هيئة الصحة بدبي
DUBAI HEALTH AUTHORITY

إجادة
EJADA

EJADA Program

Spinal Muscular Atrophy

KPIs and Recommendations

2024

Spinal Muscular Atrophy

KPIs and Recommendations

Content

Introduction

Spinal Muscular Atrophy (SMA) is a severe genetic disorder that affects the motor neurons in the spinal cord, leading to muscle weakness and atrophy. Despite advances in treatment, patients with SMA continue to face significant unmet needs. SMA affects approximately 1 in 20,000 babies, with no gender bias, underscoring the importance of addressing these needs universally.

The unmet needs of SMA patients span several dimensions, including the lack of robust treatment guidelines, limitations in diagnosis and cure, and inadequate supportive care. These gaps highlight the need for a more holistic approach to SMA care that goes beyond pharmacological treatments. Furthermore, a systematic review on caregiver burden under- scores the challenges related to mobility, breathing, swallowing, communication, caregiving, accessing appropriate medical care, and managing psychological and emotional aspects of the disease, pointing to the need for comprehensive support systems for both patients and their caregivers.

The current guidelines review the current diagnostic criteria for SMA and the scientific evidence supporting treatment at different stages of the disease, as well as the required multidisciplinary assessment and intervention required to support patients with SMA. The purpose of these guidelines is to provide practical recommendations and algorithms for the diagnosis and treatment of SMA based on current scientific evidence and clinical experience.

Scope

The Ejada KPIs are quality indicators and ratings for physicians, facilities and insurance companies based on information collected by DHA systems from providers, payers and patients. Pediatric neurologists, physiotherapists, pediatricians, occupational therapists, dentists and maxillofacial surgeons practicing in the UAE with experience in the management of SMA, met at a series of workshops sponsored by Dubai Health Authority (DHA) and Dubai Health Insurance Corporation (DHIC), to identify previously published guidelines for management of SMA, and draft guidelines for diagnosis, treatment, and management of SMA in Dubai.

To ensure accuracy and coherence, this document consolidates various sources, addressing contradictions, incorporating updates, and incorporating additional information where necessary. These sources include:

- Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care (E. Mercuri et al, 2018)
- Diagnosis and management of spinal muscular atrophy: Part 2: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care (E. Mercuri et al, 2018)
- Disease Modifying Therapies for the Management of Children with Spinal Muscular Atrophy (5q SMA): An Update on the Emerging Evidence (Helgi Thor Hjartarson1 et al, 2022)

List of Abbreviations

Sr No	Abbreviations	Full Form
1	6MWT	6 minutes walk test
2	ADL	Activities of daily living
3	CHOP INTEND	Children's Hospital Of Philadelphia Infant Test Of muscular Disorders
4	CPAP	Continuous positive airway pressure
5	DEXA	Dual energy X-Ray absorptiometry
6	DHA	Dubai Health Authority
7	DHIC	Dubai Health Insurance Corporation
8	FRC	Functional Residual Capacity
9	GMFM	Growth motor functional measure
10	HFMSE	Expanded Hammersmith Functional Motor Scale
11	HINE	Hammersmith Infant Neurologic Examination
12	IPAP	Inspiratory positive airway pressure
13	MFM	Motor Function Measure
14	MLPA	Multiplex ligation-dependent probe amplification
15	MRC	Medical Research Council
16	NIV	Non-invasive ventilation
17	NSAA	Northstar ambulatory assessment
18	PCR	Polymerase chain reaction
19	RH	Revised Hammersmith
20	ROM	Range of motion
21	RSV	Respiratory syncitial virus
22	RULM	Revised Upper Limb Module
23	SMA	Spinal muscular atrophy
24	SMN	Survival motor neuron
25	TIMP	Tes of infant motor performance

Neuro-

KPIs and their measuring parameters

Sr No	Key performance indicators	Measuring parameters
1	Screening of newborn	Medical records
2	Frequency of assessment	Neurology, rehabilitation, nutri- tionist, dietitian, pediatric den- tistry, orthopedic and respirato- ry consultation
3	CHOP INTEND Score for patients with SMA	CHOP INTEND score as per medical records
4	HINE Score for patients with SMA	HINE score as per medical re- cords
5	MFM-20 Score for patients with SMA	MFM-20 score as per medical records
6	GMFM Score for patients with SMA	GMFM score as per medical re- cords
7	RH Score for patients with SMA	RH score as per medical records
8	6-MWT Score for patients with SMA	6-MWT score as per medical re- cords
9	RULM Score for patients with SMA	RULM score as per medical re- cords
10	Evolution of the degree of scoliosis for pa- tients with SMA	X-Ray
11	NSAA score for patients with SMA	NSAA score as per medical re- cords
12	TIMP score for patients with SMA	TIMP score as per medical re- cords
13	Longitudinal anthropometrics score for pa- tients with SMA	Medical records
14	Cough peak flow in patients with SMA	Medical records

Screening and diagnosis of spinal muscular atrophy

Unless there are previous familial cases, the diagnostic process is generally prompted by the clinical signs. Clinically, these infants present with:

1. Hypotonia
2. Progressive symmetric and proximal weakness affecting the legs more than the arms.
3. Sparing of the facial muscles but often with bulbar muscle weakness.
4. There is also weakness of the intercostal muscles with relative sparing of the diaphragm, which results in the typical "bell-shaped" chest and paradoxical breathing pattern.

