated hemoglobin), especially in those with diabetes. However, there was no improvement in the time to cycle 1 km. In conclusion, while evidence is scarce, both studies suggested that, despite a very low muscle mass, wheelchair users with NMDs can benefit from exercise. There is, however, not much evidence and further research is needed to confirm these findings and explore the effects of exercise on other types of NMDs.

Jean-Yves Hogrel explored how eHealth can support an active lifestyle for people with muscle diseases, with potential applications for other conditions as well. While definitions of mHealth, eHealth, and digital health are not uniform, eHealth is a rapidly growing field with promising clinical applications. Promoting an active lifestyle is important for three reasons: preventing deconditioning [54], possibly slowing disease progression, and enhancing patient well-being. Digital solutions that support an active lifestyle can include devices (wearables), medical

services (telemedicine, coaching), social applications (online support communities), and data processing technologies like Artificial Intelligence. These solutions are often patient-centered and personalized, involving medical, social, and family networks. However, challenges exist when digital tools do not meet patient needs, or when patients are not convinced about their benefits or non-compliant for various reasons. A sociological approach, focusing on patient motivations and needs, can address these challenges. Hogrel introduced the concept of "sense of coherence" [55], which considers health from a broader perspective (*salutogenesis*) rather than just focusing on the disease (*pathogenesis*). This theory suggests that a patient's sense of coherence—shaped by cognitive, behavioral, and motivational factors—plays a crucial role in deciding to increase physical activity. Increasing physical activity requires a sense of purpose and goal, whether for life satisfaction, mood enhancement, or finding meaning in life. Digital tools can also help to administer and monitor exercise programs, using technologies like connected wearables, videos and online questionnaires to track progress. However, the effectiveness of these tools depends on patient compliance, acceptability, and the technical and environmental factors surrounding the use of these technologies.

5. Recommendations and future steps

In the various discussion rounds during the workshop, the expert group reached a consensus (i.e., all attendees agreed) on the following recommendations and future steps:

- Exercise should be encouraged for people with muscle diseases.
- Exercise prescription for people with muscle diseases should be personalized: there is no one-size-fits-all approach.
- Aerobic exercise recommendations, specified in terms of the FITT factors, are shown in Table 1. It is recommended to start with moderate (rather than high) intensity exercise. Moderate- or high-intensity continuous aerobic exercise may not be feasible for everyone because of difficulties in maintaining the intensity or duration. In this case, low-intensity continuous aerobic exercise or newer forms of aerobic exercise, such as polarized exercise (i.e., most of the exercise volume at low exercise intensities with some intense bouts) or high-intensity interval exercise may be considered depending on the (severity of) disease [56,57]. High-intensity interval exercise is contraindicated in certain metabolic myopathies (especially certain types of muscle glycogenosis) where it may increase the risk of rhabdomyolysis.
- Resistance exercise recommendations, specified in terms of the FITT factors are shown in Table 1. Exercises should be performed with correct form and technique, using muscle groups of at least Medical Research Council (MRC) grade 3 to avoid compensation and overloading. Exercise involving only eccentric contractions is not recommended for people with muscle diseases, as they can cause severe muscle damage and soreness. In certain metabolic myopathies (especially certain types of muscle glycogenosis) resistance exercise should exclusively involve low-repetition sets allowing phosphocreatine resynthesis between them.
- It is important to monitor the exercise program, especially in the early stages, so that adjustments can be made if necessary to avoid overexertion.
- Potential clinician and patient- reported outcome measures to monitor progress (including safety) and to evaluate the effects of exercise programs are shown in Table 2. Outcome measures should reflect ICF domains and include not only body structures and function, but also activity and participation measures. The choice of outcome measures depends on the exercise modality (aerobic, resistance exercise, or a combination thereof), the setting (research or clinic/at home), the level of ambulation (ambulant or non-ambulant) and on the specific muscle disease. Additional measures to consider include MRI, respiratory function (including maximal inspiratory and expiratory pressure), body composition, and disease specific outcome measures.
- To promote a physically active lifestyle that includes long-term continuation of exercise, it is recommended to address this issue in the design of exercise programs and to discuss it with the patient. Discuss the rationale for exercise, personal goals (make them relevant for life), and consider patient preferences.
- Future research on exercise in muscle diseases is required. Topics of interest include the long-term (i.e., >1 year) effects and safety, development and evaluation of strategies for continuation of physical activity and exercise, development and consensus on outcomes for monitoring of exercise programs (including eHealth), exercise studies in non-ambulant patients with very low muscle mass and in diseases where evidence is missing (such as oculopharyngeal muscular dystrophy), and evaluation of different forms of exercise programs (for example low and/or high intensities, or combinations thereof) or types of exercise (for example aerobic and resistance exercise combined).

