

# Management of motor rehabilitation in individuals with muscular dystrophies. 1<sup>st</sup> Consensus Conference report from UILDM - Italian Muscular Dystrophy Association (Rome, January 25-26, 2019)

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Received: May 10, 2021  
Accepted: June 9, 2021

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**How to cite this article:** Lombardo ME, Carraro E, Sancricca C, et al. Management of motor rehabilitation in individuals with muscular dystrophies. 1<sup>st</sup> Consensus Conference report from UILDM - Italian Muscular Dystrophy Association (Rome, January 25-26, 2019). Acta Myol 2021;40:72-87. <https://doi.org/10.36185/2532-1900-046>

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**Muscular dystrophy (MD) is a group of neuromuscular diseases characterized by progressive muscle weakness due to various mutations in several genes involved in muscle structure and function. The age at onset, evolution and severity of the different forms of MD can vary and there is often impairment of motor function and activities of daily living. Although there have been important scientific advances with regard to pharmacological therapies for many forms of MD, rehabilitation management remains central to ensuring the patient's psychophysical well-being. Here we report the results of an Italian consensus conference promoted by UILDM (Unione Italiana Lotta alla Distrofia Muscolare, the Italian Muscular**

**Dystrophy Association) in order to establish general indications and agreed protocols for motor rehabilitation of the different forms of MD.**

**Key words:** muscular dystrophy, rehabilitation, exercise

## Introduction

Muscular dystrophy (MD) is a collective term referring to a group of inherited neuromuscular diseases characterized by progressive muscle weakness due to various mutations in several genes involved in muscle structure and function.

Although the age at onset, evolution, and severity of the disease can vary, several features are common to all the forms of MD, namely progressive weakness, often accompanied by muscle contractures, spinal deformity, and an increased risk of bone fragility and fractures. Most of these conditions are associated with cardiac and respiratory involvement, and different forms of intellectual disability can also be present in some of them. For this reason, MD requires multidisciplinary management<sup>1,2</sup>.

Even though recent years have seen considerable progress in the molecular characterization and diagnosis of MD, no effective treatment is yet available for the majority of forms, and general management and rehabilitation continue to have a key role in maintaining an acceptable functional status in affected patients.

The multidisciplinary management of MD should be aimed at preserving motor function, preventing secondary complications, promoting overall health, and improving patients' autonomy and quality of life (QoL).

With regard to the aim of preserving motor function, physical exercise and management of contractures are two areas that deserve careful consideration.

The role of physical exercise in MD is still highly controversial. Some argue that it should be considered potentially harmful due to the poor regenerative ability of muscle in MD, and the possibility of wasting due to overwork in response to external stimuli/stresses<sup>3-5</sup>. On this basis, physical exercise has traditionally been discouraged in MD. On the other hand, the beneficial effects of physical activity per se could potentially help to maintain function and prevent non-use atrophy in MD patients<sup>6-11</sup>. Since it remains unclear how best to balance the drawbacks and benefits of physical exercise, we believe that there is now a fundamental need for more precise indications, based on the F.I.T.T. (frequency, intensity, time and type) model of physical exercise, in order to ensure optimal management of these patients.

Very recently, a paper was published describing a multidisciplinary rehabilitation approach involving phys-

ical activity and therapeutic exercise in late-onset Pompe disease, a severe metabolic myopathy for infant forms, while late onset cases span from asymptomatic (high CK) to relatively severe cases with respiratory insufficiency. The authors proposed operational protocols based on physical activity and on therapeutic exercise and respiratory rehabilitation<sup>12</sup>.

Joint contractures and/or deformities are frequent in several forms of MD; they are a consequence of muscle degeneration, muscle fibrosis, and reduced mobility, which together cause significant muscle imbalance. Careful management of rehabilitation interventions specifically aimed at preventing contractures is fundamental to maintaining motor function and preserving patient autonomy<sup>13</sup>.

To date, internationally validated guidelines on rehabilitation are available only for Duchenne muscular dystrophy (DMD), and it is unclear whether they can be applied to other forms of MD<sup>14,15</sup>.

In view of the afore-mentioned considerations, we performed a systematic and comprehensive analysis of the biomedical literature related to neuromuscular rehabilitation in MD with the aim of drawing up a consensus document on recommendations for clinical practice. This document was commissioned by UILDM (Unione Italiana Lotta alla Distrofia Muscolare, the Italian Muscular Dystrophy Association), which represents and supports patients suffering from neuromuscular diseases.

## Methods

The purpose of this study was to obtain consensus statements from an expert panel (the 'Jury'), after presentation and discussion of relevant literature data.

We used the consensus conference methodology, which is an excellent means of reaching conclusions and formulating crucial statements in the field of health care. It is recommended for addressing clinical issues on which available good quality evidence is limited<sup>16,17</sup>.

The consensus conference was carried out according to the US National Institutes of Health Consensus Development Program and the Methodological Handbook of the Italian National Guideline System<sup>18,19</sup>. The project was coordinated by a scientific board (the "Board") made up of nine experts: multidisciplinary clinicians (3 neurologists, 2 child neurologists, 2 physiatrists, 1 physiotherapist) plus a supervisor specialized in consensus conference methodology. In the first step, the Board generated research questions in accordance with the P.I.C.O. (i.e., Population, Intervention, Comparison, Outcome) model, used in the field of evidence-based medicine<sup>20</sup>. Nine topics were covered, in order to provide recommendations on the most important aspects of motor rehabilitation:

**Topic 1:** Outcome measures;

**Topic 2:** The rehabilitation project/program: objectives and management, based on the International Classification of Functioning, Disability and Health (ICF);

**Topic 3:** Body function – focusing on “Functions of the joints and bones” (ICF codes b710-b729): contracture management;

