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ORIGINAL ARTICLES

Emergencies cards for neuromuscular disorders 1st Consensus Meeting from UILDM – Italian Muscular Dystrophy Association Workshop report

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Acute hospitalisation may be required to support patients with Neuromuscular disorders (NMDs) mainly experiencing respiratory complications, swallowing difficulties, heart failure, urgent surgical procedures. As NMDs may need specific treatments, they should be ideally managed in specialized hospitals. Nevertheless, if urgent treatment is required, patients with NMD should be managed at the closest hospital site, which may not be a specialized centre where local emergency physicians have the adequate experience to manage these patients. Although NMDs are a group of conditions that can differ in terms of disease onset, progression, severity and involvement of other systems, many recommendations are transversal and apply to the most frequent NMDs. Emergency Cards (EC), which report the most common recommendations on respiratory and cardiac issues and provide indications for drugs/treatments to be used with caution, are actively used in some countries by patients with NMDs. In Italy, there is no consensus on the use of any EC, and a minority of patients adopt it regularly in case of emergency. In April 2022, 50 participants from different centres in Italy met in Milan, Italy, to agree on a minimum set of recommendations for urgent care management which can be extended to the vast majority of NMDs. The aim of the workshop was to agree on the most relevant information and recommendations regarding the main topics related to emergency care of patients with NMD in order to produce specific ECs for the 13 most frequent NMDs.

Key words: neuromuscular diseases, respiratory complications, cardiac complications, swallowing difficulties, anaesthesia, emergency card, critical care.

Introduction

Neuromuscular disorders (NMDs) are a heterogeneous group of diseases affecting the function of motor neurons, peripheral nerve, neuromuscular junction, or skeletal muscles. When muscle weakness involves respiratory, bulbar and/or cardiac muscles, NMD may lead to respiratory, swallowing and/or cardiac complications [1-12]. Acute hospitalization may be required to support patients with NMDs, who can experience a range of common affections or conditions (e.g., respiratory infections, heart failure, urgent surgical procedures, bone fractures, labour and delivery) [2,4,5,7,13-18]. As these patients may need specific treatments, such as non-invasive ventilation (NIV), assisted cough [4,5,7,12,14-16,19-30], and dedicated extubation strategies [31,32], they should be ideally managed in specialized hospitals that have the appropriate technical tools and human resources [33,34]. Nevertheless, if urgent treatments are required, patients should be managed at the closest hospital site, which may not be one of the specialized centres for NMD [34]. Since NMDs are rare diseases and are an uncommon cause of emergency department and ICU admissions [33], local emergency physicians and intensivists may not have the adequate experience to manage these patients [5,34].

Although NMDs are a group of conditions that may differ in terms of disease onset, progression, severity and involvement of other systems, many recommendations can apply to the vast majority of NMDs. In particular, they all may require a similar management in case of acute respiratory, cardiac and swallowing complications and may require a similar perioperative management.

The introduction of an emergency card (EC) for patients with NMDs has been identified as a possible solution to improve local acute care [5,34,35]. The EC is intended as a pocket guide for Emergency Department physicians, to provide an overview of key issues related to the emer-

gency management of patients with NMDs [34]. Patients should take it with them when they seek acute care. While EC are already actively used in some countries by patients with NMDs there is no consensus and wide use in Italy for any of the most common diseases.

To fill this gap, 50 participants from 39 Italian tertiary centres met in Milan, Italy, to agree on a minimum set of recommendations for urgent care management which can be extended to the vast majority of NMDs. The aim of the workshop was to agree on the most relevant informations and recommendations regarding the main topics related to urgent care of the vast majority of NMDs in order to produce an EC for the 13 most frequent NMDs.

An informal consensus technique was used that involved group discussions moderated by senior chairpersons. Any information or suggestion of care and management was presented and voted by the panel of experts during a plenary roundtable and two web-based surveys.

Methods

In January 2020, the UILDM (Italian Muscular Dystrophy Association) Medical Scientific Committee (UILDM-MSC) discussed on the current emergency care issues for patients with NMDs. It became immediately clear that the wide variation of medical care received by NMDs patients in the emergency setting likely increases the variability of clinical outcomes. Thus, the UILDM-MSC nominated an eight-member Core Committee (CC) with the aim of organizing a Consensus Conference that formulates the EC for the most frequent NMDs. The CC consisted of six physicians (4 neurologists, 1 pulmonologist, 1 anesthesiologist/intensivist), one physiotherapist and one patient representative from UILDM. This CC appointed two chairmen (FRac and ClB). All committee members participated on a voluntary basis, with no compensation. During the planning stages of Consensus Conference, the co-Chairs frequently communicated with the CC. It was decided to focus on the emergency management of the following NMDs: Spinal muscular atrophy type 1, type 2 and type 3, Charcot-Marie-Tooth disease, Duchenne Muscular dystrophy, Becker Muscular dystrophy, Myotonic dystrophy type 1, Limb girdle muscular dystrophy, Facioscapulohumeral muscular dystrophy, Congenital muscular dystrophy, Congenital myopathies, Mitochondrial myopathies, Glycogen storage myopathies. The CC selected seven main domains which are typically associated with clinical problems and require urgent care: i) acute respiratory failure; ii) chocking due to swallowing difficulties; iii); cardiac complications; iv) anaesthetic precautions and perioperative management; v) falls and fractures; vi) acute constipation due to bowel dysfunction; vii) other issues.

The format of EC was drafted to provide a readily accessible compilation of main topics related to the emergency care of these patients (Tab. I).

The most relevant literature in the field was identified by querying PubMed (www.pubmed.gov) from January 1991 to December 2021, including only human studies. We used the search terms “neuromuscular diseases”, “spinal muscular atrophy”, “Charcot-Marie-Tooth disease”, “myopathy”, “muscular dystrophy”, cross-referenced with the term “respiratory complications”, “cardiac complications”, “swallowing difficulties”, “anesthesia” and “fractures”. We identified 352 out of 10.000 articles as relevant to the document.

Table I. Standard format chosen for the compilation of the emergency card.

EMERGENCY CARD for patients with _____	
Name_____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____ as soon as possible on: _____	
Main topics	**Most relevant informations and recommendations related to the emergency care**
Acute respiratory insufficiency	Key issues and management
Chocking due to swallowing difficulties	Key issues and management
Acute cardiac Complications	Key issues and management
Anaesthetic precautions And perioperative management	Key issues and management
Falls and fractures	Key issues and management
Acute constipation due to bowel dysfunction	Key issues and management
Other issues	Key issues and management

The CC decided to focus on a minimum set of common recommendations for different NMDs and drafted consensus statements on each area of care based on the literature results and personal experience. The effort was to select the most important consensus-based recommendations acceptable to the panel and amenable to application by physicians not specialized in NMDs in the Emergency Departments.