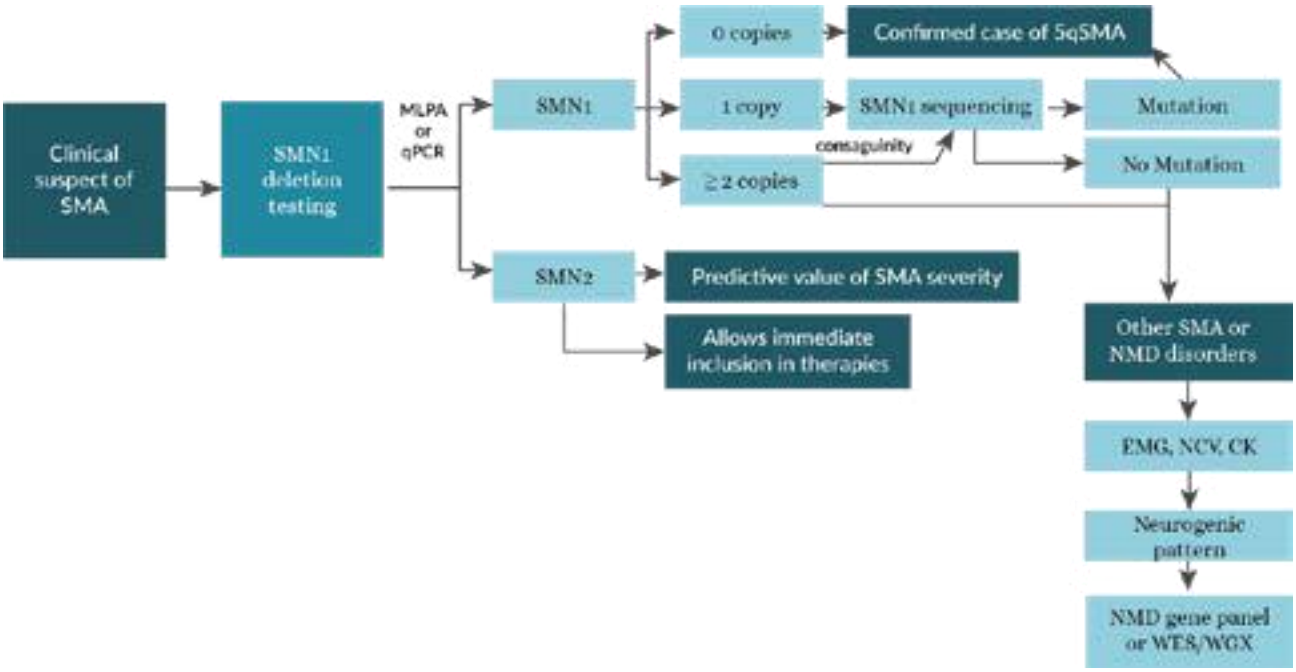
It has to be noted that:

1. Approximately 96% of patients, SMA is caused by homozygous absence of exons 7 and 8 of the SMN1 gene, or, in some cases, only of exon 7.
2. The majority of patients inherit the SMN1 deletion from their parents; in 2% de-novo deletions in one of the 2 alleles have been described. In 3–4%, other mutations in SMN1 can be found, typically with an SMN1 deletion on the other allele.

Screening for Spinal Muscular Atrophy

Routine screening for Spinal Muscular Atrophy (SMA) shall be offered to all newborns. This screening should employ real-time PCR (qPCR) as the first-tier methodology or multiplex ligation-dependent probe amplification (MLPA). The objective is to identify the deletion of exon 7+/-8 in SMN1.

Diagnosis of Spinal Muscular Atrophy



Managing Spinal Muscular Atrophy in a multidisciplinary approach

Upon the confirmation of positive SMN1 detection cases, it is essential to engage all fami- lies in genetic counseling. This counseling will not only provide crucial information but also offer guidance for future pregnancy planning.Families with a member diagnosed with SMA will be assigned a designated single point of contact within the field of Pediatric Neurology and/or Pediatric Neurorehabilitation. This professional will play a pivotal role in coordinat- ing the necessary care across various specialties within a multidisciplinary team.

The multidisciplinary team shall cover the following:

1. Pulmonary care
2. Acute care
3. Orthopedic and spine
4. Spine Rehabilitation
5. Oral & Maxillofacial
6. Gastroenterology
7. Nutritionist
8. Cardiologist
9. Physiotherapist
10. Feeding & Swallowing
11. General Pediatric

Management of asymptomatic Spinal Muscular Atrophy patients

Asymptomatic / presymptomatic patients shall be closely monitored for their developmen- tal progression every 3-6 months based on the clinical recommendations. Those patients are candidates for Spinal Muscular Atrophy therapies.

Assessment of symptomatic Spinal Muscular Atrophy patients

All assessments shall be performed routinely every 3-6 months unless there are special cir- cumstances requiring different follow up.

Recommended assessments

	Non-sitters	Sitters	Walkers
Oral assessment	✓	✓	✓
Postural control	✓	✓	✓
Scoliosis	✓	✓	✓
Hip dislocation	✓	✓	✓
Contractures	✓	✓	✓
Muscle weakness	✓	✓	✓
Functional scales	✓	✓	✓
Sitting tolerance	✓		
Foot deformity		✓	
Mobility			✓
Chest deformity	✓	✓	
Motor development	✓		
Endurance			✓

	Non-sitters	Sitters	Walkers
Pelvic obliquity		✓	
Falls			✓
Bedisde swallowing assessment	✓	✓	✓
Modified barium swallow fluoro-scopic study	✓		
Evaluation of length and weight	✓	✓	
DEXA	✓	✓	
Vitamin D levels	✓	✓	
Feeding evaluation		✓	
Evaluation of fluid & fiber intake		✓	
Obesity monitoring		✓	✓
Pulse oximetry	✓		
Capnography	✓		
Sleep study	✓	✓	✓
Pneumogram with CO_2 recording	✓		
Spirometry		✓	
Cough effectiveness			✓

Recommended assessment techniques

Oral assessment

- Evaluation of Maximal Mouth Opening should be done in all the children. Also, these children should be assessed for an-kyloglossia, Lip tie, shape of the palate, high arched or wide palate, Relative tongue size
- Masseter muscle tonicity as these can affect chewing and swallowing function.
- They should also assess dentition status (Early, Normal or Delayed)
- Presence of gingival hyperplasia should be evaluated and treated in severe case surgically.
- The above should be assessed by Oral Physician, Dentist Trained in Special needs Dentistry when possible