**Topic 4:** Body function – focusing on “Muscle functions” and “Movement functions” (b730-b789): physical exercise;

**Topic 5:** Activities and participation – focusing on “Mobility” (d4): posture and mobility management;

**Topic 6:** Activities and participation – focusing on “Self-care” (d5) and “Major life areas” (d8): activities of daily living (ADL);

**Topic 7:** Definition of the professional figures involved in the rehabilitation project/program;

**Topic 8:** The rehabilitation setting: outpatient vs home therapy;

**Topic 9:** Duration/frequency.

In step 2, the Board reviewed the specific literature, consulting several databases (i.e., EMBASE, CINAHL, PubMed, PsychINFO and Scopus). According to their area of expertise, the Board members worked in 3 groups:

- Group 1: two child neurologists and 1 physiotherapist. This group focused on pediatric-onset forms of MD: DMD/Becker muscular dystrophy, congenital muscular dystrophy, and early-onset limb-girdle muscular dystrophy (LGMD);
- Group 2: three adult neurologists and 1 physiotherapist. This group focused on adult forms of MD: Becker muscular dystrophy, LGMD, facioscapulohumeral muscular dystrophy (FSHD), myotonic dystrophy type 1;
- Group 3: two psychiatrists and 1 physiotherapist. This group focused on the concept and content of rehabilitation projects versus programs.

The literature review was performed using the following keywords: type of MD (e.g., “Duchenne muscular dystrophy”), “exercise” and “rehabilitation”.

Reviews and studies in English, Italian, French, or Spanish, of any design, and published in peer-reviewed journals in the period January 1984 - December 2018, were included on the basis of their relevance to the topic. Literature published only in abstract form was excluded.

The third step was the formation of the expert panel (the Jury) composed of 23 experts in MD/stakeholders (representatives of the MD community). This panel comprised clinicians, researchers, and members of patients’ associations. The results of the literature review were presented to the Jury and discussed among its members at the “1<sup>st</sup> UILDM Consensus Conference on neuromuscular rehabilitation in pediatric and adult MD”, held in

Rome on January 25-26, 2019. The evidence collected during the literature review and the recommendations proposed by the Board, were addressed through constructive debate involving all the participants, to ensure that all the experts/stakeholders had an active role in the consensus-reaching process.

A specific survey questionnaire was then administered to all 23 Jury members, and, under the supervision of the Board, their level of consensus on each of the proposed questions was determined, as follows:

- unanimous consensus: positive opinions expressed by 100% of the Jury members;
- majority consensus: positive opinions expressed by > 60%;
- consensus to be redefined: positive opinions expressed by between 41 and 59%;
- consensus not reached: positive opinions expressed by < 40%.

This led to the drafting of a document that was shared among all the participants for final approval. The approved draft document constitutes the basis of this paper: it extensively describes the discussion and the level of consensus reached by the panel on the above 9 questions, which apply to all forms of MD. Table I sets out specific indications for the different forms.

## Consensus document

### *TOPIC 1: outcome measures*

#### Discussion

Many difficulties surround the definition of, and the terminology used in, standardized outcome measures in the field of MD. There are several reasons for this, the most important being the still incomplete knowledge of the natural history of the different forms which, in turn, is due to their significant clinical heterogeneity.

Because of the low prevalence of these diseases, there are still few randomized clinical trials dealing with rehabilitation in patients with MD, and those that do exist present several methodological limitations. The studies are heterogeneous, in terms of both the populations selected and the rehabilitation programs followed. They often lack control groups or have a non-blinded study design; and precise endpoints, biomarkers, and clearly defined outcome measures are often lacking, too. Thus far, DMD is the only form in which these issues have been extensively addressed through validated international guidelines and standards of care, focusing on outcome measures, general management, secondary complications, and rehabilitation treatment<sup>15,16</sup>. The most standardized outcome measures used to monitor motor function in DMD include the North