The Co-Chairs and CC worked together to establish an Italian consensus working group (CWG), sharing the responsibility for nominating and approving participants. The panel selection was based on a) clinical and scientific experience in NMDs; b) involvement in acute care management of NMDs patients; c) the need to have different health-care professionals who could provide knowledge and experience in the different domains described above; d) geographic diversity; and e) ability to commit time to the CC process. Ultimately, the panel consisted of 49 clinically-active physicians, involved in acute management of paediatric and adult neuromuscular patients (24 neurologists, 5 pulmonologists, 7 anesthesiologists and intensivists, 3 emergency medicine specialists, 3 pediatricians, 3 orthopedics, 2 cardiologists, 1 physiatrist, 1 physiotherapist) and one patient representative. The panelists came from different Regions of Italy. Representatives from the medical groups such as the Italian Muscle Association (AIM, Associazione Italiana Miologia), the Italian Pulmonology Association (AIPO, Associazione Italiana Pneumologi Ospedalieri), the Italian Pediatric Respiratory Association (SIMRI, Società Italiana Medicina Respiratoria Infantile), the Italian Neonatal and Pediatric Reanimation Society (SARNePI, Società di Anestesia e Rianimazione Neonatale e Pediatrica Italiana), the Italian Emergency Care Society (SIMEU, Società Italiana della medicina di emergenza-urgenza), the Italian Pediatric Emergency Care Society (SIMEUP, Società Italiana di Medicina di Emergenza e Urgenza Pediatrica) actively partecipate to the CC.

Starting three months before the meeting, the consensus working group (CWG) completed a web-based survey. A set of 45 close-ended questions was constructed for each of the seven main topics. Panellists were encouraged to limit their responses to the respective areas of expertise. In case of disagreement with the statement proposed by the application, they were encouraged to give feedback in order to clarify the reasons for their dissent. Consensus was reached with a percentage of votes in favour greater than 85%. Points for which consensus was not reached were reviewed by the leadership team based on feedback from the panel. All responses were summarized and presented by the Co-Chairs to panel members during the in-person Consensus Conference meeting. The meeting took place on 13th April 2022 in Milan. The entire group discussed all recommendations and voted for the revised version, using the same 85% criterion. The Co-Chairs ensured that every one of the working group had the opportunity to present and debate their views and ensured that discussions were open and constructive.

At the end of the meeting, the Co-Chairs revised the recommendations for which consensus was not reached and sent a second web-based survey to obtain an additional round of votes to reach consensus on the revised statements. All the activities were completed between December 2020 and May 2022.

Results

Consensus, that was reached on keys issues and management of acute respiratory failure, chocking, cardiac complications, anaesthesia, fractures and acute constipation is summarized in four tables (Tabs. II-V) and 37 statements (Tab. VI). Subsequently, the CWG defined 13 ECs, one for each disease, all sharing the same structure but with disease-related specifities. These cards are presented as on-line support information.

The general considerations for the most frequent clinical conditions potentially requiring urgent care and the recommendations and management strategies are outlined in the following paragraphs.

Key issues and management of acute respiratory failure

The probability of occurrence of respiratory complications is different in NMDs depending on the disease and age (Tab. II) [14,16,36-38] and may be the main cause of death [13,36,39,40]. The weakness of inspiratory muscles affects the ability to ventilate and leads to alveolar hypoventilation and hypercapnia. In addition, the involvement of expiratory muscles impairs the ability to clear airway secretions, inducing mucus plugging and hypoxemia [14,38,39,41]. The presence of severe scoliosis, which develops mainly in patients with NMDs, who lose independent ambulation before adulthood, further increases the risk of respiratory complications [14,42-44].

The use of Non Invasive Ventilation (NIV) associated with cough assist device, reduces the risk of alveolar hypoventilation and airway secretion retention, decreasing the number of hospital admissions, intubation, and tracheostomy [14,19-29,45,46]. Acute intercurrent events can lead to respiratory exacerbation and acute respiratory failure (RF) [14,41]. Respiratory tract infections are the most common cause of hospitalization for patients with NMDs , triggering over 90% of episodes of acute RF [40]. In case of airway infections, the weakness of the expiratory muscles, especially when associated with weakness of the inspiratory muscles, causes cough deficit with accumulation of bronchial secretions and increased work of breath-

Table II. Respiratory complications in neuromuscular disorders.

Disorder	Respiratory complications
SMA type 1	Always present (early onset; frequent exacerbation)
SMA type 2	Frequent (progressive)
SMA type 3	Occasional (progressive)
CMT	Occasional in some subtypes (progressive)
DMD	Always present in adulthood (progressive; frequent exacerbation)
BMD	Occasional (progressive)
DM1	Frequent (progressive; central sleep apnea is also reported)
LGMD	Frequent in some subtypes (LGMD1, LGMD2C/D/E/F)
FSHD	Occasional (progressive)
CMD	Frequent in some subtypes (Ullrich's CMD, LAMA 2 deficient CMD)
CM	Frequent in some subtypes (nemaline, myofibrillary and centro-nuclear CM)
Mitochondrial (encephalo) myopathies	Frequent (progressive, infantile onset and late onset; abnormalities of respiratory drive due to dysfunction of the respiratory centers are very frequently reported in pediatric cases)
Glycogen storage myopathies	Frequent in Pompe disease (infantile onset and late onset)

Occasional: < 10%; frequent: 10-50%; very frequent: > 50%; always present: 100%. DMD: Duchenne Muscular dystrophy; BMD: Becker Muscular dystrophy; DM1: Myotonic dystrophy type 1; LGMD: Limb girdle muscular dystrophy; FSHD: Facioscapulohumeral muscular dystrophy; CMD: Congenital muscular dystrophy; CM: Congenital myopathies; SMA: Spinal muscular atrophy; CMT: Charcot-Marie-Tooth disease

Table III. Swallowing difficulties in neuromuscular disorders.

Disorder	Swallowing difficulties
SMA type 1	Always present
SMA type 2	Very frequent
SMA type 3	Occasional
CMT	Occasional
DMD	Always present in the late stages of the disease
BMD	Occasional
DM1	Very frequent
LGMD	Occasional in some subtypes
FSHD	Occasional
CMD	Frequent in some subtypes
CM	Frequent in some subtypes
Mitochondrial (encephalo) myopathies	Frequent (more often due to central involvement than primary muscular impairment)
Glycogen storage myopathies	Frequent in Infantile onset Pompe Disease/rare in late onset Pompe Disease

Occasional: < 10%; frequent: 10-50%; very frequent: > 50%; always present: 100%. DMD: Duchenne Muscular dystrophy; BMD: Becker Muscular dystrophy; DM1: Myotonic dystrophy type 1; LGMD: Limb girdle muscular dystrophy; FSHD: Facioscapulohumeral muscular dystrophy; CMD: Congenital muscular dystrophy; CM: Congenital myopathies; SMA: Spinal muscular atrophy; CMT: Charcot-Marie-Tooth disease

ing [13,14,41]. The use of NIV associated with cough assist device (Mechanical Insufflation-Exsufflation, MI-E). and the early use of antibiotics are the standard of care in the event of airway infection both at home [28,29,42,46,47] and in hospitals [13,21,48-50]. In addition, oxygen should never be used unless associated with NIV and CO2 monitoring [13,28,29,36].