Table 1
Aerobic and resistance exercise recommendations.

Aerobic exercise	
Frequency	3 to 5 days per week
Intensity	50 to 80 % of peak oxygen uptake or heart rate (moderate to high intensities)
Time	10 to 20 min at high intensity (70 to 80 % of peak) or 20–60 mins at lower intensities (50 to 70 % of peak) per exercise session
Type	Any type of exercise that involves greater muscle groups
Progression	Gradual progression of exercise volume by adjusting time, frequency and/or intensity until the desired exercise goal (maintenance) is attained.
Resistance exercise	
Frequency	2 to 3 days per week
Intensity	25 to 85 % of the 1 repetition maximum (1RM) 25 to 70 % of the 1RM, light to moderate intensity 70 to 85 % of the 1RM, high intensity
Time (i.e., sets and repetitions)	2 to 4 sets, 2 to 3 min rest intervals between sets 5 to 15 repetitions at high intensity to improve muscle strength 15 to 25 repetitions at lower intensities to improve muscle endurance
Type	Machines, free weights, elastic bands, or own body weight
Progression	A gradual progression of greater resistance (to improve strength), or number of repetitions (to improve endurance) until the desired exercise goal (maintenance) is attained.

6. Discussion and conclusion

As a next step to build on the momentum of the workshop, the workshop study group agreed for two manuscripts to follow this workshop report. The first will be a position stand aimed at providing practical guidance for prescribing personalized exercise for people with muscle diseases. The manuscript will present the aerobic and strengthening exercise recommendations discussed above, together with a detailed description of diseases requiring special attention, and recommendations for pre-exercise screening procedures, baseline intensity assessment, monitoring, and outcome assessment. Potential long-term risks and recommendations for continuing exercise are also discussed. The key message of the manuscript will be to encourage HCPs to prescribe exercise to people with muscle diseases, to do so in a more standardized way, and to raise awareness of this patient-prioritized topic. The second manuscript will present the results of the patient and HCP surveys on the application of exercise in daily practice. It will provide information on barriers and facilitators to exercise, as well as the need for support, which may guide future initiatives. Potential differences between continents and countries will also be explored.

In conclusion, this workshop brought together leading international experts in the field of exercise in muscle diseases. Patient engagement

Table 2
Potential outcome measures.

	Research	Clinic/at home
Evaluation of effects		
Body functions		
Muscle function	- Muscle strength, using quantitative muscle testing (fixed dynamometer, hand-held dynamometer) - Muscle power using sports science equipment	- Manual muscle testing - Number of repetitions (similar weight/load)
Aerobic capacity/ endurance	- Peak oxygen uptake (VO_{2peak}) by cardiopulmonary exercise testing - Motor-assisted cycling (no or constant load), with measurement of distance, heart rate, and blood lactate*	- Submaximal heart rate or rating of perceived exertion during fixed distance physical activity (e.g., bicycling, walking or moving in a wheelchair)
Pain	- Visual analogue scale - PROMIS pain	- Visual analogue scale - PROMIS pain
Fatigue	- Fatigue severity scale - Checklist individual strength - PROMIS fatigue	- Fatigue severity scale - Checklist individual strength - PROMIS fatigue
Activities		
Functional capacity	- Appropriate walking test (e.g., 2- or 6-minute walk test [or push test*], 100 meter timed test, 10 meter walk/run test) - Timed Up and Go test - 5 or 10 times Sit to Stand test	- Appropriate walking test (e.g., 10 meter walk/run test) - Timed Up and Go test - 5 or 10 times Sit to Stand test
Physical activity	- Accelerometry	- Wearables, smartphone apps
Functional activities of daily living	- ACTIVLIM - Egen Klassifikation 2* - Validated and disease specific measure of motor function (e.g., North Star for Limb-Girdle Type Dystrophies [NSAD], Revised Upper Limb Module for Spinal Muscular Atrophy (RULM)	- ACTIVLIM - Egen Klassifikation 2* - Validated and disease appropriate functional measure of motor function (e.g., NSAD, RULM)
Participation		
Quality of life	- SF-36 - Quality of Life for NMD - PROMIS quality of life	- SF-36 - Quality of Life for NMD - PROMIS quality of life
Personal goals	- Goal Attainment Scale - Canadian Occupational Performance Measure	- Discuss during intake and follow-up
Monitoring of progress (during training sessions)		
Training load	- Heart rate using heart rate monitors - Workload, resistance level - Ratings of perceived exertion - Blood lactate	- Heart rate using wearables or smartphone apps - Distance covered, weight/ load lifted - Ratings of perceived exertion
Recovery	- Physical complaints (e.g., muscle soreness, [excessive] fatigue) - Sleep quality - Serum creatine kinase	- Physical complaints, (e.g., muscle soreness, [excessive] fatigue) - Sleep quality