**Table I.** Specific recommendations for different types of muscular dystrophy.

<p>Duchenne muscular dystrophy (DMD) <i>Standard of care</i><sup>14,15</sup>:</p>	<p><b>Contracture management</b> Stretching/orthoses based on the natural history and stage of the disease (see standard of care for details)  <ul style="list-style-type: none"> <li>• Recommended frequency of stretching: at least 4 to 6 times a week, on the basis of personalized evaluation</li> </ul> </p> <p><b>Physical exercise</b>  <ul style="list-style-type: none"> <li>• Feasibility and safety of low-intensity endurance training with assisted cycle training, during ambulatory or late-ambulatory and wheelchair-dependent phases</li> <li>• Personalized protocols with regular, gentle aerobic exercise (like aquatics or cycling), especially in early stages of the disease</li> <li>• Spontaneous non-structured daily activity (e.g., play)</li> <li>• Need for specific cardiological evaluation.</li> </ul> </p> <p><b>Other issues</b>  <ul style="list-style-type: none"> <li>• Cognitive, nutritional and psychosocial evaluation, speech therapy, and cardiac and respiratory management are fundamental for these patients (see standard of care)</li> <li>• Always keep in mind pain management and promotion of ADL participation, use of assistive technology, and customized powered wheelchairs</li> </ul> </p>
<p>Congenital MUSCULAR Dystrophies <i>Guidelines</i><sup>33,54,77</sup>:</p>	<p><b>Contracture management</b> Joint contractures: typical in both the lower and the upper limbs, often accompanied by foot and spinal deformities, hip dislocation, and joint hypermobility. Early intervention with stretching, orthoses, standing, and assistive equipment is fundamental.  <ul style="list-style-type: none"> <li>• LMNA, LMNA2, and COL6: early and adequate posture of feet and neck is of supreme importance for prevention of foot deformities and hyperextension of the neck</li> <li>• Emery Dreifuss muscular dystrophy (EDMD): pay specific attention to early severe elbow contractures, also in ambulant patients</li> </ul> </p> <p><b>Physical exercise</b>  <ul style="list-style-type: none"> <li>• There are no specific conclusive data on the possible beneficial or detrimental effects of muscle exercise</li> <li>• Hydrokinesitherapy to preserve range of motion and prevent edema and swelling of extremities is recommended</li> </ul> </p> <p><b>Other issues</b>  <ul style="list-style-type: none"> <li>• Pain management and promotion of ADL participation, use of assistive technology and customized powered wheelchairs</li> </ul> </p>
<p>Limb-Girdle muscular dystrophy (LGMD) <i>Guidelines</i><sup>30,31</sup>:</p>	<p><b>Contracture management</b> Periodic assessment to define personalized contracture program and mobility support</p> <p><b>Physical exercise</b>  <ul style="list-style-type: none"> <li>• Strength training and aerobic exercise training are both safe and potentially beneficial: recommendation for combined supervised programs</li> <li>• Low-impact aerobic exercise (swimming, stationary cycling) improves cardiovascular performance and muscle efficiency and reduces fatigue</li> <li>• Need to monitor the risk of damage due to supramaximal high-intensity exercise. This is very important in LGMD (in childhood, eccentric sport activities for LGMD 2B can exacerbate muscle damage progression)<sup>78</sup></li> <li>• Need for specific cardiological evaluation (bear in mind the potential positive effect of aerobic training for cardiovascular function and metabolic issues)</li> </ul> </p>
<p>Becker muscular dystrophy (BMD)</p>	<p><b>Contracture management</b> There are no specific data concerning the management of joint contractures (see general recommendations)</p> <p><b>Physical exercise</b>  <ul style="list-style-type: none"> <li>• Endurance training is safe (also in the presence of significant cardiomyopathy) and can increase performance and daily function<sup>79</sup>.</li> <li>• Aerobic/resistance training (studies including LGMD/BMD patients): both low- and high-intensity resistance training showed positive effects on muscle strength and endurance and were well tolerated<sup>80-82</sup>.</li> <li>• Need to monitor the risk of damage due to supramaximal high-intensity exercise. This is very important in BMD, particularly in more severely affected patients</li> <li>• Need for specific cardiological evaluation (bear in mind the potential positive effect of aerobic training for cardiovascular function and metabolic issues)</li> </ul> </p>

**Table I.** Specific recommendations for different types of muscular dystrophy.

<p>Myotonic dystrophy <i>Guidelines</i><sup>61</sup>:</p>	<p><b>Contracture management</b> There are no specific data concerning the management of joint contractures (see general recommendations)</p> <p><b>Physical exercise</b></p> <ul style="list-style-type: none"> <li>• Moderate physical exercise should be strongly encouraged since it does not worsen the disease progression and can minimize the disuse weakness<sup>64</sup></li> <li>• Always consider the patient's basal activity level: sedentary patients may benefit from a physical exercise program, while further activity may be fatiguing for individuals with an active lifestyle</li> <li>• Equipment such as elastic bands, free weights, and machines can, very carefully, be included in the program, as can certain types of exercise, like yoga and pilates</li> <li>• To be performed at least 3 times a week</li> <li>• Low-moderate aerobic training is highly recommended after appropriate cardiological assessment<sup>63</sup>. Definition: <i>moderate exercises are defined as activities that you can perform while still continuing a conversation – without having to stop to catch your breath</i></li> <li>• Frequency: 2 hours and 30 minutes per week of moderate-intensity exercise, in sessions of at least 10 minutes spread throughout the week</li> <li>• Examples include: walking briskly, cycling on level ground or on a stationary bicycle, ballroom and line dancing, general gardening, household activities, canoeing, using a manual wheelchair, and water aerobics</li> </ul> <p><b>Other issues</b></p> <ul style="list-style-type: none"> <li>• Balance training/reduction of falls rate/foot drop management: very important to consider, due to the specific weakness distribution and balance impairment in these patients (concomitant neuropathy, proprioceptive deficits, etc.). Also consider use of AFOs when appropriate</li> <li>• Cognitive behavior management, nutritional therapy, speech therapy, and occupational therapy: it is fundamental to include these in the neuro-rehabilitation program (OPTIMISTIC trial)<sup>84</sup></li> </ul>
<p>Facioscapulohumeral muscular dystrophy (FSHD) <i>Tawil 2010</i><sup>27</sup> <i>Tawil 2015</i><sup>28</sup></p>	<p><b>Contracture management</b> There are no specific data concerning the management of joint contractures (see general recommendations).</p> <p><b>Physical exercise</b></p> <ul style="list-style-type: none"> <li>• Low-intensity aerobic exercise: safe and potentially beneficial, always target exercise on the basis of weakness distribution (to avoid falls or over-use damage)</li> <li>• Strength training: its role is controversial. Propose safe and personalized programs using appropriate low/medium weights/resistance and taking into consideration the patient's physical limitations</li> </ul> <p><b>Other issues</b></p> <ul style="list-style-type: none"> <li>• Balance training/reduction of falls rate/foot drop management: very important to consider, due to the specific weakness distribution and balance impairment in these patients (concomitant neuropathy, proprioceptive deficits etc.). Also consider the use of AFOs when appropriate</li> <li>• Surgical scapular fixation for periscapular muscle weakness: this should be considered for selected patients after careful evaluation of: potential gain in range of motion, patient's rate of disease progression, possible adverse consequences of surgery, and prolonged postsurgical bracing</li> </ul>

Star Ambulatory Assessment, the timed function tests, the 6-Minute Walking Test (6MWT), and the Performance of the Upper Limb tool<sup>21-26</sup>. For other neuromuscular diseases, expert networks have been created in order to seek to develop reliable and valid outcome measures<sup>27-34</sup>. In clinical practice, the 6MWT and the Performance of the Upper Limb tool<sup>21-26</sup> can be used in MD, as can other specific outcome measures, such as the Egen Klassifikation Scale

Version 2<sup>35</sup>, the Motor Function Measurement scale, and the GSGC (Gait, Stairs, Gower, Chair), as confirmed by recent validation studies<sup>36-38</sup>.

