Spinal muskelatrofi:
- *Tverrfaglig oppfølging*

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Oslo universitetssykehus

SMA:
- *Oppfølging I Norge*

- Oppfølging
  - Consensus retningslinjer
  - Standardisert etter nye behandlinger

- Tverrfaglig oppfølging
  - Tverrfaglig møter OUS-RH
- Nasjonal interesse gruppe
- Nordisk samarbeid

SMA: Klassifikasjon – skal dette endres?

International SMA consortium:			
TYPE	DEBUT	MOTOR FUNCTION	LIFE EXP
SMA 1 - alvorlig	< 6 mndr	Sitt aldri	< 2 år
SMA 2 - intermediare	6 – 18 mndr	Sitt; Går aldri	50% 20 – 30 år
SMA 3 - mild	> 18 mndr	Går	Normal

Also type 0 and Type 4

Hvordan klassifisere vi pasienter som har fått behandling ?

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Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care

Eugenio Mercuri [a,b,l,*], Richard S. Finkel [c,l], Francesco Muntoni [d], Brunhilde Wirth [e], Jacqueline Montes [f], Marion Main [d], Elena S. Mazzone [a,b], Michael Vitale [g], Brian Snyder [h], Susana Quijano-Roy [i,j], Enrico Bertini [k], Rebecca Hurst Davis [l], Oscar H. Meyer [m], Anita K. Simonds [n], Mary K. Schroth [o], Robert J. Graham [p], Janbernd Kirschner [q], Susan T. Iannaccone [r], Thomas O. Crawford [s], Simon Woods [t], Ying Qian [u], Thomas Sejersen [v] for the SMA Care Group

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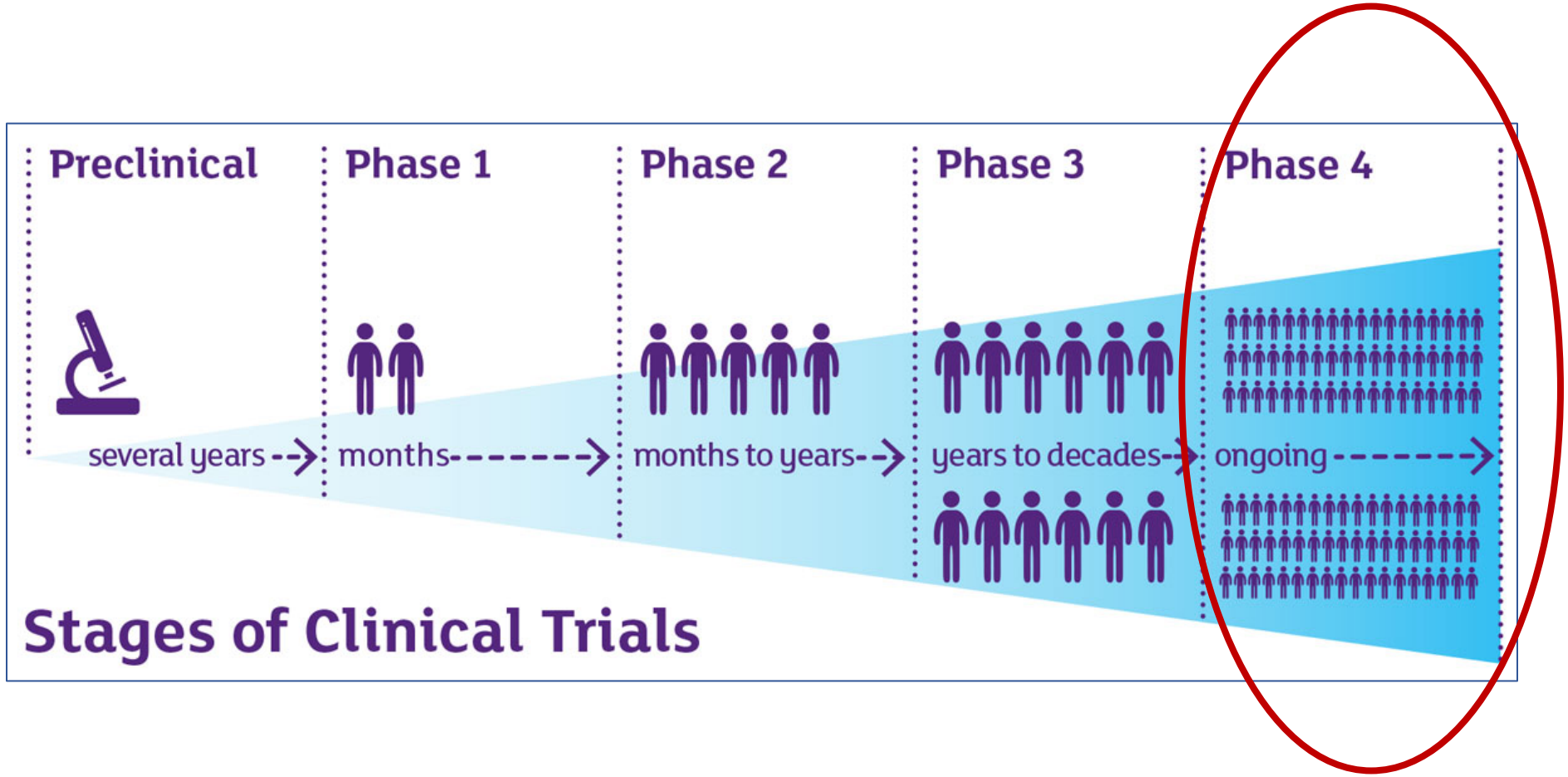
Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics

Oppfølging

Effekt av behandling: 1


Preclinical
Phase 1
Phase 2
Phase 3
Phase 4
several years
months
months to years
years to decades
ongoing
Stages of Clinical Trials

2.2 Multi-disciplinary

Testing

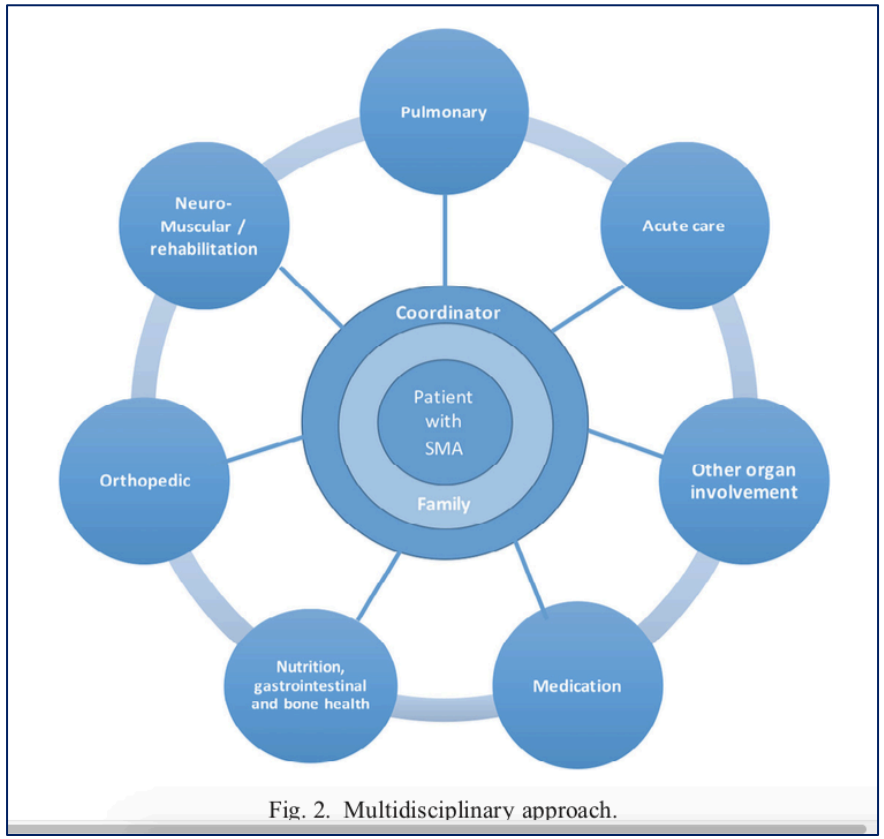


Fig. 2. Multidisciplinary approach.

- Range of Motion
- CHOP
- HINE
- HFMSE
- 6 MWT
- RULM
- MFM
- *EQS*

Standardised Follow-up

- Studiene
  - Overlevelse og/eller Respirasjonsstøtte

• Milepæler	WHO, HINE
• Funksjonsnivå	CHOP intend, HFMSE, RULM (*6MWT*)
• Respirasjon	RFTs, Søvn studier, FVC,
• Ernæring	
• Biomarkører	

MEASURE: MOTOR MILESTONES
INFANTS (2-24 months of age)

The Hammersmith Infant Neurological Examination (HINE) is designed to be a simple and scorable method for evaluating infants from 2 months to 2 years of age. The HINE includes 3 sections containing 26 items that assess different aspects of neurologic function[7,8]:

- **Section 1:** Neurologic examination assessing cranial nerve function, posture, movements, tone, reflexes, and reactions
- **Section 2:** Developmental milestones (head control, sitting, voluntary grasp, ability to kick, rolling, crawling, standing, and walking)
- **Section 3:** Behavioral assessment (state of consciousness, emotional state, social orientation)

HINE Section 2 (motor milestones) includes 8 items scored on a 5-point scale with 0 as the absence of activity, and a maximum score of 4 points[9]