Contractures Muscle weakness Functional scales Motor development	ROM, Goniometry MRC grading, strengths tests CHOP INTEND, HFMSE, RULM, MFM HINE, Bayley-4
Endurance	6MWT
Capnography	End tidal CO_2 ($P_{Et}CO_2$) or transcutaneous CO_2 ($P_{Tc}CO_2$)

Rehabilitation management in symptomatic Spinal Muscular Atrophy patients Stretching

Non-sitters	Sitters	Walkers
• Orthoses and splints, active-assistive and passive techniques, supported supine/ standing/standing frames and serial casting. • Thoracic bracing is recommended for postural stabilization and to promote function. • Cervical bracing is often used for head support particularly to minimize risk of asphyxiation while upright. • Upper and lower limb orthoses are used to promote function and range of motion. • Mild isotonic midrange stretches to maintain the muscle length band promoting passive/assisted mobility as well as improving Neuromuscular properties of the muscle. • Mild isotonic, midrange stretches to maintain the muscle length promoting passive assist mobility as well as improving neuromuscular properties of the muscle.	• Modalities for stretching include techniques that can be achieved manually and through the use of orthoses, splints, active-assistive stretching, support- ed standing/standing frames and positioning techniques such as serial casting. • Stretching modalities should be performed and/or supervised by physical or occupational therapists. • Joint approximations to promote weight bearing on the upper limbs to facilitate neuromuscu- lar control. • Weight bearing on lower limbs should be done without Orthosis as well as with orthosis intra-sessions of physiotherapy as it is shown to improve the knee control in sitters. • Parents and caregivers should also be instructed in daily stretching activities. • Session duration for effective stretching depends on specific patient needs, joints, and rehabilitation aims.	• Passive stretching and active-assistive techniques. • Lower limb orthoses are mainly used for maintaining flexibility, posture and function at the ankle and knee. • Thoracic bracing is not typically used during walking as it may adversely affect ambulation ability and limit effective compensatory strategies but, when needed, may be used to promote posture in sitting.

Positioning

Non-sitters	Sitters	Walkers
• Seating systems and postural supports that shall supine positioning with rolls, beanbags, molded pillows or wedges. • Custom and molded wheelchair seating systems as well as custom sleeping sys- tems are recommended. To promote mobility and transfers the use of strollers and power wheelchairs with re- cline/tilt options and adapted seating sys- tems are recommended. • Mandatory review peri- ods of 3 months should be emphasized in case of orthosis as well as aggressive monitoring of postural deformities. • Education and cues to parents by advising them to take pho- tographs and videos periodically can be an added monitoring data as well.	• Thoraco-lumbar sacral orthoses are recom- mended for posture and to promote func- tion. • Cervical bracing is often used for safety and transportation. • Usually in sitters we do encourage them to sit independent of cervi- cal supports as thora- columbar corsets are stabilizers for the neck in such cases. • Static, dynamic and functional orthoses are used for positioning and standing and, when possible, for supported ambulation. • Supported standing is important to facil- itate lower extremity stretching but also to promote bodily func- tions and bone health, enable upright partic- ipation, and promote spine and trunk pos- ture.	

Mobility and exercise

Non-sitters	Sitters	Walkers
• Assistive technology and adaptive equip- ment are recommend- ed.	• Oral exercises, Intra and extra oral should be ad- vised to the parents as the regimen, which they should do at least three times a day.	• Balance exercise, both dynamic and static forms. • Functional Activities or ADL should be incorpo- rated in Mobility exer- cises.

Non-sitters	Sitters	Walkers
• The use of eye tracking devices is recommend- ed to improve commu- nication. • Some non-sitters can participate safely in aquatic therapy with proper head and neck support and constant supervision. • Tactile cues are also helpful in non-sitters to initiate movements.	• All sitters should have electric/power wheel- chairs with custom postural support and seating systems. As- sessments for power wheelchair mobility can begin before 2 years of age. • Light-weight manual wheelchairs or power assist wheels are ideal to promote self- pro- pulsion in stronger patients. • Exercise programs and activities that encour- age muscle activation should be encouraged since it can have an effect on maintaining and improving function, strength, range of mo- tion, endurance, bal- ance, activities of daily living, and participation in school, social activ- ities and occupation. Recommended exer- cise for sitters include aquatic therapy, con- centric and eccentric exercise and aerobic and general condition- ing exercise with and without resistance.	• Exercise programs and activities that encour- age muscle activation should be encouraged. Recommended exer- cise for walers includes aquatic therapy, con- centric and eccentric exercise and aerobic and general condition- ing exercise with and without resistance. • Lightweight manual wheelchairs or power assist wheels are rec- ommended when en- durance is limited. Simi- larly, electric/ power wheelchairs or powered scooters may also be considered. • Graded gradual weight bearing exercises pro- gression to resisted exercises especially in larger groups namely gluts and antigravity muscles should be en- couraged. • Use of Surged Faradic stimulation to promote muscle contractions with dynamic activities can be an added initia- tive for faster muscle recruitment.

Respiratory

Non-sitters	Sitters	Walkers
• Chest Physiotherapy: Manual techniques include percussion, vibration and position-ing to promote postural drainage. • It is recommended to incorporate assist- ed upright sitting (as tolerated) and Chest drainage procedures prior and intra sessions especially for tracheos-tomized patients . • Upright assisted sitting and mobility exercises promotes respiratory endurance and does have a factor of fatigue which should be timed, and progression should be monitored subse- quent sessions.	• Chest Physiotherapy: Manual techniques include percussion, vibration and position-ing to promote postural drainage. • Incentive spirometry to promote inspiratory capacity and acapella Deceives to promote coughing can be en-couraged in conjunction with Respiratory team.	