In case of hospitalization, chest x-ray should be performed as soon as possible to assess the presence of pneumonia or atelectasis. Furthermore, if there is no clear infectious cause, non-infectious causes of acute RF (pneumothorax, pulmonary thromboembolism, adipose embolism) should be excluded [13,36,51]. In patients with myopathy complicated by cardiomyopathy, an echocar-

Table IV. Cardiac complications in neuromuscular disorders.

	Cardiomyopathy	Arrhythmias	Conduction defects	Structural cardiac abnormalities
SMA type 1	Very rare (only one case reported)	Not reported	Not reported	Occasional
SMA type 2/3	Occasional	Occasional	Not reported	Occasional
CMT	Not reported	Not reported	Not reported	Not reported
DMD/ BMD	Very frequent (dilated cardiomyopathy)	Very frequent	Occasional	Occasional
DM1 (adult onset)	Occasional	Very frequent	Very frequent	Not reported
LGMD	Very frequent in some subtypes (LGMD1B and LGMD2C/D/E/I)	Occasional but very frequent in LGMD1B and frequent in LGMD2E	Occasional but very frequent in LGMD1B	Not reported
FSHD	Occasional	Occasional	Occasional	Not reported
CMD	Frequent in Fukuyama CMD; Occasional in other subtypes	Occasional	Occasional	Not reported
CM	Occasional	Occasional (Long QT)	Occasional	Not reported
Mitochondrial (encephalo) myopathies	Very frequent	Frequent	Frequent	Occasional
Glycogen storage myopathies	Very frequent in some subtypes (type II, III, IV, VII and IX)	Very frequent	Frequent	Not reported

Occasional: < 10%; frequent: 10-50%; very frequent: > 50%; always present: 100%. DMD: Duchenne Muscular dystrophy; BMD: Becker Muscular dystrophy; DM1: Myotonic dystrophy type 1; LGMD: Limb girdle muscular dystrophy; FSHD: Facioscapulohumeral muscular dystrophy; CMD: Congenital muscular dystrophy; CM: Congenital myopathies; SMA: Spinal muscular atrophy; CMT: Charcot-Marie-Tooth disease

Table V. Use of succinylcholine and inhaled anaesthetics in patients with NMDs.

	Use of succinylcholine	Use of halogenated agents
DMD/BMD	Must be avoided	Must be avoided
DM1	Must be avoided	Must be avoided
LGMD	Must be avoided	Must be avoided
FSHD	Must be avoided	Must be avoided
CMD	Must be avoided	Must be avoided
CM	Must be avoided	Must be avoided
Mitochondrial (encephalo) myopathies	Must be avoided	May be used
Glycogen Storage myopathies	Must be avoided	Must be avoided
SMA	Must be avoided	May be used
CMT	Must be avoided	May be used

DDMD: Duchenne Muscular dystrophy; BMD: Becker Muscular dystrophy; DM1: Myotonic dystrophy type 1; LGMD: Limb girdle muscular dystrophy; FSHD: Facioscapulohumeral muscular dystrophy; CMD: Congenital muscular dystrophy; CM: Congenital myopathies; SMA: Spinal muscular atrophy; CMT: Charcot-Marie-Tooth disease

diogram should also be performed in order to rule out the possibility of cardiogenic pulmonary oedema [13,36]. If the chest x-ray does not justify the clinical picture of acute RF, a chest CT scan must be required to exclude an anterior pneumothorax, not visible by the chest x-ray [13,36,51]. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism [13,36].

If non-invasive treatment (NIV and coughing assistance) fail, tracheal intubation must not be delayed [13,36,48]. In this case, difficulty in performing tracheal intubation

Table VI. Consensus summary of the 37 most relevant recommendations related to the urgent care of patients with NMDs

Section 1. ACUTE RESPIRATORY INSUFFICIENCY
1.1 Respiratory muscle weakness can impair the pump function of the respiratory system, upper airway muscle tone and secretion clearance efficiency. The respiratory consequences are retention of secretions, upper airway obstruction, nocturnal and finally daytime hypoventilation
1.2 Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections
1.3 If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax, adipose embolism or atelectasis). Cardiogenic pulmonary oedema should be ruled out in case of patients with myopathy
1.4 Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case, chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism
1.5 NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available
1.6 O2 must never be used except in association with NIV. If supplementary oxygen is required, titrate oxygen therapy to achieve a SpO2 94-98%, and monitor CO2
1.7 In the case of an acute, reversible event, intubation and invasive ventilation are indicated when NIV fails, unless prior directives are known to state otherwise. When indicated, tracheal intubation must not be delayed. It should be noted that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia, narrow and high-arch hard palate or limited mobility of the cervical spine
1.8 Upon recovery from acute illness, these patients should be promptly extubated by switching to NIV in combination with MI-E
1.9 Tracheotomy can be considered, in particular in patients with severe bulbar dysfunction. However, in acute phases it should only be considered in case of multiple weaning protocol failures including preventive application of NIV combined with MI-E after extubation
Section 2. CHOCKING DUE TO SWALLOWING DIFFICULTIES:
2.1 Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered
2.2 Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV
2.3 In case of choking, use MI-E or manual assisted coughing; if it is ineffective, consider emergent tracheal intubation
Section 3. CARDIAC COMPLICATIONS:
3.1 Cardiac dysfunction (i.e., cardiomyopathies or abnormalities of the conduction system and arrhythmias) may be present in these patients,in particular in patients with myopathies. However, the clinical manifestations of heart failure are often not recognized until very late, due to skeletal muscle limitations
3.2 As cardiomyopathy is progressive, consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias
3.3 Request patient's baseline test results, including echocardiogram and electrocardiogram
3.4 Obtain a brief history with particular attention to underlying cardiac status, including medication use
3.5 Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2
3.6 Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest x-ray and/or chest ultrasound may be useful if pulmonary oedema is suspected.
3.7 Obtain an echocardiogram and prompty consult a cardiologist.
3.8 As in patients with myopathies, the blood cardiac Tropo nin T (cTnT) levels may be chronically high, while the blood cardiac Troponin I (cTnI) level are more rarely elevated, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI

Table VI. continues

Section 4. ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT:
4.1 Ideally, surgery should occur in a specialist centre with staff experienced in managing these patients. Otherwise, urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management
4.2 Obtain a pre-operative evaluation that include lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. FVC less than 50% the predicted value, or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure, whenever possible
4.3 Patients and in particular patients with myopathies should also undergo careful assessment of heart function and optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram are mandatory before anaesthesia
4.4 In many patients with NMDs the use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis (see table 5)
4.5 Patients with NMDs may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex)
4.6 Tracheal intubation may be difficult in patients with NMDs and a frequent use of fiberoptic-assisted endotracheal intubation is reported
4.7 The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia side-effects and reduction of postoperative respiratory complications
4.8 Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea.
4.9 Admission to an Intensive Care Unit (ICU) should be considered in patient at risk for respiratory or cardiac complications
4.10 Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation and switching to NIV with aggressive use of MI-E. O2 must never be used, except in association with NIV
Section 5. FALLS AND FRACTURES:
5.1. Due to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures
5.2 In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows for early walking recovery while preserving muscle function
5.3 In non-ambulatory adult patients, conservative management may be considered for non-displaced sub capital femoral neck fractures. Conversely, internal fixation is required in diaphyseal or trochanteric femoral fractures.
5.4 The treatment of femoral fractures in paediatric patients is strictly related to the child's age, site of the fracture, and disability related to muscle weakness. Conservative treatment may be considered in patients younger 5-6 years, with non-displaced fractures, and when a short period of immobilization is expected. In other cases, surgical fixation using minimally invasive techniques (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators) is preferred
Section 6. ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION:
6.1 Patients with NMDs and especially older patients can experience constipation due to abnormal gastrointestinal motility
6.2 Gastric and/or abdominal distention can cause acute respiratory failure in patients at high risk of respiratory complications. In these cases, gastrointestinal decompression by nasogastric tube and/or rectal tube is often an effective therapy
Section 7. OTHER ISSUES
7.1 Blood transaminases and creatine kinase levels may be increased in patients with myopathies. If other hepatic function tests (e.g., bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy liver disease and may be due to muscle involvement

is frequently reported [30,52,53]. This may be due to several factors such as jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia, narrow and high-arch hard palate or limited mobility of the cervical spine [52,53].