**Panel consensus**

The Jury recognizes and accepts the published standardized outcome measures for DMD, which should be performed periodically in order to monitor clinical pro-

gression of the disease and the progress of the rehabilitation program. All the members confirm the need for better definition of outcome measures for other forms of MD, in order to achieve validation of tools already proposed, or the creation of new quantitative ones. *Unanimous consensus.*

*TOPIC 2: The Rehabilitation Project/Program: objectives and management based on the International Classification of Functioning, Disability and Health (Icf)*

### Discussion

It is widely recognized that rehabilitation should focus on patient functional status and on improvement of well-being, and not simply on the specific disease in question.

The ICF is an internationally approved classification system that aims to ‘provide a unified and standard language and framework for the description of health and health-related states’<sup>39</sup>. It describes all aspects of disability (i.e., ‘impairments, activity limitations or participation restrictions’), together with possible contextual factors (environmental and personal)<sup>41</sup>. A recent study recommended using the ICF in rehabilitation studies<sup>42</sup>. To our knowledge, there are only 7 published studies in which the ICF was used to explore neuromuscular diseases<sup>42-49</sup>. While none of these considered use of the ICF in rehabilitation planning, a single study, applying a qualitative method, examined the content validity of the ICF Core Set as a basis for enhancing overall care in patients with neuromuscular diseases<sup>49</sup>.

In the rehabilitation process, it is necessary to distinguish between the *project*, which aims to achieve the expected level of long-term functioning in a given patient, and the *program*, which identifies and sets out the short-term goals, the methodology to be used to reach them, the timing, and the milestones along the way<sup>50</sup>.

### Panel consensus

The Jury unanimously supports the need to define rehabilitation projects/programs on the basis of the ICF.

The main objectives of the motor rehabilitation plan should refer, in particular, to the following ICF categories:

#### 1. Body Functions (b):

*Neuromusculoskeletal and movement-related functions (b7):* Mobility of joint functions (b710), Muscle power functions (b730), Muscle endurance functions (b740) and Gait pattern functions (b770);

*Functions of the cardiovascular, hematological, immunological and respiratory systems (b4):* Exercise tolerance functions (b455);

*Sensory functions and pain (b2):* Pain (b280).

#### 2. Activities and Participation (d):

d. *Mobility (d4);*

e. *Self-care (d5);*

f. *Major life areas (d8).*

#### 3. Environmental Factors (e):

*Products and technology (e1)* for personal use in daily living (e115) and for personal indoor and outdoor mobility and transportation (e120). *Unanimous consensus.*

*TOPIC 3: Body function – focusing on “functions of the joints and bones” (b710-b729): contracture management*

### Discussion

The term “contractures” denotes lack of full passive range of motion due to joint, muscle, or soft tissue limitations. Although joint contractures may in some cases have a compensatory function, their progression over time has a significant negative impact on motor function and autonomy, leading to fixed deformities and pain. The pathogenesis involves various factors, both intrinsic (muscle structural changes and fibrosis) and extrinsic (reduced active joint mobilization due to muscle weakness associated with a static position, compensatory postures, and agonist-antagonist muscle imbalance)<sup>13</sup>. It is important to consider the main clinical characteristics of the different forms of MD in order to identify joint groups and muscles at greater risk of tightness. Knowledge of specific natural histories is fundamental to identifying the progression phases and providing specific need-based preventive and personalized interventions (Tab. I). The degree of muscle pathology progression is related to the frequency and severity of contractures. Lower limb contractures appear earlier and are more frequent, while upper limb contractures usually develop later, when ambulation is lost.

Although contractures are unavoidable in some cases, a preventive rehabilitation intervention, even for mild contractures, is important to minimize their negative effects on global function. For the lower limbs, careful stretching of muscles and joints (each position should be held for at least 15 seconds, and this should be repeated 10 to 15 times during a session) and daily standing or walking (a minimum of 2 to 3 hours) are recommended; so too, if necessary, are splinting and the use of orthoses to promote body segment alignment and proper posture<sup>13</sup>. For upper limb contractures, careful stretching is mandatory to maintain distal functions such as wheelchair driving.

In DMD, recent updated standards of care guidelines define the rehabilitation management of contractures on the basis of the natural history and stage of the disorder<sup>14,15</sup>. Muscle and joint groups at risk of tightness are

well documented<sup>15</sup>. Lower limb contractures should be managed early starting from the ambulation stages, and continued into adulthood. Upper limb contractures should be monitored mainly from the stages of loss of ambulation. All interventions must be coordinated throughout all the stages of the disease. Stretching is recommended at least 4 to 6 times a week. Night-time use of resting and stretching ankle-foot orthoses (AFOs) is recommended from the early stages of ambulation, also to improve their tolerability. Daytime use of AFOs is indicated in the stages of loss of ambulation, to ensure adequate foot position in a wheelchair, or even in the ambulation stages (during “non-loading” time) in cases where they are not tolerated at night. Knee-ankle-foot orthoses (KAFOs) have a rehabilitation and non-functional purpose. They are indicated when contractures are mild or absent, and when the trunk still has good residual strength, in the late ambulation and early non-ambulation stages, in order to maintain standing and correct lower limb alignment. It has been reported that using KAFOs may extend walking ability in DMD by between 2 and 4 years. Standing can also be promoted through the use of standing devices, which are safer than KAFOs, reducing the risk of falls. Finally, serial casting is indicated in DMD when ankle-foot contractures are not manageable by means of stretching and orthoses, but surgery is not yet indicated<sup>51,52</sup>. As regards other childhood and adult forms of MD, there is a lack of outcome measures, well defined natural history and recommendations on the management of contractures. Table I highlights the principal issues in this regard.