Nutritional and swallowing management in symptomatic Spinal Muscular Atrophy patients

Non-sitters

Interventions	Notes
• Oral exercises (intra and extra oral) should be advised to the parents. • For proactive care following a failed swallow study or growth failure, placement of a short-term nasogastric or nasojejunal tube is recommended until long term gastrostomy tube can be placed • Many experts prefer that Nissen fundoplication be performed in conjunction with gastrostomy tube placement secondary to decreased gastrointestinal motility, reflux, and increased pressure related to respiratory treatments	• Oral exercises to be done at least three times a day • DEXA to be performed yearly • Vitamin D levels at least every six months, unless there is a clinical indi-cation to increase the frequency, particularly in cases of osteopenia.

Interventions	Notes
• Diet type and administration should be based on individual tolerance • Adequate hydration as well as bowel regulating agents, probiotics, and motility medications are recommended to ease symptoms of constipation and gastrointestinal dysmotility. • During acute care, it has been strongly suggested that fasting should be avoided to prevent including metabolic acidosis, fatty acid metabolism abnormalities, and hyper/hypoglycemia. Adequate hydration and electrolyte balance is imperative during illness.	

Sitters

Interventions	Notes
• Feeding tubes are commonly used for supplementary nutrition rather than total nutrition and suggestions for feeding tubes and GI surgical recommendations depend on the individual situation. • Calories, protein, fat and carbohydrate, are initially estimated using common standardized equations and should be adjusted as appropriate growth and labs indicate. • Fasting times should be limited during acute circumstances and electrolyte and fluids should be moni- tored and repleted as indicated • Depending on severity of constipation, fiber intake, probiotics, and bowel regulating agents may be used to improve symptoms. • Oral exercises (intra and extra oral) should be advised to the parents. • Growth modifications of maxilla and mandible can be considered by utilizing Myofunctional Appliances for correction of cross bites, narrow arched palate and Retrognathism • In the case of frequent fracture, review may be given to use of bisphosphonates.	• Nutrition evaluations are recommended after diagnosis and periodically, every 3–6 months for younger children and annual evaluations afterwards • Periodic Dual energy x-ray absorptiometry analysis (DEXA) to be done yearly • Vitamin D levels should be monitored at least annually, and supplements should be given in the presence of low levels or of osteopenia • Oral exercises to be done at least 3 times per day

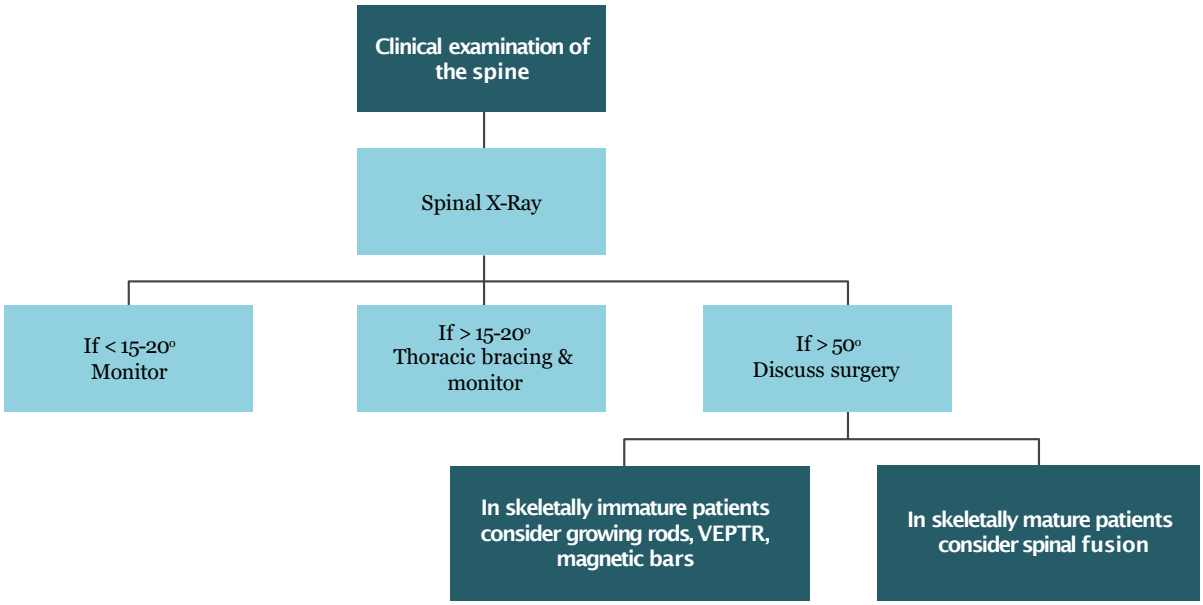
Walkers

Interventions	Notes
• In the case of frequent fracture, review may be given to use of bisphosphonates.	• Periodic DEXA to be done yearly

Interventions	Notes
• Focus should be on improving flexibility of the neck and temporomandibular joint, tactile oral stimulation, passive and active oropharyngolaryngeal exercises, and supraglottic swallowing maneuvers • Growth modifications of maxilla and mandible can be considered by utilizing Myofunctional Appliances for correction of cross bites, narrow arched palate and Retrognathism Dysphagia.	• Vitamin D levels should be monitored at least annually, and supplements should be given in the presence of low levels or of osteopenia

Orthopaedic management in symptomatic Spinal Muscular Atrophy patients

Spine deformity management



Chest deformity, thoracic insufficiency and pulmonary health management

Children with hypotonic scoliosis treated with either rib- or spine-based growth-friendly instrumentation systems have shown poor efficacy in ameliorating parasol rib deformity or increasing thoracic volume, and therefore are not recommended

Hip instability management

Unilateral and bilateral hip instability should be surgically managed only in patients with significant pain or impaired function

Contractures management

Surgical management of contractures of the upper or lower extremities should be considered when they cause pain or impaired functions.