In addition, it is important to verify whether an invasive cure plan has been shared before with the referral medical team and the patient had previously approved invasive manoeuvres such as tracheostomy, also in the context of expressed end-of-life decisions depending of

time of progression of the NMDs. A consultation with the referring team may be sometimes essential. If there are not informations regarding a previously approved invasive cure plan by the patient, it is important to verify if the patient is able to do it during the acute setting.

This should be done prior to proceeding with invasive manoeuvres. If the patient is unable to express end-of-life decisions due to age, severe clinical conditions or inability to communicate for other reasons (e.g., anarthria, cognitive impairment), it is good clinical practice to discuss about the patient choices with caregivers or close family members.

In the acute phase, tracheostomy should be considered only after failure of multiple attempts at proper weaning, that includes preventive application of NIV combined with MI-E immediately after extubation [31,32].

Based on these considerations, the section on respiratory involvement in the EC includes the following statements.

1.1 Respiratory muscle weakness can impair the pump function of the respiratory system, upper airway muscle tone and secretion clearance efficiency. The respiratory consequences are retention of secretions, upper airway obstruction, nocturnal and finally daytime hypoventilation.

1.2 Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute RF and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections.

1.3 If no infectious cause of acute RF is evident, consider non-infectious causes (e.g., pneumothorax, adipose embolism or atelectasis). Cardiogenic pulmonary oedema should be ruled out in case of patients with myopathy.

1.4 Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 < 95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case, chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism.

1.5 NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an AMBU bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available.

1.6 O2 must never be used except in association with NIV. If supplementary oxygen is required, titrate oxygen therapy to achieve a SpO2 94-98%, and monitor CO2.

1.7 In the case of an acute, reversible event, intubation and invasive ventilation are indicated when NIV fails, unless prior directives are known to state otherwise. When indicated, tracheal intubation must not be delayed. It should be noted that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia, narrow and high-arch hard palate or limited mobility of the cervical spine.

1.8 Upon recovery from acute illness, these patients should be promptly extubated by switching to NIV in combination with MI-E.

1.9 Tracheotomy can be considered, in particular in patients with severe bulbar dysfunction. However, in acute phase it should only be considered in case of multiple weaning protocol failures including preventive application of NIV combined with MI-E after extubation.

Chocking due to swallowing difficulties

Inadequate strength and coordination of the bulbar muscles, is common in patients with NMDs and leads to difficulty in swallowing (dysphagia) and managing saliva (sialorrhea) [54,55]. A meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, malnutrition, sialorrhea and choking when eating or drinking are signs and symptoms potentially associated with swallowing difficulties [54,56]. The swallowing impairments vary with the natural course of the underlying NMD (Tab. III). Bulbar dysfunction may cause chocking, aspiration pneumonia and other pulmonary sequelae, such as pulmonary fibrosis [54,57-59]. In addition, it impairs the ability to clear airway secretions [14]. The association of a weak cough with dysphagia increases the risk for choking and aspiration pneumonia [60]. On the other hand, bulbar dysfunction may impede the successful use of NIV [32,48].

In case of choking, the use of MI-E may reverse hypoxemia [61]; if hypoxemia cannot be corrected by MI-E, emergent tracheal intubation should be immediately considered [13].

Based on these considerations, the section on swallowing difficulties in the EC includes the following statements.

2.1 Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered.

2.2 Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV.

2.3 In case of choking, use MI-E or manual assisted coughing; if it is ineffective, consider emergent tracheal intubation.

Cardiac complications

Cardiac involvement is frequently reported in patients affected by NMDs with a growing impact on mor-

bidity and mortality [62-66]. Two major features are usually described: i) cardiomyopathy; and ii) conduction defects with arrhythmias [63,66-69]. The incidence and nature of cardiac involvement vary according to the type of NMD (Tab. IV).

Cardiac evaluation includes physical examination, electrocardiogram, transthoracic echocardiogram, Holter monitoring, cardiac MRI and laboratory analysis including B-type natriuretic peptide [63,73-76]. A scheduled follow up is usually preferred because most of these patients are asymptomatic due to musculoskeletal limitations [63,73,78,79]. Symptoms of cardiac insufficiency in wheel-chair-bound patients may present with loss of appetite, weight reduction, gastrointestinal disorders (slow digestion, stomach pain, pain in the upper right side of the abdomen), palpitations, dyspnoea at rest, orthopnoea, pre-syncope, syncope [80].

Appropriate cardiac treatment significantly improves the overall long-term outcome of NMDs [67]. Standard heart failure treatment, such as ACE inhibitors and/or beta-blockers, is currently used in patients presenting with dilated cardiomyopathy [70,80,81]. However, beta-blockers should be avoided in patients with conduction system disorders [73,82]. New drugs for heart failure improving survival in NMDs are now available [83-86].

Electrical therapy can also be useful in NMD patients: the implant of pacemakers (PMs) is indicated in case of bradycardia or atrioventricular blocks, whereas ventricular arrhythmias and/or severe congestive heart failure may require automatic implantable cardioverter defibrillator (ICD) placement [73,87]. Heart transplantation is an effective treatment for a selected group of patients with NMDs and end-stage heart failure (e.g., Becker MD or Steinert disease) [88-91]. Left ventricular–assist devices can be used for long term treatment in patients with Duchenne MD and severe cardiomyopathy [80].

Patients with heart failure may also benefit of the use of nocturnal NIV for respiratory support. Indeed, NIV results in improved gas exchange and heart pump function [73].

The following statements are suggested for patients with NMDs at risk of cardiac complications.

3.1 Cardiac dysfunction (i.e., cardiomyopathies or abnormalities of the conduction system and arrhythmias) may be present in these patients, in particular in patients with myopathies. However, the clinical manifestations of heart failure are often not recognized until very late, due to skeletal muscle limitations.

3.2 As cardiomyopathy is progressive, consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias.

3.3 Request patient's baseline test results, including echocardiogram and electrocardiogram.

3.4 Obtain a brief history with particular attention to underlying cardiac status, including medication use.

3.5 Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2.

3.6 Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest x-ray and/or chest ultrasound may be useful if pulmonary oedema is suspected.