Another frequent orthopedic complication in MD is scoliosis, which frequently develops in patients with childhood-onset forms (such as congenital ones) in whom the skeletal apparatus is still growing and therefore much more susceptible to deforming forces<sup>53</sup>. The development of scoliosis is a frequent complication of the late or non-ambulatory stages of DMD; bracing should be considered in order to maintain midline support and encourage symmetrical spinal alignment, so as to prevent or minimize the development/progression of scoliosis<sup>15,54</sup>. From the neuromotor development perspective, it is important to define which function or activity to promote, always bearing in mind the presence of the brace (e.g., manipulation activities are easier in the sitting position).

In severe scoliosis, surgical intervention may be recommended; candidates for surgical intervention are non-ambulatory individuals with DMD who have a spinal curve greater than 20-30° in the sitting position, have not yet reached puberty, and have not been treated with corticosteroids because the curve is expected to progress<sup>55</sup>.

In other forms of MD, other spinal abnormalities can be present, such as bent spine syndrome, rigid spine, or hyperlordosis, as seen in LGMD<sup>56</sup>; plaster casts or brac-

es could be useful to support an antigravity posture but their use should be considered in relation to the specific patient’s activities and motor performances. Moreover, it is very important to use adequate customized postural supports that ensure body alignment and counteract abnormal positions, especially when the patient spends a lot of time in a wheelchair.

### Panel consensus

Although joint contracture management is not extensively described for all forms of MD, the Jury agrees that it is crucial to maintain the patient’s motor function. A coordinated and integrated intervention, consisting of passive or active assisted stretching, and the use of orthoses, standing devices, and customized seating solutions is strongly recommended for all forms of MD. The intervention must be preventive, preferably starting before the development of contractures, and it should target the muscles and joints at greatest risk of tightness, on the basis of the natural history and stage of the single disorder (Tab. I).

As previously mentioned, the best characterized form of MD is DMD; in other forms, in the absence of natural history data, the Jury suggests that joint function should be managed with reference to the DMD classification, on the basis of the single patient’s functional stage<sup>15</sup>.

In consideration of the above, the Jury reached the following consensus on statements:

- The main objective of the rehabilitation project/program (with regard to b710: Mobility of joint functions):
  - to prevent and counteract the progression of contractures, retractions and deformities. *Unanimous consensus.*
- Terminology:
  - Stretching can be active (involving specific muscle contraction with elongation of a joint, performed by the patient as indicated by the therapist) or passive/“manual” (performed manually by therapist or the caregiver, without muscle contraction by the patient). *Unanimous consensus;*
  - Stretching can be “self-managed” (performed, after adequate training, by the patient or by the caregiver) or “rehabilitative” (performed by the therapist). *Unanimous consensus.*
- Frequency and duration:
  - Both in ambulant and in non-ambulant patients, stretching (self-managed and rehabilitative) of muscles and structures at risk of tightness in the different forms of MD should be performed not less than 4 to 6 times a week. If only self-managed stretching is performed, supervision by the therapist once a month is required. *Unanimous consensus;*

- In non-ambulant patients, stretching (self-managed and rehabilitative) should be performed only for mild contractures (e.g., joint tightness with preserved range of motion) or medium contractures (e.g., joint tightness with impaired range of motion). It should not be performed in the case of fixed contractures (such as in severe deformities). *Unanimous consensus*;
- The use of orthoses can be integrated with, but cannot substitute, stretching. *Unanimous consensus*.

#### TOPIC 4: BODY function – targeting “muscle functions” and “movement functions”

##### Discussion

The most controversial issue when considering exercise training in MD is the potential for exacerbation of the muscle damage as a consequence of the exercise itself<sup>3,57</sup>. This phenomenon has various possible underlying causes. For example, it may be a direct effect of the exercise (especially eccentric high-resistance exercise) on muscle fibers, or due to various metabolic mechanisms (hypoxic/ischemic, adenosine triphosphate (ATP) deficit, oxidative stress, nitric oxide (NO) pathway impairment)<sup>58</sup>.

On the other hand, muscle weakness can also be a consequence of disuse, muscular atrophy, and deconditioning due to a sedentary lifestyle. In the healthy population, physical activity exerts several benefits, such as protection from obesity, metabolic syndrome, coronary heart disease, hypertension, and (at least in part) osteoporosis, and improvement of psychological and general well-being<sup>11,59</sup>.

The panel discussed training and physical activity in MD, considering the World Health Organization’s standard definition of different types of exercise, according to which moderate-intensity aerobic activity is a physical activity that is performed at between 3 and < 6 times the intensity of rest, and is therefore relative to an individual’s personal capacity<sup>60</sup>. In a consensus on care recommendations for physical therapy in DM1, “moderate exercises” are defined as activities that the individual can perform while still continuing a conversation and without having to stop to catch his/her breath<sup>61</sup>. With regard to muscle-strengthening activity (defined as exercise that increases skeletal muscle strength, power, endurance, and mass; e.g., strength training, resistance training, and muscle strength and endurance exercises), an updated Cochrane review examined clinical trials focusing on the effects of strength and aerobic exercise training in muscle diseases<sup>62</sup>. Among the studies considered, only five were randomized and met all the criteria for inclusion in the review. Two of these dealt with DM1 and one with

FSHD<sup>63-65</sup>. The authors concluded that moderate-intensity strength training and aerobic exercise training appear to do no harm since no signs of overuse were reported, and that normal participation in sports and daily activities appeared to be safe.