Fractures management

1. Closed treatment with cast immobilization is generally recommended for non-ambulatory patients, but prolonged cast immobilization (>4 weeks) that aggravates muscle wasting and disuse osteoporosis should be avoided.
2. Ambulatory patients with long bone fractures of the lower extremities and non-ambulatory patients with hip fractures generally benefit from surgical stabilization using intramedullary rods or bridging fracture plates to restore immediate bone stability to allow early range of motion of the extremity and to promote accelerated fracture healing.
3. In case of frequent fractures with evidence of osteopenia as evidenced by DEXA, it is recommended to use Bisphosphonates.

Respiratory management in symptomatic Spinal Muscular Atrophy patients

Non-sitters

Interventions	Notes
• A respiratory therapist should be involved to initiate, and support assisted airway clearance and respirato- ry range of motion therapy before the appearance of any symptom • Manual chest physiotherapy combined with mechan- ical insufflation–exsufflation (e.g., Cough Assist® or VitalCough®) should be the primary mode of airway clearance therapy and should be made available to all non-sitters. When initiating cough assist devices, the insufflation and exsufflation pressures should be increased gradually to 30–40 cm H_2O of positive or negative pressure, respectively, or instead increase them to the maximal tolerated pressure. • In the absence of significant parenchymal lung dis- ease with small airway obstruction and air trapping there is no significant risk of pneumothorax in us- ing the cough assist. While there is the potential of aerophagia and gastric distention in using the cough assist, this risk and the subsequent risk of aspiration can be mitigated in GTube venting to prevent gastric distention. • Airway clearance techniques should be introduced proactively in patients based on either clinical assess- ment of cough effectiveness or by measuring peak cough flow (not a routinely performed test in infants)	• Clinic visits are rec- ommended initially for every 3 months for non- sitting patients with SMA.

Interventions	Notes
• Oral suctioning with a mechanical suction pump and catheter is a critical part of airway clearance and should be used with any patient with an ineffective cough. • The high frequency chest wall oscillation (Vest) ther- apy does not improve clearance of secretions in the setting of an ineffective cough or improve clearance of secretions. • Non-invasive positive pressure ventilation (NIV) should be used in all symptomatic infants prior to signs of respiratory failure, to be “prepared” for respi- ratory failure, prevent/minimize chest wall distortion, and palliate dyspnea. • Continuous positive airway pressure (CPAP) should not be used to treat chronic respiratory failure but may be used with caution temporarily to help main- tain resting lung volume (functional residual capacity (FRC)) in younger patients who are unable to syn- chronize with the ventilator in NIV mode, and who are not markedly hypercapnic. • Interface selection and fitting to the patient by an ex- perienced clinician is strongly recommended, as was using at least two comfortable interfaces with differ- ent facial contact points and using a nasal interface initially. • The initiation of non-invasive ventilation (NIV) is advised through clinical titration,. It is not routinely recommended to exceed a maximum inspiratory pos- itive airway pressure (IPAP) value of 16 cmH_2O for children with neuromuscular disorders. Values sur- passing 18 cmH_2O should only be applied briefly for recruitment purposes • Tracheotomy ventilation is an option in selected pa- tients in whom NIV is insufficient or fails, or if there is no effective interface for providing ventilation. • Gastroesophageal reflux should be proactively man- aged.	

Interventions	Notes
• Nebulized bronchodilators should be available if bron- chospasm is suspected. Nebulized mucolytics, 3% or 7% hypertonic saline or dornase-β should not be used long-term as there is no evidence to support its use. Furthermore, if 3% or 7% saline is used beyond the therapeutic need it can thin secretions of normal viscosity thereby increasing secretion burden. • Glycopyrrolate should be used with caution to treat hypersalivation with great care to adjust the dose to attain the proper effect, and avoid over drying of secretions, which may contribute to the development of mucus plugs. There was no consensus for the injection of botulinum toxin into the salivary glands or other methods to reduce production of oral secre- tions.	

Sitters

Interventions	Notes
• Manual chest physiotherapy combined with mechan- ical insufflation-exsufflation (e.g., Cough Assist® or VitalCough®) should be made available to all patients with an ineffective cough. It should be introduced proactively in patients using either clinical assess- ment of cough effectiveness or by measuring peak cough flow. The issues related to settings are similar to those described for non-sitters. • Non-invasive positive pressure ventilation (NIV) should be used in all symptomatic patients. The best approach is individualized to each patient's need and quality of life. • A sleep study should be used to determine when a patient has sleep disordered breathing or respirato- ry failure and needs to use bilevel NIV, and to titrate settings • Continuous positive airway pressure (CPAP), with rare exceptions, should not be used. • The need for tracheostomy ventilation is less fre- quent than in non-sitters but in some weak sitters bilevel NIV can be insufficient or fail. As for non-sit- ters this should be a decision based on clinical status and discussion with the family and patient, if age appropriate.	• Clinic visits are rec- ommended, every 6 months for sitters

Interventions	Notes
• Nebulized bronchodilators should be available if there is high suspicion of asthma or a clear clinical im- provement after administration. Nebulized mucolytics should not be used long-term. • Annual influenza and pneumococcal immunizations should be administered per standard pediatric recom- mendations for patients with chronic neuromuscular conditions.	

Walkers

Interventions	Notes
• Supportive care should be provided when there are specific concerns identified in the clinical assessment. • Immunizations are the same as for sitters.	

Acute care management in symptomatic Spinal Muscular Atrophy patients

Acute care management at home

1. Individualized anticipatory care plans should be developed and include review of vital signs (e.g., oxygen desaturation and tachycardia) and symptom parameters and prompting escalation of care with specific recommendations for airway clearance, ventilation, nutrition, hydration, antibiotics, and emergency contact measures.
2. Supportive care should be provided when there are specific concerns identified in the clinical assessment.
3. When appropriate, families should be provided with homecare technology for monitoring respiratory function and providing related support, such as augmented secretion clearance, bilevel NIV to prevent hospitalization, and to optimize status prior to presentation. This equipment, when available, should be, brought by the family for possible use during transport.