3.7 Obtain an echocardiogram and promptly consult a cardiologist.

3.8 As in patients with myopathies, the blood cardiac Troponin T (cTnT) levels may be chronically high, while the blood cardiac Troponin I (cTnI) level are more rarely elevated, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.

Anaesthetic and perioperative management

Patients with NMDs may have abnormal vital functions (e.g., respiratory and/or cardiac involvement), which increase the risk of surgical procedures requiring general anaesthesia [92,93]. In addition, some anaesthetic agents can trigger life-threatening reactions (i.e., malignant hyperthermia, rhabdomyolysis and hyperkaliaemic cardiac arrest secondary to denervation) [94-96]. As a consequence, patients with NMDs are at high risk of intra-operative and post-operative complications, and surgery should be, ideally, performed in a fully equipped hospital with extensive experience in NMDs management [93].

Pre-operative assessment of respiratory function should include lung function tests and cough assessment [92,93]. Patients with respiratory muscle weakness [i.e. forced vital capacity (FVC) less than 50% of predicted value, or peak cough less than 270 l/min], should be trained pre-operatively on the use of NIV and mucus clearance techniques [92,93]. Indeed, when general anaesthesia is necessary, these patients should be extubated by switching directly to NIV in combination with MI-E [30,92,93, 97,98].

Patients with myopathies should also undergo a careful assessment of heart function and optimize cardiac therapy in the pre-operative period [93,94,98].

Patients with NMDs may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants [94]. Moreover, the use of inhaled anaesthetics and succinylcholine is contraindicated in myopathic patients due to the high risk of acute rhabdomyolysis [93-96,99-100] (Tab. V). In addition, difficulty in performing direct laryngoscopy and the frequent use of fibreoptic-assisted endotracheal intubation is frequently reported [30,52,53]. As a consequence, regional anaesthesia should be warranted whenever possible [30,93,94,98].

Based on these considerations, the following statements are suggested, in the section on anaesthetic and perioperative management.

4.1 Ideally, surgery should occur in a specialist centre with staff experienced in managing these patients. Otherwise, urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

4.2 Obtain a pre-operative evaluation that include lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. FVC less than 50% the predicted value, or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure, whenever possible.

4.3 Patients with NMDs, in particular patients with myopathies, should also undergo careful assessment of heart function and optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram are mandatory before anaesthesia.

4.4 In many patients with NMDs the use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis (see table V).

4.5 Patients with NMDs may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex).

4.6 Tracheal intubation may be difficult in patients with NMDs and a frequent use of fiberoptic-assisted endotracheal intubation is reported.

4.7 The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia side-effects and reduction of postoperative respiratory complications.

4.8 Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea.

4.9 Admission to an Intensive Care Unit (ICU) should be considered in any patient who is at risk for respiratory or cardiac complications.

4.10 Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation and switching to NIV with aggressive use of MI-E. O2 must never be used, except in association with NIV.

Falls and fractures

Fractures are quite common in patients with NMDs, as they present marked disuse osteoporosis and are at high risk of falls [101]. Decreased bone mass and osteopenia are reported in approximately 2/3 of these patients, resulting in frequent fragility fractures [102]. Goals of the treatment are to promptly restore function and to reduce immobilization in order to prevent bed rest consequences, such as muscular and bone weakness that may increase the risk of re-fractures [103].

In adult patients, non-surgical treatment with cast immobilization is generally recommended for non-ambulatory patients, except for patients with inter-trochanteric, sub-trochanteric, and diaphyseal fractures. On the other hand, a prolonged immobilization (> 4 weeks) that aggravates muscle wasting and disuse osteoporosis, should be avoided in ambulatory patients. As a consequence, all ambulatory and non ambulatory patients, who present inter-trochanteric, sub-trochanteric, and diaphyseal fractures, generally benefit from surgical stabilization. Intramedullary nails or plates are used to allow early extremity range of motion and to promote acceleration of the fracture healing [1]. However, the level of independence and disability before the fall and fracture is usually unlike to be maintained after surgery, regardless of the level of surgery because of the underlying muscle weakness.

In paediatric patients, conservative treatment may be considered in children younger than 5-6 years, with non-displaced fractures and when a short period of immobilization is expected. In other cases, surgical fixation using minimally invasive techniques (e.g., flexible intramedullary nailing) is preferred [104].

Based on these considerations, the section on falls and fractures in EC includes the following statements.

5.1 Due to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures.

5.2 In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows for early walking recovery while preserving muscle function.

5.3 In non-ambulatory adult patients, conservative management may be considered for non-displaced sub capital femoral neck fractures. Conversely, internal fixation is required in diaphyseal or trochanteric femoral fractures.

5.4 The treatment of femoral fractures in paediatric patients is strictly related to the child's age, site of the fracture, and disability related to muscle weakness. Conservative treatment may be considered in patients younger than 5-6 years, with non-displaced fractures, and when a short period of immobilization is expected. In other cases, surgical fixation using minimally invasive techniques (e.g., percutaneous fixation by Kirshner wires and plaster casts, flexible intramedullary nailing or light external fixators) is preferred.

Acute constipation due to bowel dysfunction

Constipation characterized by abdominal pain and distension, associated with the inability to defecate, is

extremely common in patients with NMDs [1,105]. Multiple potential risk factors can contribute to the development of constipation in NMDs, including underlying motility dysfunction due to involvement of smooth muscle fibres, lack of mobility, dehydration due to swallowing dysfunction, and lack of dietary fibre. Gastric or abdominal distention can cause acute RF in patients with severe respiratory muscle weakness. Treatment strategies include increasing water and fibre intake, and using osmotic laxatives. Decompressive manoeuvres (i.e., placing nasogastric and/or rectal tubes) are the mainstay of acute management [105].

Based on these considerations, the following statements are suggested in the section on acute constipation due to bowel dysfunction.

6.1 Patients with NMDs and especially older patients can experience constipation due to abnormal gastrointestinal motility.

6.2 Gastric and/or abdominal distension can cause acute respiratory failure in patients at high risk of respiratory complications. In these cases, gastrointestinal decompression by nasogastric tube and/or rectal tube is often an effective therapy.

Other issues

Muscle can also be a source of elevation in serum aminotransferases. As a consequence, abnormal liver function tests are frequently observed in cases of myopathies. Serum aminotransferases lack tissue specificity to allow clinicians to distinguish primary liver injury from muscle damage [106,107]. This can raise the question of liver injury and often triggers a false pathway of investigation.

Based on these considerations, the following statement is included in EC.

7.1 Blood transaminases and creatine kinase levels may be increased in patients with myopathies. If other hepatic function tests (e.g., bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy liver disease and may be due to muscle involvement.

Discussion

This paper reports the results of the first Consensus Conference organized to build specific ECs for NMDs. Aim of the workshop was to agree on a minimum set of the most relevant management information and recommendations related to urgent care, and to produce ECs dedicated to patients with NMDs.

Consensus was reached on key issues and management of the main clinical problems requiring urgent care (i.e., acute RF, chocking, cardiac complications, anaesthesia, fractures and acute constipation) and are summarized in 4 tables and 37 statements. Based on these statements the CWG defined 13 ECs, one for each NMD, all sharing the same structure but with disease-related specificities.