For other forms of MD (LGMG, Becker muscular dystrophy, etc.), the available studies are few in number, and moreover report different protocols and heterogeneous results (see Table I). However, knowledge of specific natural histories is always fundamental before suggesting physical exercise, given the need to avoid possible harmful effects (in terms of disease progression) of strength training.

Besides classical muscle exercise, neuromuscular electrical stimulation (NMES) is widely used in rehabilitation, offering the advantage of producing activation of fast fibers. However, data regarding the possible application of NMES in MD are still controversial due to the potential harmful effects of excessive muscle stimulation<sup>66-69</sup>.

##### Panel consensus

The Jury reached the following consensus statements:

- The main objectives of a rehabilitation project/program (with regard to b730: Muscle power functions, b740: Muscle endurance functions, b770: Gait pattern functions; b455: Exercise tolerance functions) are:
  - to prevent no-use atrophy;
  - to maintain and optimize residual muscle strength;
  - to minimize progression of weakness when possible;
  - to support and optimize cardiorespiratory function;
  - to optimize exercise tolerance, energy efficiency, and energy conservation;
  - to contain stasis edema. *Unanimous consensus*.
- Terminology:
  - Physical activity: this includes “spontaneous non-structured activity” (i.e., normal activity during daily life), sports and “structured activity” (i.e., therapeutic exercise). *Unanimous consensus*.
  - Therapeutic exercise, prescribed by a specialist, should be defined by the following components: frequency, intensity, time, and type (F.I.T.T.). *Unanimous consensus*.
  - Both non-structured and structured activities and sports can include the two main exercise types: aerobic/cardiovascular fitness training (designed to improve cardiorespiratory endurance) and strength/resistance training (performed to im-



prove muscle strength and endurance). The latter can consist of concentric (shortening), isometric or eccentric (lengthening) contractions. *Unanimous consensus.*

- The term “muscle activation” should be used in rehabilitation programs rather than “muscle strengthening” or “strength training” or “resistance training”, to underline the importance of avoiding excessive loading (overload work) of dystrophic muscle. *Unanimous consensus.*
- General recommendations:
  - Spontaneous non-structured physical activity (ADL, free play) should always be encouraged. *Unanimous consensus.*
  - Sports activities:
    - Avoid contact sports, and competitive and non-competitive sports involving mainly eccentric exercise/activities. *Unanimous consensus.*
    - Competitive sports without specific eccentric exercise can be considered, exceptionally, in selected situations after critical clinician evaluation. *Majority consensus.*
    - Sports activities should always be readily accepted by the patients; swimming/water sports and low-resistance cycling are particularly recommended, while regular football training and tennis should be avoided. Wheelchair hockey and use of new technologies (e.g., Wii) are also encouraged. *Unanimous consensus.*
- Therapeutic exercise:
  - Eccentric exercise must be avoided, whereas concentric sub-maximal resistance exercises (“muscle activation”) and moderate aerobic training are recommended. Balance training should be included when deemed indicated and as prescribed by the clinician and rehabilitation team (patients can be evaluated by means of specific functional balance scales, such as the Berg Balance Test, gait analysis, and by recording the number of falls, which can indicate a balance impairment). *Unanimous consensus.*
  - Mean frequency: at least 3 times a week, for at least 30 minutes per session. *Unanimous consensus.*
  - Always consider patient-specific conditions, including compliance and any relational issues, and avoid unnecessary clinical interventions<sup>70</sup>, which could have a negative impact on ADL. *Unanimous consensus.*
  - The 6MWT can be used as an outcome measure for endurance. Conversely, no reliable and feasible outcome measure for aerobic training is

available at present, and more focused investigation is needed to fill this gap. *Unanimous consensus.*

- Postural hygiene and lymphatic drainage techniques including massage and compression garments should be promoted whenever these are deemed indicated by clinical experts. *Unanimous consensus.*
- Personalization and monitoring:
  - The patient’s status (including disease genotype, concomitant diseases, severity of weakness, pre-training level of activity – sedentary versus active) must always be carefully evaluated by the multidisciplinary team before a rehabilitation project/program or sports activities are prescribed. Outcome measures of muscle function (e.g., strength, endurance) and aerobic capacity (e.g., work capacity), and functional assessments are necessary. This evaluation must also include cardiological and respiratory assessment. *Unanimous consensus.*
  - Clinicians, patients and caregivers should bear in mind the possible risk of overwork weakness, and should be extensively warned about and trained to promptly recognize the following red flags:
    - significant muscle pain/soreness/cramps during or after exercise, or myoglobinuria in the 24 hours following a specific activity;
    - significant and prolonged weakness/fatigue after exercise (compared with basal condition);
    - significant (as per clinical judgment) elevation of CK compared with the patient’s basal CK level. N.B. The panel agreed that no specific or absolute cut-off values of CK can be established as a basis for clinical management decisions, given that this parameter is highly variable (being influenced by the specific form of MD, its phase, the severity of the disease, etc.). With regard to this parameter, the judgment of the physician in charge of the patient remains mandatory. *Unanimous consensus*

#### TOPIC 5: Activities and participation – focusing on mobility (d4): posture and mobility management

#### Discussion

Few studies have specifically explored the management of gait, balance, and manual abilities in MD. Øygaard and co-authors demonstrated some improvements in gait spatiotemporal parameters after Bobath sessions in pa-

tients with LGMD and FSHD<sup>71</sup>. Targeted exercises (focusing for example on ankle dorsiflexion, hand/finger movements, the diaphragm), balance training (to prevent falls), and aquatic therapy could be particularly appropriate especially in certain forms of MD<sup>59</sup>.