ACTIVLIM, activity limitations questionnaire; PROMIS, patient-reported outcomes measurement information system.
* Specific outcomes for non-ambulatory people with muscle diseases.

was of great value, as evidenced by the high number of responses to the patient survey, which also highlighted the importance of addressing this topic from the patient perspective. There was a consensus that personalized exercise is safe and beneficial for people with muscle diseases and should be recommended.

7. The 281st ENMC workshop study group

Helene Alexanderson (Karolinska Institutet, Stockholm, Sweden), Linda van den Berg (Erasmus MC, Rotterdam, The Netherlands), Asunción Bustos (Universidad Europea de Madrid, Madrid, Spain), Elise Duchesne (Université Laval, Québec, Canada), Charlotte van Esch (Spierziekten Nederland, Baarn, The Netherlands), Ingrid de Groot (The Netherlands), Jean-Yves Hogrel (Hospitalier Pitié Salpêtrière, Paris, France), Meredith K. James (The John Walton Muscular Dystrophy Research Centre, Newcastle Upon Tyne, United Kingdom), Hans Knoop (Amsterdam UMC, Amsterdam, The Netherlands), Madelon Kroneman (The Netherlands), Thomas Krag (Rigshospitalet, Copenhagen, Denmark), Alejandro Lucia (Universidad Europea de Madrid, Madrid, Spain), Sander Oorschot (Amsterdam UMC, Amsterdam, The Netherlands), Kristin Ørstavik (Oslo University Hospital, Oslo, Norway), Pim Pijnappel (Erasmus MC, Rotterdam, The Netherlands), Alfredo Santalla (Universidad Pablo Olavide, Sevilla, Spain), Nanna Scharff Poulsen (Rigshospitalet, Copenhagen, Denmark), Tanja Taivassalo (University of Florida, Gainesville, United States of America), John Vissing (Rigshospitalet, Copenhagen, Denmark), Nicole Voet (Radboudumc, Nijmegen, The Netherlands), Eric Voorn (Amsterdam UMC, Amsterdam, The Netherlands).

CRediT authorship contribution statement

Eric Lukas Voorn: Conceptualization, Writing – original draft, Writing – review & editing. **Alejandro Lucia:** Conceptualization, Writing – original draft, Writing – review & editing. **John Vissing:** Conceptualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

Eric Voorn: none.
Alejandro Lucia: none.
John Vissing: none.

Acknowledgments

The workshops and next generation programme are made possible thanks to the financial support of the European Neuromuscular Centre (ENMC) and its Full Partners: Association Française contre les Myopathies (France), Deutsche Gesellschaft für Muskelkranke (Germany), Muscular Dystrophy Campaign (UK), Muskelsvindfonden (Denmark), Prinses Beatrix Spierfonds (The Netherlands), Schweizerische Stiftung für die Erforschung der Muskelkrankheiten (Switzerland), Spierziekten Nederland (The Netherlands), Telethon Foundation (Italy). In addition, we would like to thank the Associated Partners: Österreichische Muskelforschung (Austria), SMA Europe, TREAT-NMD, World Duchenne Organisation, World Muscle Society (WMS), and the members of the ENMC Company Forum: Amicus Therapeutics, Dyne Therapeutics, Lupin Neuroscience, Novartis, Roche, Sanofi and Santhera.