Although NMDs may lead to severe disability and may shorten the life-expectancy, improvements in the function, quality of life and longevity of these patients have been achieved through a multidisciplinary management approach [2,4,8,10,11,12,14,18]. Consequently, when these patients come to the Emergency Department due to acute life-threatening complications, they deserve full appropriate care and treatment. In order to optimise patient outcomes, the medical providers should have a good background in the issues relevant for individuals with NMDs. However, these diseases are rare and are an uncommon cause of admission to Emergency Departments [33]. For this reason, the local ED physicians might be inexperienced in the management of these patients [5,34]. The ECs proposed in this paper may provide not only a rapid overview of key issues related to the more frequent acute complications in patients with NMDs, but also describe the background information which is required to better improve local urgent care.

We are aware that this study has several limitations. One may argue that the level of information is high for an acute setting, but we believe that providing the background of the disease issues for the specific domain or organ involved will help the physicians in the emergency setting. A second limitation may be that we considered different forms of NMDs, which may differ in terms of disease onset, progression and severity. However, many studies have shown that several NMDs share common features and issues concerning respiratory and cardiac impairment, swallowing difficulties and perioperative management, while retaining disease-specific problems [13,14,62,86]. Another limitation may be that many statements selected by the Consensus panel were mainly derived from observational studies and expert's opinion rather than evidence-based guidelines. However, prospective randomized controlled trials aimed at supporting the utility of some therapies such as NIV and MI-E, would be difficult to carry out for ethical reasons. Indeed, in developed Countries of the world NIV and MI-E are routinely used to treat patients with NMDs and acute respiratory complications.

In conclusion, this paper reports a minimum set of management recommendations for urgent care dedicated to patients with NMDs, suggested by a panel of Italian experts. Based on these statements, we propose an EC for each selected NMD. The usefulness of these ECs in improving local acute care will be verified in the acute setting and real-world evidence.

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Conflict of interest statement

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Not applicable.

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ON-LINE SUPPORTING INFORMATION

Table S1: Emergency card for patients with Spinal muscular atrophy (SMA) type 1

EMERGENCY CARD for patients with **Spinal muscular atrophy (SMA) type 1**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are always present (early onset; frequent exacerbation). Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and daytime hypoventilation.. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are always present. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Cardiomyopathy is very rare (only one 1 case reported). Conduction defects and arrhythmia are not reported. Structural cardiac abnormalities are occasional.
ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management. ✓ Familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Use of succinylcholine must be avoided to prevent succinylcholine-induced hyperkalaemia. Inhaled anaesthetics may be used. ✓ They may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex).

	✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Osteoporosis increases the risk of fractures ✓ In adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ Gastroesophageal reflux can occur in SMA. Symptoms may be subtle (weight loss, poor feeding, crying after feed or when lying down and coughing). If a gastrostomy is performed, and reflux is present, a Nissen fundoplication should be associated

Table S2: Emergency card for patients with Spinal muscular atrophy (SMA) type 2

EMERGENCY CARD for patients with **Spinal muscular atrophy (SMA) type 2**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are very frequent. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Cardiomyopathies, arrhythmias and structural cardiac abnormalities are occasional. Conduction defects are not reported.
ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management. ✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Use of succinylcholine must be avoided to prevent succinylcholine-induced hyperkalaemia. Inhaled anaesthetics may be used. ✓ They may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported.

	✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility. ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ Gastroesophageal reflux can occur in SMA. Symptoms may be subtle (weight loss, poor feeding, crying after feed or when lying down and coughing). If a gastrostomy is performed, and reflux is present, a Nissen fundoplication should be associated.

Table S3: Emergency card for patients with Spinal muscular atrophy (SMA) type 3

EMERGENCY CARD for patients with **Spinal muscular atrophy (SMA) type 3**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are occasional. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation.. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are occasional. ✓ Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Cardiomyopathies, arrhythmias and structural cardiac abnormalities are occasional. Conduction defects are not reported.
ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management. ✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Use of succinylcholine must be avoided to prevent succinylcholine-induced hyperkalaemia. Inhaled anaesthetics may be used. ✓ They may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex).

	✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ Gastroesophageal reflux can occur in SMA. Symptoms may be subtle (weight loss, poor feeding, crying after feed or when lying down and coughing). If a gastrostomy is performed, and reflux is present, a Nissen fundoplication should be associated

Table S4: Emergency card for patients with Charcot-Marie-Tooth disease (CMT)

EMERGENCY CARD for patients with **Charcot-Marie-Tooth disease (CMT)**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are occasional in some subtypes. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation.. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are occasional. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Not reported
ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management. ✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Use of succinylcholine must be avoided to prevent succinylcholine-induced hyperkalaemia. Inhaled anaesthetics may be used. ✓ They may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported.

	✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ Pain is a very common. It can be caused by altered loading of the joints, because of muscle weakness, or neuropathic pain, owing to damage to the pain nerve endings.

Table S5: Emergency card for patients with Duchenne Muscular Dystrophy

EMERGENCY CARD for patients with **DUCHENNE MUSCULAR DYSTROPHY (DMD)**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are always present in adulthood. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). In case of long-bone or vertebral fractures consider fat embolism syndrome if patient has dyspnoea or altered mental status. Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are always present in the late stage of the disease. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy and arrhythmia are very frequent. Conduction defects are occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement. ✓ In case of chronic corticosteroid therapy consider adrenal insufficiency. Determine whether stress steroid dosing is necessary. For critical adrenal insufficiency, administer 100 mg hydrocortisone by slow intravenous injection or intramuscular. In less critical situations, consult the PJ Nicholoff Steroid and obtain early consultation with an endocrinologist.

Table S6: Emergency card for patients with Becker Muscular dystrophy (BMD)

EMERGENCY CARD for patients with **Becker Muscular dystrophy (BMD),**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are occasional. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). In case of long-bone or vertebral fractures consider fat embolism syndrome if patient has dyspnoea or altered mental status. Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are occasional. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy and arrhythmia are very frequent. Conduction defects are occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement. ✓ In case of chronic corticosteroid therapy consider adrenal insufficiency. Determine whether stress steroid dosing is necessary. For critical adrenal insufficiency, administer 100 mg hydrocortisone by slow intravenous injection or intramuscular. In less critical situations, consult the PJ Nicholoff Steroid and obtain early consultation with an endocrinologist.

Table S7: Emergency card for patients with Myotonic dystrophy type 1 (DM1)

EMERGENCY CARD for patients with **Myotonic dystrophy type 1 (DM1)**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. Central sleep apnoea are also reported. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are very frequent. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Conduction defects and arrhythmia are very frequent. Dilated cardiomyopathy is occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV. ✓ In these patients respiratory insufficiency may be caused both by weakness or myotonic reactions, which may involve laryngeal and respiratory. Many factors like hypothermia, postoperative shivering, dyskalemia, mechanical and electrical stimulation or drugs (i.e., propranolol, succinylcholine and anticholinesterase agents) can precipitate myotonic contractures. Myotonia occurs for an intrinsic change in the muscle and not in the peripheral nerve or neuromuscular junction. Thus, it cannot be abolished by peripheral nerve blockades or neuromuscular blockers. Myotonia may be treated with midazolam, otherwise the treatment is mainly preventive, avoiding all triggering factors.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases, gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement. ✓ Intellectual impairment and cognitive dysfunction are often present. ✓ Excessive daytime sleepiness (EDS) is common and is most often owing to CNS involvement. Sleep apnoea and chronic respiratory failure also need to be considered and sleep study should be considered to assess possible obstructive sleep apnoea and CNS mediated sleep apnoea. ✓ DM1 may be associated with insulin resistance and cataract.