Supported ambulation involving the use of assistive devices of different types (such as body-weight-supported treadmill, robotic-assisted training with exoskeleton) is anecdotally reported in MD patients, but these systems need further investigation<sup>72,73</sup>.

The most updated Cochrane review on foot drop management evaluated possible therapeutic approaches that included ‘wait and see’ (i.e., no intervention), physiotherapy, surgery, and drug treatment<sup>74</sup>. It was concluded that targeted strength training shows no positive effects in the treatment of foot drop in myotonic dystrophy and FSHD patients, and that early lower limb surgery in DMD children lacks consensus and remains controversial.

Loss of ambulation is a frequent complication in MD and, due to the significant variability of the different forms, can occur at different ages and be associated with different degrees of general motor disability. In these cases, products and technologies codified in the Environmental Factors chapter of the ICF (e.g., [e115] “Products and technology for personal use in daily living” – [e120] “Products and technology for personal indoor and outdoor mobility and transportation”) are very important to support mobility. The choice of a personalized manual or electric powered, indoor/outdoor wheelchair is fundamental and related not only to mobility factors, but also to the single patient’s expectations in terms of community participation at different stages of his/her life.

The guidelines for LGMD recommend the “prescription of assistive devices that are adapted specifically for the patient’s deficiencies”; in the same way, standards of care for DMD underline the importance of assistive technology and manual/powered wheelchairs as part of the rehabilitation management of these patients<sup>14,15,30,31</sup>.

The Consensus Statement on Standard of Care for Congenital Muscular Dystrophies highlighted the importance of appropriate wheelchair prescription and customization, according to the child’s needs and level of disability<sup>53</sup>. Standing and ambulation should be encouraged if deemed achievable on the basis of the individual child’s assessment.

The benefits of powered mobility are universally recognized, and consist of greater independence, increased QoL, and potential savings in social costs. Indeed, powered wheelchairs are no longer seen as simple mobility aids but as facilitators of participation and occupation. Additionally, they have direct therapeutic effects: powered wheelchairs are fundamental in optimizing medical management of patients with chronic disabilities, and

they are equally important for minimizing discomfort and postural abnormalities<sup>75</sup>. In the late stages of DMD, patients lose postural control, and need to use personalized adaptive seats, even in addition to wearing a brace<sup>76</sup>. When the use of a brace is no longer feasible or tolerable, the half-reclining position, facilitated by the use of a chair with an anatomically adjustable back or with a padded seating shell, remains the only possible solution<sup>54</sup>. In these stages, the major clinical issues are orthopedic complications, including fractures and (kypho)scoliosis, cardiopulmonary involvement, and pain. At this point, powered wheelchairs offer major therapeutic benefits, particularly in the management of pain and for pressure relief.

Tilt-in-space systems are necessary to reduce pain and prevent bedsores, always bearing in mind the degree of spinal deformities, and should be considered even before the loss of independent pressure relief<sup>76</sup>.

In patients with respiratory involvement, the wheelchair often requires specific adjustments to accommodate ventilatory equipment. For self-feeding, anterior trunk support and an elevated support for leverage to enable propping and leaning forward can also be necessary. To facilitate toileting routines, the use of a semi-reclining wheelchair can be helpful.

### Panel consensus

In consideration of the above, the Jury reached the following consensus statements:

- The main objective of the rehabilitation project/program (with regard to d4: Mobility) is:
  - to maintain and optimize movement skills, manual skills, and postural changes and transfers. *Unanimous consensus.*
- General recommendations:
  - Functional orthoses should be considered to improve mobility and autonomy. *Unanimous consensus.*
  - Training for walking safety, including balance exercises, is suggested for as long as is possible; training for safe postural changes and transfers is essential. *Unanimous consensus.*
  - Appropriate manual or powered electric wheelchair prescription and customization is essential. *Unanimous consensus.*

*TOPIC 6: Activities and participation – focusing on “self-care” (d5) and “major life areas” (d8): activities of daily living (adl)*

### Discussion

Improvement of QoL is one of the main targets in MD due to the progressive nature of these diseases<sup>77</sup>.

ADL and function should be regularly assessed, so as to be able to increase the patient's independence and safety through the use of transfer aids and adaptive equipment<sup>53</sup>.

Assistive devices, including ones incorporating robotic technologies, can play a significant role in increasing the daily-life autonomy of individuals with disability, but there are no specific studies on their use in MD patients.

Assessing cognitive and psychosocial aspects in relation to patient autonomy is also important as some forms of MD are also characterized by cognitive impairment, which further impacts on ADL management. Dany and colleagues, after investigating QoL in people with slowly-progressive neuromuscular diseases, emphasized that issues concerning the environment, social relationships, and the individual's psychological state can be much more important than physical symptoms, which, from the patients' perspective, do not always reflect their overall wellbeing<sup>47</sup>. The psycho-emotional dimension of disability can include feelings like anger, disability non-acceptance, and in some cases feelings of rejection or humiliation. These elements are often difficult to address, but rather than allowing them to be overlooked, the rehabilitation project/program should take into account the psychosocial dimension.

#### Panel consensus

The Jury reached the following consensus statements:

- The main objectives of the rehabilitation project/program (with regard to d5: Self-care; d8: major life areas) are:
  - to support functional independence in ADL;
  - to support and optimize participation at school, work, and in the social environment;
  - to optimize and improve QoL. *Unanimous consensus.*
- General recommendations:
  - Promote sport to improve participation;
  - Include transfer aids and adaptive equipment to ensure the highest possible degrees of independence and safety;
  - Assistive technologies (e.g., ergonomic support, robotic manipulators, home automation, environmental control) should be considered in order to improve autonomy. *Unanimous consensus.*

*TOPIC 7: Definition of the professional figures involved in the rehabilitation project/program*

#### Discussion

An interesting debate has unfolded in recent years concerning the specific roles of the different professional figures involved in the management of rehabilitation programs<sup>1</sup>. Due to the heterogeneity of national regulations

and health systems, there is not always a complete correspondence between the roles, skills, and responsibilities of the various rehabilitation professionals in different countries. In Italy, these professional figures and specific roles still need to be defined.