Transportation to a medical facility and emergency department evaluation

1. Presentation to the closest facility should be considered based upon the goals of care, distance from a tertiary facility, availability of pediatric transport team, and other aspects such as environmental considerations.
2. Emergency medical services should be provided by certified staff who have the capacity to provide the most appropriate level of ventilation and cardiac and respiratory life support.
3. Mode of transportation between home and acute care facility should be considered on

a case-by-case basis involving the neuromuscular team.

Recommendations for acute care management at medical care site

1. Respiratory assessment and support should be of highest priority
2. The management approach should encompass proactive measures, including:
   a. The optimization of bilevel positive airway pressure (NIV rather than CPAP) respiratory support
   b. Incorporating a backup respiratory rate administered through noninvasive meth- ods, tracheostomy, or an endotracheal tube.
   c. Enhanced secretion clearance should precede empiric oxygen supplementation.
   d. Whenever feasible, it is advisable to utilize the patient's own ventilator and mask. However, in cases involving atelectasis and heightened oxygen requirements, a tran- sition to full face or oronasal interfaces is recommended. This transition minimizes leaks and facilitates improved lung recruitment.
   e. If necessary, patients can be transferred to hospital-based specific NIV ventilators, particularly when the medical team is more proficient in their use.
3. Oxygen supplementation:
   a. Should not be provided empirically in the absence of NIV or without monitoring CO2 gas exchange.
   b. Should not be withheld but weaned to minimal provision prior to extubation and not employed in lieu of positive pressure ventilatory support.
   c. When supplemental oxygen is introduced, the maximum achievable fraction of inspired oxygen (FiO2) is limited to 50%. The oxygen supply should be connected at the patient's end. In situations where a FiO2 requirement exceeds 50%, the utilization of conventional invasive ventilation (NIV) option or dedicated NIV ventilators equipped with a blender option becomes necessary.

1. Fasting should be avoided to prevent metabolic acidosis, hyper/hypoglycemia or fatty acid metabolism abnormalities. Despite respiratory distress, it is advisable to refrain from fasting. In cases where necessary, the use of tube feeding rather than oral feeding should be continued. However, it is crucial not to withhold feeding in an effort to prevent catabolic states, whenever possible. Temporary shift to NG or other tube feeding method can be taken to protect the airways during active illness for weaker kids
2. Attention should be paid to the risk of aspiration, when orally feeding a weaker child during illness.
3. Criteria establishing the threshold for endotracheal intubation should be established considering several factors including limited neck and mandibular mobility, and positioning restrictions and patient and family preference.
4. Extubating criteria and procedure should be established. It is recommended to minimize the use of neuromuscular blocking agents in the perioperative periods, with a preference for faster-acting agents.

8. There is no clear evidence to support empiric use of antibiotics or volume resuscitation (except for sepsis management in the general population) during acute illness or to guide viral testing or other diagnostics. For these issues, providers should consider presentation characteristics, the presence of indwelling devices and history of recent surgical interventions, and recurrent antibiotics.

Hospital discharge during acute care

Discharge planning should begin shortly after admission to identify goals with the patient/ family, inpatient team, and primary care providers. Planning should consider threshold for discharge, need to augment outpatient services, follow-up care, and indications for urgent re-hospitalization. Threshold for discharge based on medical status will depend on the com- fort and skill of family and outpatient medical care team. It is highly recommended to wean off patients to home ventilators wherever indicated

Preprocedural screening, anesthesia/sedation considerations and pain management

1. Polysomnograms and nutritional assessment may be considered as part of a pre-anesthetic evaluation.
2. Cardiology screening is not recommended, unless there is a concern for cardiac dysfunction in older individuals or conditions unrelated to SMA.
3. Difficult airway status should be considered based upon mandibular contractures, limited neck mobility, positioning restrictions and other factors.
4. A low threshold for deferring elective/non-emergent sedation/anesthesia should be considered during intercurrent illness across all SMA types.
5. Opiate-based analgesia should be considered as part of routine post-procedural management with anticipation of providing appropriate NIV and cough assistance.
6. Regional analgesia may be considered for all SMA types and may allow for lower amounts of systemic analgesics with subsequent effects on respiratory drive and intestinal motility.
7. Practical consideration must be taken into account when evaluating epidural catheter placement in context of pre-existing scoliosis.
8. Monitoring during procedural sedation and anesthesia should include capnography to complement oximetry, as apneic or hypopneic oxygenation should be avoided.

Use of medication, supplements and immunizations

1. Antibiotics or medications/supplements for bone health, such as vitamin D and calcium and bisphosphonate, or drugs for gastroesophageal reflux, are recommended with the exception of vitamin D, rarely used prophylactically, and mainly used if needed/ deficient.
2. Annual influenza, RSV and pneumococcal immunizations are strongly recommended

Spinal Muscular Atrophy therapies

Nusinersen

1. Nusinersen is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.
2. Nusinersen is administered intrathecally.
3. Recommended dosage:
   a. The recommended dosage is 12 mg (5 mL) per administration.
   b. Initiate Nusinersen treatment with 4 loading doses.
      i. The first three loading doses should be administered at 14-day intervals.
      ii. The 4th loading dose should be administered 30 days after the 3rd dose.
   c. A maintenance dose should be administered once every 4 months thereafter. If a loading dose is delayed or missed, administer Nusinersen as soon as possible, with at least 14-days between doses and continue dosing as prescribed. If a maintenance dose is delayed or missed, administer Nusinersen as soon as possible and continue dosing every 4 months.
4. Conduct the following laboratory tests at baseline and prior to each dose of Nusinersen and as clinically needed:
   a. Platelet count
   b. Prothrombin time; activated partial thromboplastin time.
   c. Quantitative spot urine protein testing

Onasemnogene abeparvovec

1. Onasemnogene is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of:
   a. Patients with 5q SMA with biallelic mutations in the SMN1 gene and a clinical diagnosis of SMA type 1, or
   b. Patients with 5q SMA with a biallelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene
2. Onasemnogene is a single-dose intravenous infusion only.
   a. The recommended dose of is 1.1×10^{14} vector genomes per kilogram (vg/kg) of body weight.
   b. One day prior to infusion, begin administration of systemic corticosteroids equiv- alent to oral prednisolone at 1 mg per kg of body weight per day (mg/kg/day) for a total of 30 days. This dose is to be adjusted based on post dose transaminitis or thrombocytopenia like complications.
   c. If stable, prednisolone is weaned off while monitoring bloods for LFT, FBC, Troponin-I like parameters over the period of 6-8 weeks.