Table S8: Emergency card for patients with Facio-scapulo-humeral muscular dystrophy (FSHD)

EMERGENCY CARD for patients with **Facio-scapulo-humeral muscular dystrophy (FSHD)**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are occasional. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are occasional. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy, conduction defects and arrhythmia are occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management. ✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible.

	✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement. ✓ Conjunctivitis and ulceration of the cornea can occur owing to limited blinking and inability to properly close the eyes, also when sleeping.. ✓ Substantial facial muscle weakness may lead to misinterpretation of emotional expression, particularly in those with severe, childhood-onset FSHD.

Table S9: Emergency card for patients with Limb girdle muscular dystrophy (LGMD)

EMERGENCY CARD for patients with **Limb girdle muscular dystrophy (LGMD)**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent in some subtypes (LGMD1, LGMD2C/D/E/F). Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation.. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are occasional in some subtypes. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy is very frequent in some subtypes (LGMD1B and LGMD2C/D/E/I). Conduction defects and arrhythmia are occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement. ✓ Some subtypes of LGMD can have central nervous system involvement with intellectual disability and/or epilepsy and, rarely, movement disorders.

Table S10: Emergency card for patients with Congenital muscular dystrophy (CMD)

EMERGENCY CARD for patients with **Congenital muscular dystrophy (CMD)**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent in some subtypes (Ullrich's CMD, LAMA 2 deficient CMD). Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are frequent in some subtypes. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy is frequent in Fukuyama CMD and occasional in other subtypes. Conduction defects and arrhythmia are occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement.

Table S11: Emergency card for patients with Congenital Myopathies

EMERGENCY CARD for patients with **Congenital Myopathies**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent in some subtypes (Nemaline, Myofibrillary and Centro-nuclear CM). Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that in these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are frequent in some subtypes. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy, conduction defects and arrhythmia (Long QT) are occasional. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis and malignant hyperthermia. ✓ Malignant hyperthermia is a medical emergency characterized by pathological hyperthermia, muscle rigidity, and hypermetabolism in response to triggering anaesthetic agents (i.e., succinylcholine and inhaled anaesthetics), It must be treated with dantrolene and additional supportive care measures. ✓ They may experience increased sensitivity to sedatives, anaesthetics agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement.

Table S12: Emergency card for patients with Mitocondrial myopathies

EMERGENCY CARD for patients with **Mitocondrial myopathies**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent (Progressive, infantile onset and late onset). Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation. Abnormality of respiratory drive due to dysfunction of the respiratory centers are very frequently reported in pediatric cases ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that n these patients tracheal intubation may be difficult. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are frequent (more often due to central involvement than primary muscular impairment). Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy is very frequent Conduction defects and arrhythmia are frequent. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist.
ANAESTHETIC PRECAUTIONS AND PERIOPERATIVE MANAGEMENT	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management. ✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia.

	✓ As these patients may have increased lactate levels during periods of physiological stress, preoperative fasting could be particularly hazardous. Thus, i.v. isotonic fluid containing dextrose (e.g., 0.9% sodium chloride with 5% dextrose) should be started during preoperative fasting period to allow maintenance of normoglycemia to avoid excessive glycolytic oxidation that may increase plasma lactate levels. ✓ Use of succinylcholine must be avoided to prevent rhabdomyolysis. Inhaled anaesthetics can be administered in order to avoid prolonged use of propofol, which can increases lactic acidosis. ✓ They may experience increased sensitivity to sedatives, inhaled anaesthetics and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general a and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 should not be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures. ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required. ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ A major clue to mitochondrial disease is a multisystem involvement, that may include: o Brain – stroke-like episodes, seizures, myoclonus, ataxia, developmental delay or regression, dementia, migraine, and dystonia o Eye – pigmentary retinopathy, optic atrophy, and cataracts o Neuropathy and dysautonomia o Endocrine – diabetes and hypoparathyroidism o Kidney – proximal nephron dysfunction and glomerulopathy o Gastrointestinal – altered motility, liver disease, episodes of nausea and vomiting, and exocrine pancreatic dysfunction o Hematologic – sideroblastic anaemia and pancytopenia o Metabolic acidosis due to elevated levels of lactate ✓ Lactate levels may be elevated, normal or only minimally elevated. These patients may have elevated lactate levels only during periods of physiologic stress. It is controversial whether IV sodium bicarbonate should be used. Many authors recommended that it should be reserved for cases of extreme acidosis when the blood pH is <7.2. ✓ Intellectual impairment and cognitive dysfunction may be present. ✓ Mitochondrial myopathies may worsen during periods of increased physiologic stress, such as an illness or surgery/anaesthesia. During these periods rhabdomyolysis may occur. ✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement.

Table S13: Emergency card for patients with Metabolic (Glycogen storage) myopathies