References

[1] Pate RR, Pratt M, Blair SN, Haskell WL, Macera CA, Bouchard C, et al. Physical activity and public health: a recommendation from the centers for disease control and prevention and the American college of sports medicine. Jama 1995;273:402–7.
[2] Ginis KAM, van der Ploeg HP, Foster C, Lai B, McBride CB, Kwok Ng, et al. Participation of people living with disabilities in physical activity: a global perspective. The Lancet 2021;398:443–55.
[3] McDonald CM. Physical activity, health impairments, and disability in neuromuscular disease. Am J Phys Med Rehabil 2002;81:S108–20.
[4] Oorschot S, Brehm M-A, Daams J, Nollet F, Voorn EL. Efficacy of aerobic exercise on aerobic capacity in slowly progressive neuromuscular diseases: a systematic review and meta-analysis. Ann Phys Rehabil Med 2023;66:101637.
[5] Voet NB, van der Kooi EL, van Engelen BG, Geurts AC. Strength training and aerobic exercise training for muscle disease. Cochrane Database Systemat Rev 2019.
[6] Stefanetti RJ, Blain A, Jimenez-Moreno C, Errington L, Ng YS, McFarland R, et al. Measuring the effects of exercise in neuromuscular disorders: a systematic review and meta-analyses. Wellcome Open Res 2020;5.
[7] Voorn EL, Koopman F, Nollet F, Brehm MA. Aerobic exercise in adult neuromuscular rehabilitation: a survey of healthcare professionals. J Rehabil Med 2019;51:518–24.

[8] Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, et al. American college of sports medicine position stand. quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc 2011;43:1334–59.

[9] Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep 1985;100:126.

[10] Raben N, Nagaraju K, Lee E, Plotz P. Modulation of disease severity in mice with targeted disruption of the acid α-glucosidase gene. Neuromusc Disord 2000;10: 283–91.

[11] Pederson BA, Cope CR, Schroeder JM, Smith MW, Irimia JM, Thurberg BL, et al. Exercise capacity of mice genetically lacking muscle glycogen synthase: in mice, muscle glycogen is not essential for exercise. J Biol Chem 2005;280:17260–5.

[12] Pagliarani S, Lucchiari S, Ulzi G, Violano R, Ripolone M, Bordoni A, et al. Glycogen storage disease type III: a novel Agl knockout mouse model. Biochimica et Biophysica Acta (BBA)-Mol Basis Dis 2014;1842:2318–28.

[13] Nogales-Gadea G, Pinos T, Lucia A, Arenas J, Camara Y, Brull A, et al. Knock-in mice for the R50X mutation in the PYGM gene present with McArdle disease. Brain 2012;135:2048–57.

[14] Krag TO, Pinós T, Nielsen TL, Brull A, Andreu AL, Vissing J. Differential muscle involvement in mice and humans affected by McArdle disease. J Neuropathol Exp Neurol 2016;75:441–54.

[15] Schaaf GJ, Van Gestel TJ, in 't Groen SL, de Jong B, Boomaars B, Tarallo A, et al. Satellite cells maintain regenerative capacity but fail to repair disease-associated muscle damage in mice with Pompe disease. Acta Neuropathol Commun 2018;6: 1–16.

[16] 't Groen SL, Franken M, Bock T, Krüger M, de Greef JC, Pijnappel WP. A knock down strategy for rapid, generic, and versatile modelling of muscular dystrophies in 3D-tissue-engineered-skeletal muscle. Skelet Muscle 2024;14:3.

[17] Iuliano A, van der Wal E, Ruijmbeek CW, in 't Groen SLM, Pijnappel WWMP, de Greef JC, et al. Coupling 3D printing and novel replica molding for in house fabrication of skeletal muscle tissue engineering devices. Adv Mater Technol 2020; 5:2000344.

[18] van der Wal E, Herrero-Hernandez P, Wan R, Broeders M, van Gestel TJM, van IJcken WFJ, et al. Large-scale expansion of human iPSC-derived skeletal muscle cells for disease modeling and cell-based therapeutic strategies. Stem Cell Rep 2018;10:1975–90.

[19] Iuliano A, Haalstra M, Raghuraman R, Bielawksi K, Bholasing AP, van der Wal E, et al. Real-time and multichannel measurement of contractility of hiPSC-derived 3D skeletal muscle using Fiber optics-based sensing. Adv Mater Technol 2023;8: 2300845.

[20] Harber MP, Myers J, Bonikowske AR, Muntaner-Mas A, Molina-Garcia P, Arena R, et al. Assessing cardiorespiratory fitness in clinical and community settings: lessons and advancements in the 100th year anniversary of VO2max. Prog Cardiovasc Dis 2024.