3. Prior to infusion:
    a. Due to the increased risk of serious systemic immune response, administer Onasemnogene to patients who are clinically stable in their overall baseline health status (e.g., hydration and nutritional status, absence of infection) prior to infusion.
    b. Postpone Onasemnogene in patients with infections until the infection has resolved and the patient is clinically stable. Clinical signs or symptoms of infection should not be evident at the time of infusion.
    c. Assess liver function.
    d. Obtain creatinine, complete blood count (including hemoglobin and platelet count), coagulation profile, and troponin-I.
    e. Perform baseline testing for the presence of anti-AAV9 antibodies.
3. It is advisable to finish life vaccine before starting the gene therapy

Risdiplam

1. Risdiplam is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.
2. It is recommended that a healthcare provider discuss with the patient or caregiver how to prepare the prescribed daily dose prior to administration of the first dose. Instruct patients or caregivers to prepare the dose using the reusable oral syringe provided.
3. Risdiplam must be taken immediately after it is drawn up into the oral syringe. If it is not taken within 5 minutes, it should be discarded from the oral syringe, and a new dose should be prepared.
4. It is taken orally once daily after a meal at approximately the same time each day.
5. In infants who are breastfed, it should be administered after breastfeeding, and it cannot be mixed with formula or milk. Instruct patients to drink water after taking Risdiplam to ensure the drug has been completely swallowed.
6. If the patient is unable to swallow and has a nasogastric or gastrostomy tube, Risdiplam can be administered via the tube. The tube should be flushed with water after delivering Risdiplam
7. Risdiplam is administered orally once daily. The recommended dosage is determined by age and body weight.
    a. Less than 2 months of age 0.15 mg/kg
    b. 2 months to less than 2 years of age 0.2 mg/kg
    c. 2 years of age and older weighing less than 20 kg 0.25 mg/kg
    d. 2 years of age and older weighing 20 kg or more- 5 mg per day

HEALTH OUTCOME INDICATORS

Description title	Screening of newborn
Definition	Percentage of newborn infants screened for SMA out of the total newborn population
Numerator	Newborn infants tested by qPCR or MLPA for SMA
Denominator	Total newborn population
Exclusion criteria	Newborn identified as low risk
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better
Rationale	Delays in diagnosis of SMA resulted from patient visits to mul- tiple health care professionals to rule out the possibility of oth- er illnesses before genetic testing for SMA was performed and a confirmed diagnosis was obtained. This “diagnostic odyssey” from the time first symptoms are noticed to a confirmed ge- netic diagnosis of SMA puts patients and caregivers through physical and mental stress. A later diagnosis may result in a missed opportunity for optimal early intervention for SMA. Early diagnosis and care of SMA also can lead to lower patient and caregiver burden; therefore, tools for improving the appro- priate and early detection of SMA, such as newborn screening, shall be warranted

Description title	Frequency of assessment
Definition	Percentage of patients who went through a multidisciplinary evaluation at least twice per year out of the total number of patients diagnosed with SMA
Numerator	Number of patients who were consulted by Neurology, reha- bilitation, nutritionist, dietitian, pediatric dentistry, orthopedic and respiratory specialists at least twice a year
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better
Rationale	All SMA patients shall be assessed by a multidisciplinary team every 3-6 months whether they are symptomatic or asymp- tomatic

Description title	**CHOP INTEND (The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders) Score for patients with SMA**
Definition	Percentage of patients with positive progression of CHOP INTEND score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of CHOP INTEND score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Sitting patients • Ambulatory patients
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better
Rationale	The significance of the CHOP INTEND score lies in its ability to monitor disease progression, evaluate treatment efficacy, inform clinical decision-making, and assess functional abilities

Description title	**HINE (Hammersmith Infant Neurological Examination) Score for patients with SMA**
Definition	Percentage of patients with positive progression of HINE score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of HINE score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Sitting patients • Ambulatory patients • Patients <2 months • Patients >24 months
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better
Rationale	The HINE score measures changes in key developmental motor milestones in infants and weaker children with SMA. Results are measured on a point system used to score improvement or worsening in motor milestone achievement.

Description title	**MFM-20 (Motor Function Measure - 20) Score for patients with SMA**
Definition	Percentage of patients with positive progression of MFM-20 score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of MFM-20 score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Patients <24 months
Unit of measure	Percentage

Description title	MFM-20 (Motor Function Measure - 20) Score for patients with SMA
Measure target and/or threshold	Higher percentage of patients is better
Rationale	The MFM-20 assesses a wide range of motor abilities. It provides a detailed and comprehensive evaluation of motor func- tion across various domains relevant to SMA. It also provides quantitative scores that allow healthcare providers to objectively measure motor function and track changes over time. This enables longitudinal assessment of disease progression and response to treatment in individuals with SMA. It can serve as a prognostic tool to predict disease severity and functional outcomes in individuals with SMA.

Description title	GMFM (Growth Motor Function Measure) Score for patients with SMA
Definition	Percentage of patients with positive progression of GMFM score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of GMFM score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Patients <5 years
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better
Rationale	The GMFM assesses a wide range of motor abilities. It provides a detailed and comprehensive evaluation of motor func- tion across various domains relevant to SMA. It also provides quantitative scores that allow healthcare providers to objectively measure motor function and track changes over time. This enables longitudinal assessment of disease progression and response to treatment in individuals with SMA. It can serve as a prognostic tool to predict disease severity and functional outcomes in individuals with SMA.