EMERGENCY CARD for patients with **Metabolic (Glycogen storage) myopathies**	
Name _____ Date of birth _____ Fiscal Code _____ If presenting at an emergency department, contact the neuromuscular and/or respiratory team at: _____as soon as possible on: _____	
MAIN TOPICS	***MOST RELEVANT INFORMATIONS AND RECOMMENDATIONS RELATED TO THE EMERGENCY CARE***
ACUTE RESPIRATORY INSUFFICIENCY	✓ Respiratory complications are frequent in Glycogen storage disease type II (Pompe Disease) both in infantile and late onset form. Respiratory muscles weakness can compromise pump function of the respiratory system, upper airway muscles tone and efficiency of secretion clearance. The respiratory consequences are secretion retention, upper airway obstruction, nocturnal and finally daytime hypoventilation.. ✓ Respiratory infections (i.e., tracheobronchitis or pneumonia) are the most frequent cause of acute respiratory failure and require early management. Low threshold for empiric antibiotic therapy is recommended for chest infections. ✓ If no infectious cause of acute respiratory failure is evident, consider non-infectious causes (e.g., pneumothorax or atelectasis). Cardiogenic pulmonary oedema should be also ruled out. ✓ Collect respiratory symptoms and monitor SpO2 levels via pulse oximetry; even mild hypoxaemia (e.g., SpO2 <95% in room air) is a concern and requires a chest x-ray and a blood gas analysis test. Chest x-ray may be difficult to interpret, especially in the presence of scoliosis. In this case chest CT scan may be useful in order to rule out pneumothorax, pneumonia or atelectasis. If even chest CT scan does not show any cause for acute RF, it is useful to deepen the examination by administering contrast medium to exclude a pulmonary thromboembolism. ✓ NIV is often required. In addition, assisted coughing (i.e., breath-stacking techniques with an Ambu bag combined with compression of the chest wall or abdomen) or cough assist device (MI-E) help to clear airways secretions. Use the patient's home equipment when available. ✓ O2 must never be used without associating it with NIV. If supplemental oxygen is required titrate oxygen therapy to achieve SpO2 94-98% and monitor CO2. ✓ In case of an acute, reversible event intubation and invasive ventilation is indicated when NIV failure occurs (unless there is a known advance directive stating otherwise). When indicated tracheal intubation must not be delayed. Consider that n these patients tracheal intubation may be difficult due to jaw ankylosis, atrophy of the masseter muscle and/or other masticatory muscles, macroglossia or limited mobility of the cervical spine. ✓ After recovery from the acute illness, these patients should be promptly extubated to NIV combined with MI-E. Tracheotomy can be evaluated in particular in patients with severe bulbar dysfunction. However, in the acute phase it should be considered only in the case of multiple failures of weaning protocol including preventive application of NIV combined with MI-E after extubation.
CHOCKING DUE TO SWALLOWING DIFFICULTIES	✓ Swallowing difficulties are frequent in Infantile onset Pompe Disease, rare in late onset Pompe Disease. Signs and symptoms of swallowing difficulties such as a meal time longer than 30 minutes, recurrent chest infections, unintentional weight loss, and choking when eating or drinking should be considered. ✓ Severe bulbar dysfunction increases the patient risk for aspiration and hampers the elimination of airway secretions. In addition, it may impede successful use of NIV. ✓ In case of choking use MI-E or manual assisted coughing; if it is ineffective consider emergent tracheal intubation
ACUTE CARDIAC COMPLICATIONS	✓ Dilated cardiomyopathy is very frequent in some subtypes (type II, III, IV, VII and IX). In the infantile form of Pompe disease hypertrophic cardiomyopathy may be present. Conduction defects and arrhythmia are frequent. However, clinical manifestations of heart failure are often unrecognized until very late, owing to musculoskeletal limitations. ✓ Consider worsening cardiomyopathy and rule out congestive heart failure, atrio-ventricular blocks and arrhythmias. ✓ Ask for the patient's baseline test results, including echocardiogram and electrocardiogram. ✓ Obtain a brief history with a focus on baseline cardiac status, including use of medications. ✓ Ask about cardiac symptoms and monitor heart rate rhythm, blood pressure and SpO2. ✓ Measure blood levels of B-type natriuretic peptide and obtain an electrocardiogram; a chest radiograph and/or chest ultrasound may be useful if pulmonary oedema is suspected. ✓ Obtain an echocardiogram and early consultation with a cardiologist. ✓ In these patients blood level of cardiac Troponin T (cTnT) may be chronically high, while blood level of cardiac Troponin I (cTnI) are more rarely high. Consequently, in the case of suspected myocarditis or myocardial ischemia, it is recommended to measure cTnI.
ANAESTHETIC PRECAUTIONS AND	✓ Ideally, surgery should occur in a specialist centre with staff experienced in managing these individuals. Otherwise, the urgent surgical interventions may be performed in non-specialized centres following recommendations regarding anaesthesia and perioperative management.

PERIOPERATIVE MANAGEMENT	✓ Obtain a pre-operative evaluation including lung function tests and cough assessment; if respiratory muscle weakness is present (i.e. forced vital capacity less than 50% of predicted value or peak cough less than 270 l/min), familiarization with ventilatory support (i.e., MI-E and NIV) should be warranted prior to procedure whenever possible. ✓ Patients should also undergo careful assessment of heart function as well as optimization of cardiac therapies in the pre-operative period. An electrocardiogram and echocardiogram should be performed before anaesthesia. ✓ Use of succinylcholine and inhaled anaesthetics must be avoided to prevent rhabdomyolysis ✓ They may experience increased sensitivity to sedatives, anaesthetic agents and muscle relaxants; thus, the depth of anaesthesia and the neuromuscular function should be monitored in order to titrate the appropriate dose of those drugs. In addition, the effect of muscle relaxants should be completely reversed at the end of surgery (i.e., rocuronium should be used and must be reversed by sugammadex). ✓ In the infantile form of Pompe disease with significant hypertrophic cardiomyopathy, decreased cardiac output and myocardial ischemia have been observed during anaesthesia. In fact, stiffness of the hypertrophied ventricular walls can induce abnormal diastolic relaxation and lead to dynamic left ventricular outflow tract obstruction, elevated left ventricular end-diastolic pressure and reduced diastolic filling. Such a condition may precipitate as a consequence of a decrease in systemic vascular resistance, preload, or both eventually induced by anaesthetic agents, with an increased risk of intraoperative cardiac arrest. ✓ Tracheal intubation may be difficult in patients with NMDs and frequent use of fibreoptic-assisted endotracheal intubation is reported. ✓ The use of regional or local anaesthesia offers a significant advantage in term of avoidance of general anaesthesia and reduction of postoperative respiratory complications. ✓ Morphine infusions should be avoided, mainly in patients with reduced respiratory function or obstructive sleep apnoea ✓ Admission to an Intensive Care Unit should be considered in any patient who is at risk for respiratory or cardiac complications. Patients with decreased respiratory muscle strength require close monitoring and aggressive post-operative respiratory management including early extubation to NIV with aggressive use of MI-E. O2 must never be used without associating it with NIV.
FALLS AND FRACTURES	✓ Owing to weakness, contractures and poor balance, patients with NMDs are at high risk of frequent falls. On the other hand, osteoporosis increases the risk of fractures ✓ In ambulatory adult patients, internal fixation of femoral fracture is preferable to conservative treatment because it allows early walking recovery, preserving muscle function. ✓ In non-ambulatory adult patients, conservative treatment can be considered in case of non-displaced sub capital femoral neck fracture. On the contrary, in diaphyseal or trochanteric femoral fracture internal fixation is required ✓ In paediatric patients the treatment of femoral fractures is strictly related with the age of the child, the site of the fracture and the disability related to muscle weakness. Conservative treatment can be considered in patients under 5-6 years of age, with non-displaced fractures and when a short period of immobilization is expected. In the other cases surgical fixation using minimally invasive techniques is preferred (e.g., percutaneous fixation by Kirshner wires and plaster casts, Flexible Intramedullary Nailing or light external fixators).
ACUTE CONSTIPATION DUE TO BOWEL DYSFUNCTION	✓ Some patients can experience constipation due to abnormal gastrointestinal motility ✓ Gastric and/or abdominal distention may cause acute respiratory failure in patients at high risk of respiratory complications. In these cases gastrointestinal decompression by using of a nasogastric tube and/or rectal tubes is often an effective therapy.
OTHER ISSUES	✓ In these patients blood levels of transaminases and creatine kinase may be increased. If other hepatic function tests (e.g. bilirubin and gamma GT) are normal, this pattern doesn't necessarily reflect hepatopathy and may be due to muscle involvement. ✓ Metabolic myopathy presenting with exercise intolerance (e.g. McArdle's disease) may present with acute rhabdomyolysis with severe hyperCKemia, muscle pain, and myoglobinuria. During such events, there is a risk of acute renal failure.