[21] Taivassalo T, Dysgaard Jensen T, Kennaway N, DiMauro S, Vissing J, Haller RG. The spectrum of exercise tolerance in mitochondrial myopathies: a study of 40 patients. Brain 2003;126:413–23.

[22] Taivassalo T, Gardner JL, Taylor RW, Schaefer AM, Newman J, Barron MJ, et al. Endurance training and detraining in mitochondrial myopathies due to single large-scale mtDNA deletions. Brain 2006;129:3391–401.

[23] Veneman T, Koopman FS, Oorschot S, de Koning JJ, Bongers BC, Nollet F, et al. Validity of cardiopulmonary exercise testing for assessing aerobic capacity in neuromuscular diseases. Arch Phys Med Rehabil 2024;105:1846–53.

[24] Morse CI, Bostock EL, Twiss HM, Kapp LH, Orme P, Jacques MF. The cardiorespiratory response and physiological determinants of the assisted 6-minute handbike cycle test in adult males with muscular dystrophy. Muscle Nerve 2018; 58:427–33.

[25] Veneman T, Koopman FS, Daams J, Nollet F, Voorn EL. Measurement properties of aerobic capacity measures in neuromuscular diseases: a systematic review. J Rehabil Med 2022;54.

[26] Gagnon C, Petitclerc É, Kierkegaard M, Mathieu J, Duchesne É, Hébert LJ. A 9-year follow-up study of quantitative muscle strength changes in myotonic dystrophy type 1. J. Neurol. 2018;265:1698–705.

[27] Petitclerc É, Hébert LJ, Mathieu J, Desrosiers J, Gagnon C. Relationships between lower limb muscle strength impairments and physical limitations in DM1. J Neuromuscul Dis 2018;5:215–24.

[28] Morin M, Hébert LJ, Perron M, Petitclerc É, Lake S-R, Duchesne E. Psychometric properties of a standardized protocol of muscle strength assessment by hand-held dynamometry in healthy adults: a reliability study. BMC Musculoskelet Disord 2023;24:294.

[29] Roussel MP, Hebert LJ, Duchesne E. Intra-rater reliability and concurrent validity of quantified muscle testing for maximal knee extensors strength in men with myotonic dystrophy type 1. J Neuromuscul Dis 2019;6:233–40.

[30] Hébert LJ, Maltais DB, Lepage C, Saulnier J, Crête M. Hand-held dynamometry isometric torque reference values for children and adolescents. Pediatric Phys Therapy 2015;27:414–23.

[31] Lucia A, Martinuzzi A, Nogales-Gadea G, Quinlivan R, Reason S, Bali D, et al. Clinical practice guidelines for glycogen storage disease V & VII (McArdle disease and Tarui disease) from an international study group. Neuromuscular Disord 2021; 31:1296–310.

[32] Rodriguez-Lopez C, Santalla A, Valenzuela PL, Real-Martínez A, Villarreal-Salazar M, Rodriguez-Gomez I, et al. Muscle glycogen unavailability and fat oxidation rate during exercise: insights from McArdle disease. J. Physiol. (Lond.) 2023;601:551–66.

[33] Wallace A, Pietrusz A, Dewar E, Dudziec M, Jones K, Hennis P, et al. Community exercise is feasible for neuromuscular diseases and can improve aerobic capacity. Neurology 2019;92:e1773–85.

[34] Oorschot S, Brehm MA, van Groenestijn AC, Koopman FS, Verhamme C, Eftimov F, et al. Efficacy of a physical activity programme combining individualized aerobic exercise and coaching to improve physical fitness in neuromuscular diseases (I'M FINE): study protocol of a randomized controlled trial. BMC Neurol 2020;20:1–10.

[35] Knak KL, Andersen LK, Witting N, Vissing J. Reliability of the 2-and 6-minute walk tests in neuromuscular diseases. J Rehabil Med 2017;49:362–6.

[36] Andersen LK, Knak KL, Witting N, Vissing J. Two-and 6-minute walk tests assess walking capability equally in neuromuscular diseases. Neurology 2016;86:442–5.

[37] Voet N, Pater R, Garmendia J, Sistiaga A, Labayru G, Gallais B, et al. Patient-reported outcome measures in neuromuscular diseases: a scoping review. J Neuromuscul Dis 2024:1–11.