#### Panel consensus

The Jury reached the following consensus statements:

- The rehabilitation project/program must be considered the result of a team effort.
- General recommendations:
  - Physicians must have specific expertise in MD rehabilitation management, as it is their task to draw up and prescribe specific projects/programs; they can be psychiatrists, neurologists, or (within the Italian health system) other types of specialist, provided they work in rehabilitation settings specialized in MD. *Unanimous consensus.*
  - Therapists are expected to discuss and share clinical indications, evaluate compliance and motor performances, critically select specific rehabilitation techniques, train patients and caregivers, and finally monitor the achievement of objectives. In the field of motor rehabilitation, therapists include the physiotherapist, the occupational therapist, and the neurodevelopmental therapist. *Unanimous consensus.*

*TOPIC 8: The rehabilitation setting: outpatient vs home therapy*

#### Discussion

When available, outpatient settings offer several advantages for the realization of the rehabilitation program, such as appropriate equipment, appropriate environments and devices, opportunities for socialization, and easier collaboration between the members of the multidisciplinary team. However, in some cases, for clinical and/or logistic reasons, a home therapy program can be required (e.g., when patients depend on vital equipment or lack adequate transportation, or when the journey would take too long).

#### Panel consensus

The Jury reached the following consensus statement:

- Home therapy should be considered for patients with severe motor impairment (i.e., bedridden patients, or those with severe cardiorespiratory impairment), for those needing very frequent treatments, and in situations where significant problems getting to the rehabilitation center (transport and travel problems, including lengthy or complex journeys) could un-

determine the objectives of the treatment. *Unanimous consensus.*

#### TOPIC 9: Duration/frequency

##### Discussion

Given the chronic and progressive nature of MD, the management of patients with these diseases needs to be understood as a life-long process. However, in defining the timing of rehabilitation projects/programs, it is very important to consider several clinical and logistic variables. The Jury agrees that rehabilitation interventions in children should generally be ongoing, as reported for all stages of DMD<sup>14</sup>. According to expert opinion in this growing area of research, MD can interfere with several levels of neurodevelopment. However, it is important to avoid unnecessary and excessive interventions, so as to safeguard socialization and ADL participation, which are equally important.

With regard to adult patients, there is a heated debate, given the greater clinical variability in this population, even within single types of MD. It was generally agreed that, when drafting a rehabilitation project/program, it is very important to consider the specific rehabilitation objective of the treatment, which is based on the patient's clinical condition, motor function, and compliance. Since all forms of MD are progressive, it is inappropriate to speak of a "stabilization" or "maintenance" phase.

##### Panel consensus

After extensive discussion, the Jury reached the following consensus statements:

- In children, the rehabilitation project/program should generally be ongoing, while avoiding excessive interventions that can interfere with socialization/ADL participation. *Unanimous consensus.*
- In adults, the definition of the rehabilitation objectives, and of the duration and frequency of interventions, must be the result of a careful multidisciplinary evaluation of the characteristics of the MD and of the patient's clinical and functional conditions. *Majority consensus.*

## Conclusions

The pressing need for appropriate and precise clinical recommendations for use in drawing up rehabilitation projects/programs is felt daily in the management of patients with MD. The purpose of this document, based on practical recommendations shared by a multidisciplinary panel of MD experts, is to provide clinicians, patients and caregivers with detailed, updated indications on the rehabilitation of MD patients, both children and adults. It is based on the main literature evidence and on expert

opinions; it outlines the specific roles and responsibilities of the professional figures involved in the rehabilitation project/program, and provides technical indications in line with the F.I.T.T. model of physical therapy. Furthermore, it details practical measures for managing contractures, mobility and ADL. The document is valuable both for clinicians, being a tool that can be rapidly consulted in order to counsel patients, and for patients themselves, who need to be sure they are getting the right care at the right time in their disease history.

This study presents some methodological limitations, in part due to the heterogeneity of the scientific literature and outcome measures, and the lack of a precise definition of natural history data in most forms of MD. Moreover, the analysis does not cover important "modern tools" such as robotic assistive technology, digital platforms, and telerehabilitation systems, which are increasingly being developed, and whose importance has been especially appreciated in the course of the COVID-19 pandemic.

Despite these limitations, we anticipate that this Italian consensus document, commissioned by UILDM, may provide a basis for official standardized guidelines and open up a new scenario with regard to the patient-clinician alliance.

##### Ethical consideration

None.

##### Acknowledgement

This project was promoted and sponsored by the Association Unione Italiana Lotta alla Distrofia Muscolare (UILDM). The authors thank UILDM, as well as Clara Chiuso, for their support. They also thank the scientific societies that took part in the project: AIM (Associazione Italiana di Miologia), SIF (Società Italiana di Fisioterapia), SIMFER (Società Italiana di Medicina Fisica e Riabilitativa), SIMPIA (Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza), SIN (Società Italiana di Neurologia), SIRN (Società Italiana di Riabilitazione Neurologica). Thanks also to ERN-EURO NMD members. We thank Dr. Catherine J. Wrenn for editorial and language assistance.

##### Funding

None.

##### Conflict of interest

The Authors declare there are no conflict of interest.

##### Author contributions

ME Lombardo participated in the consensus conference and wrote the text.

All the Authors and The Italian Consensus Conference Groupe participated in the consensus conference and reviewed and approved the text.

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