Description title	RH (Revised Hammersmith) Score for patients with SMA
Definition	Percentage of patients with positive progression of RH score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of RH score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Non-ambulatory • Patients <1 year
Unit of measure	Percentage

Description title	RH (Revised Hammersmith) Score for patients with SMA
Measure target and/or threshold	Higher percentage of patients is better
Rationale	RH is a valuable tool for evaluating motor function and disease progression in individuals with SMA, contributing to compre- hensive clinical care, treatment monitoring, rehabilitation plan- ning, and research advancements in the field of neuromuscular disorders

Description title	6-MWT (6 Minute Walk Test) Score for patients with SMA
Definition	Percentage of patients with positive progression of 6-MWT score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of 6-MWT score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Non-sitting patients • Sitting patients • Patients <4years
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better
Rationale	The 6MWT serves as a crucial tool in SMA management by providing a comprehensive measure of walking ability, endur- ance, and functional exercise capacity. It's instrumental in clini- cal settings for assessing disease progression, evaluating treat- ment efficacy, and guiding therapeutic interventions, making it an invaluable asset in SMA research and patient care.

Description title	RULM (Revised upper limb module) Score for patients with SMA
Definition	Percentage of patients with positive progression of RULM score compared to their baseline among patients with SMA compared to their baseline score
Numerator	Number of patients with positive progression of RULM score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Asymptomatic patients • Non-sitting patients
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage of patients is better

Description title	RULM (Revised upper limb module) Score for patients with SMA
Rationale	RULM score is a critical component of the SMA assessment toolkit, offering valuable insights into patient motor function, treatment response, and disease progression. Its application across various studies and clinical settings highlights its im- portance in guiding therapeutic decisions and improving pa- tient outcomes in SMA.

Description title	Evolution of the degree of scoliosis for patients with SMA
Definition	Percentage of patients with progression of spine curvature compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of spine curva- ture
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage indicates poor quality
Rationale	Scoliosis is still highly prevalent in children with SMA 1 and 2, with an incidence of 60–90% and initial presentation in early childhood. The hypotonic spinal curves continuously progress through childhood. The degree of scoliosis in patients with SMA is an important prognostic factor, influencing outcomes such as respiratory function and the effectiveness of treat- ments. The progression of scoliosis can significantly affect the quality of life and medical management in SMA patients, with operative treatment showing varying results based on the de- gree of curvature

Description title	NSAA (Northstar Ambulatory Assessment) score for patients with SMA
Definition	Percentage of patients with positive progression of NSAA score compared to their baseline among patients with SMA
Numerator	Number of patients with positive progression of NSAA score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	• Non-ambulatory patients
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage indicates better quality

Description title	NSAA (Northstar Ambulatory Assessment) score for patients with SMA
Rationale	NSAA score plays a crucial role in evaluating disease progres- sion, functional ability, and treatment outcomes in individuals with SMA. It has been widely recognized as a valuable tool for assessing disease severity and progression across different SMA populations, including both pediatric and adult patients. Moreover, the NSAA score has been integrated into broader assessments of health utility and quality of life in SMA pa- tients, highlighting its relevance beyond mere clinical outcomes to encompass patient and caregiver perceptions of disease im- pact. This underscores the multifaceted importance of NSAA in guiding clinical decision-making, monitoring therapeutic in- terventions, and evaluating long-term outcomes in SMA.

Description title	Longitudinal anthropometrics score for patients with SMA
Definition	Percentage of patients with positive progression of Longitu- dinal anthropometrics score compated to expected growth charts among patients with SMA
Numerator	Number of patients with positive progression of longitudinal anthropometrics score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage indicates better quality
Rationale	Longitudinal anthropometric studies offer insights into dis- ease progression, impact of treatments, and patients' growth trajectories. These studies provide a systematic way to track changes in physical measurements over time, shedding light on how SMA affects individuals' physical development. One of the primary benefits of longitudinal anthropometric studies in SMA is the detailed observation of disease progression and the efficacy of treatments.

Description title	TIMP (Test of Infant Motor Performance) score for patients with SMA
Definition	Percentage of patients with positive progression of TIMP score compated to expected growth charts among patients with SMA
Numerator	Number of patients with positive progression of TIMP score
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	
Unit of measure	Percentage

Description title	TIMP (Test of Infant Motor Performance) score for patients with SMA
Measure target and/or threshold	Higher percentage indicates better quality
Rationale	The TIMP is designed to assess the motor skills of infants, and in the context of SMA, it could offer early insights into the disease's impact on motor function development. This is particularly relevant for evaluating the efficacy of treatments such as nusinersen, where improvements or stabilizations in motor functions are significant treatment goals. Moreover, the relevance of the TIMP score could extend to evaluating disease severity and progression, providing a quantitative measure that can be tracked over time to assess the impact of SMA on motor function from an early age. This could aid in the timely initiation of treatments and interventions aimed at mitigating disease progression and improving quality of life for affected individuals.

Description title	Cough peak flow in patients with SMA
Definition	Percentage of patients diagnosed with SMA and whose cough peak flow >270/min expected out of the total number of SMA patients
Numerator	Number of patients with cough peak flow >270/min
Denominator	Total number of patients diagnosed with SMA
Exclusion criteria	
Unit of measure	Percentage
Measure target and/or threshold	Higher percentage indicates better quality
Rationale	The prognostic value of cough peak flow in SMA in assessing respiratory muscle strength and the risk of respiratory complications is high. Its use as a prognostic tool in SMA is supported by research showing its effectiveness in evaluating respiratory function and predicting the risk of respiratory complications. For instance, mechanical insufflation/exsufflation, which can increaseit, has been shown to improve cough efficacy in patients with neuromuscular diseases, including SMA, suggest- ing its potential as a prognostic indicator