[38] Seedat F, James MK, Rose MR. Activity rating scales in adult muscle disease: what do they actually measure? Muscle Nerve 2014;50:14–23.

[39] Seedat F, James MK, Rose MR. Activity rating scales in adult muscle disease: how well do they actually measure? Muscle Nerve 2014;50:24–33.

[40] Schwartz CE, Andresen EM, Nosek MA, Krahn GL, REPoHS Measurement. Response shift theory: important implications for measuring quality of life in people with disability. Arch Phys Med Rehabil 2007;88:529–36.

[41] Pijpers EJ, Bloemen B, Cup EH, Groothuis JT, Oortwijn WJ, van Engelen BGM, et al. The capability approach in rehabilitation: developing capability care. Disabil Rehabil 2024:1–13.

[42] Andries A, Van Walsem MR, Ørstavik K, Frich JC. Functional ability and physical activity in hereditary neuromuscular diseases. J Neuromuscul Dis 2022;9:437–46.

[43] Bull FC, SS Al-Ansari, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 2020;54:1451–62.

[44] van den Berg LE, Favejee MM, Wens SC, Kruijshaar ME, Praet SFE, Reuser AJJ, et al. Safety and efficacy of exercise training in adults with Pompe disease: evalution of endurance, muscle strength and core stability before and after a 12 week training program. Orphanet J Rare Dis 2015;10:1–8.

[45] Ismailova G, Wagenmakers MA, Brusse E, van der Ploeg AT, Favejee MM, van der Beek NAME, et al. Long-term benefits of physical activity in adult patients with late onset Pompe disease: a retrospective cohort study with 10 years of follow-up. Orphanet J Rare Dis 2023;18:319.

[46] Okkersen K, Jimenez-Moreno C, Wenninger S, Daidj F, Glennon J, Cumming S, et al. Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. Lancet Neurol 2018;17:671–80.

[47] Üstün TB, Chatterji S, Bickenbach J, Kostanjsek N, Schneider M. The international classification of functioning, disability and health: a new tool for understanding disability and health. Disabil Rehabil 2003;25:565–71.

[48] Poulsen NS Kraglund LR, Vissing J. Physical training of wheelchair users with neuromuscular disorders: a systematic review. J Neuromuscul Dis 2025.

[49] Bora G, Subaşı-Yıldız Ş, Yeşbek-Kaymaz A, Bulut N, Alemdaroğlu I, Tunca-Yılmaz Ö, et al. Effects of arm cycling exercise in spinal muscular atrophy type II patients: a pilot study. J. Child Neurol. 2018;33:209–15.

[50] Cumplido-Trasmonte C, Ramos-Rojas J, Delgado-Castillejo E, Garcés-Castellote E, Puyuelo-Quintana G, Destarac-Eguizabal MA, et al. Effects of ATLAS 2030 gait exoskeleton on strength and range of motion in children with spinal muscular atrophy II: a case series. J Neuroeng Rehabil 2022;19:75.

[51] Nozaki S, Kawai M, Shimoyama R, Futamura N, Matsumura T, Adachi K, et al. Range of motion exercise of temporo-mandibular joint with hot pack increases occlusal force in patients with Duchenne muscular dystrophy. Acta Myologica 2010;29:392.

[52] Wanke T, Toifl K, Merkle M, Formanek D, Lahrmann H, Zwick H. Inspiratory muscle training in patients with Duchenne muscular dystrophy. Chest 1994;105: 475–82.

[53] Gozal D, Thiriet P. Respiratory muscle training in neuromuscular disease: long-term effects on strength and load perception. Med Sci Sports Exerc 1999;31: 1522–7.

[54] Voet NB. Exercise in neuromuscular disorders: a promising intervention. Acta Myologica 2019;38:207.

[55] Antonovsky A. The salutogenic model as a theory to guide health promotion. Health Promot Int 1996;11:11–8.

[56] Voorn EL, Koopman FS, Nollet F, Brehm M-A. Individualized aerobic exercise in neuromuscular diseases: a pilot study on the feasibility and preliminary effectiveness to improve physical fitness. Phys Ther 2021;101:pzaa213.

[57] Andersen G, Heje K, Buch AE, Vissing J. High-intensity interval training in facioscapulohumeral muscular dystrophy type 1: a randomized clinical trial. J. Neurol. 2017;264:1099–106.