- Some items have a maximum score of 2 or 3 points (see table below)

HINE Section 2 scoring chart illustrating the motor developmental milestones[9]

Milestone					
Head control	**Unable to maintain head upright** (normal up to 3 months)	**Wobbles** (normal up to 4 months)	**Maintained upright all the time** (normal from 5 months)		
Sitting	**Cannot sit**	**Sits with support at hips** (normal at 4 months) 	**Props self up** (normal at 6 months) 	**Stable sitting** (normal at 7–8 months) 	**Pivots** (rotates) (normal at 9 months) 
Voluntary grasp (note L or R side)	**No grasp**	**Uses whole hand**	**Index finger and thumb, but immature grasp**	**Pincer grasp**	
Ability to kick (supine)	**No kicking**	**Kicks horizontally but legs do not lift**	**Upward** (vertical) (normal at 3 months) 	**Touches leg** (normal at 4–5 months) 	**Touches toes** (normal at 5–6 months) 
Rolling	**No rolling**	**Rolls to side** (normal at 4 months)	**Prone to supine** (normal at 6 months)	**Supine to prone** (normal at 6 months)	
Crawling or bottom shuffling	**Does not lift head**	**On elbow** (normal at 3 months) 	**On outstretched hand** (normal at 4 months) 	**Crawling flat on abdomen** (normal at 8 months) 	**Crawling on hands and knees** (normal at 10 months) 
Standing	**Does not support weight**	**Supports weight** (normal at 4 months)	**Stands with support** (normal at 7 months)	**Stands unaided** (normal at 12 months)	
Walking		**Bouncing** (normal at 4 months)	**Cruising** (walks holding on) (normal at 12 months)	**Walking independently** (normal at 15 months)	
SCORE	0	1	2	3	4

MEASURE: MOTOR FUNCTION
INFANTS AND CHILDREN WITH SMA
(≈4 months to >4 years of age)

The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) may be used to evaluate the motor skills of infants with SMA[10,11]:

- CHOP INTEND was developed by evaluating infants (n=26) with Type I SMA, mean age 11.5 months (1.4-37.9 months), and has been shown to be valid for the assessment of children ranging in age from 3.8 months to over 4 years who have an infant's repertoire of motor skills
- Includes 16 items used to assess motor skills. Each item is graded on a scale of 0-4[12]:
  0=No response
  4=Complete response
- Total score ranges from 0-64

1	**Spontaneous movement** (upper extremity)
2	**Spontaneous movement** (lower extremity)
3	Hand grip
4	Head in midline with visual stimulation
5	Hip adductors
6	Rolling: elicited from legs
7	Rolling: elicited from arms
8	Shoulder and elbow flexion and horizontal abduction
9	Shoulder flexion & elbow flexion
10	Knee extension
11	Hip flexion and foot dorsiflexion
12	Head control
13	Elbow flexion
14	Neck flexion
15	Head/Neck extension
16	Spinal incurvation

The Hammersmith Functional Motor Scale—Expanded (HFMSE), developed to evaluate motor function in non-ambulatory and ambulatory individuals with later-onset SMA, is a measure that has been used in several clinical trials to evaluate the motor function of individuals with later-onset (Types II and III) spinal muscular atrophy.

The HFMSE includes 13 clinically relevant items from the Gross Motor Function Measure (GMFM) related to lying/rolling, crawling, crawling/kneeling, standing, and walking/running/jumping[4,14,15]:

- Exam has 33 items that are scored on a scale of 0-2
- Total score ranges from 0 to 66, with lower scores indicating poorer motor function
- Patient fatigue is an important consideration; the HFMSE can be conducted in 12 minutes (mean time)

SITTING	ROLLING	TRANSITIONS/ CRAWLING	STANDING/ STEPPING	TRANSITIONS/ KNEELING	SQUAT/JUMP	STAIRS
ITEMS 1-4	ITEMS 5-9	ITEMS 10-17	ITEMS 18-20	ITEMS 21-27	ITEMS 28-29	ITEMS 30-33

HAMMERSMITH FUNCTIONAL MOTOR SCALE-EXPANDED (HFMSE) EXAM

Child depicted in graphic above is >2 years of age.

“The burden of disease”

Quality of life

Independance

Length of life

Effekt av behandling: 2

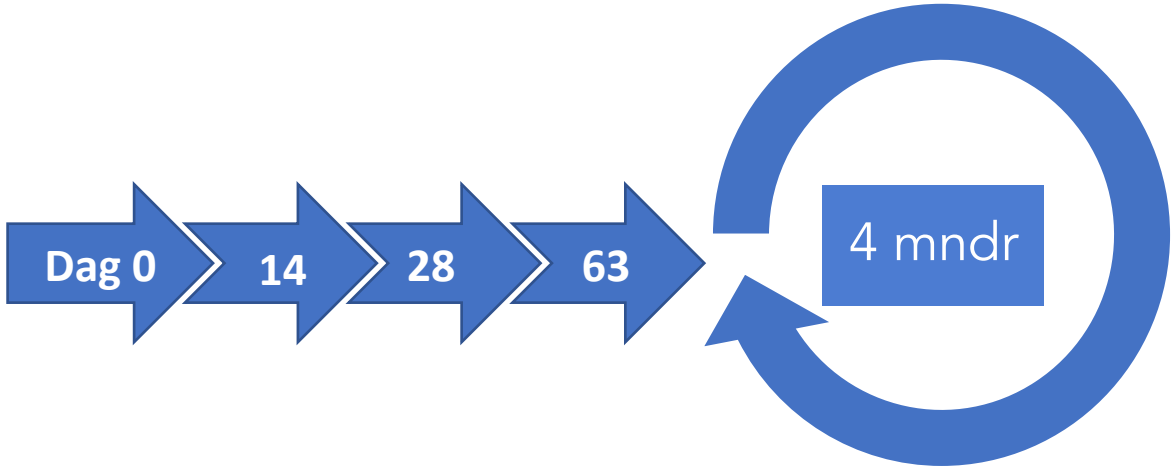
Tverrfaglig møte: OUS-RH"

- Møte en gang per mnd
- Diskutere alle pasienter siste 4 uker
  - Leger
    - Barnenevro, Lungeseksjon
  - Fysio
  - Spiseteamet
  - Sykepleie
  - Koordinator

Sett behov for
"ekstra" oppfølging ved
mer aggresiv lunge behadnling

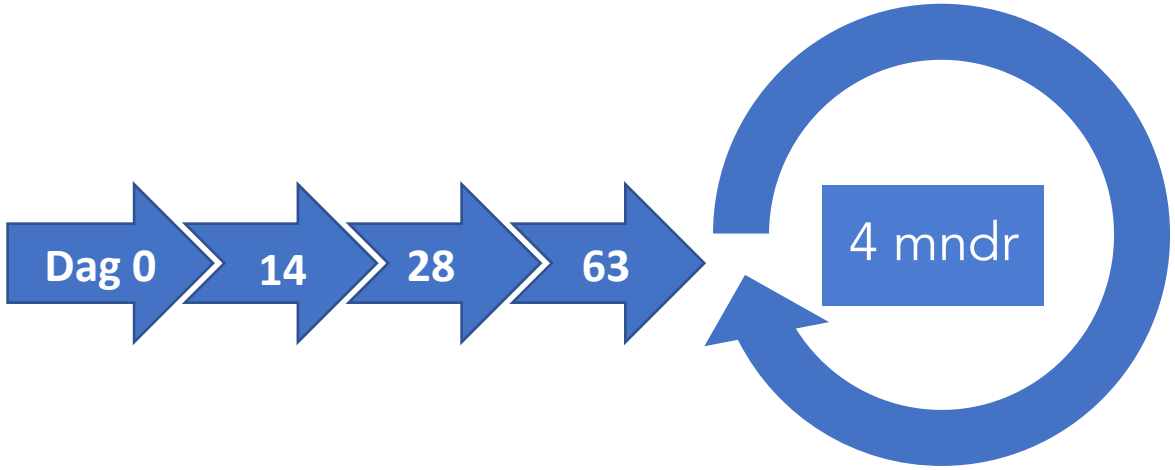
Behandling:

- Intrathecal behandling
- Oppstart og 1 års oppfølging
  - OUS
- Fysio, Lunge, Nevro, Ernæring...



Bdehanling:


Monday
Tuesday
Wednesday
Thursday
Friday
Busy
Election Day
Veterans Day
Thanksgiving Day


Dag 0
14
28
63
4 mndr

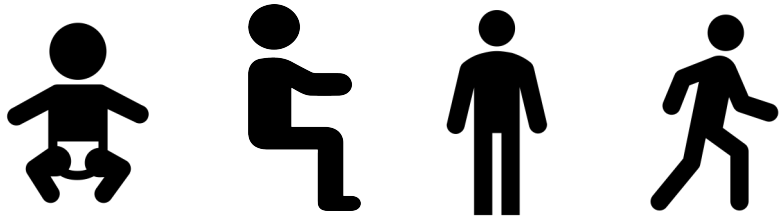
Tverrfaglig Nasjonal interresse gruppe

- Møte 4 - 6 ganger per år
  - Alle 4 helseregioner
  - Barnenevrologi
  - Nevrologi
  - Lungelege
  - Anestesi

Oppfølging

Consensus retningslinjer

- Non-sitters
- Sitters
- Walkers



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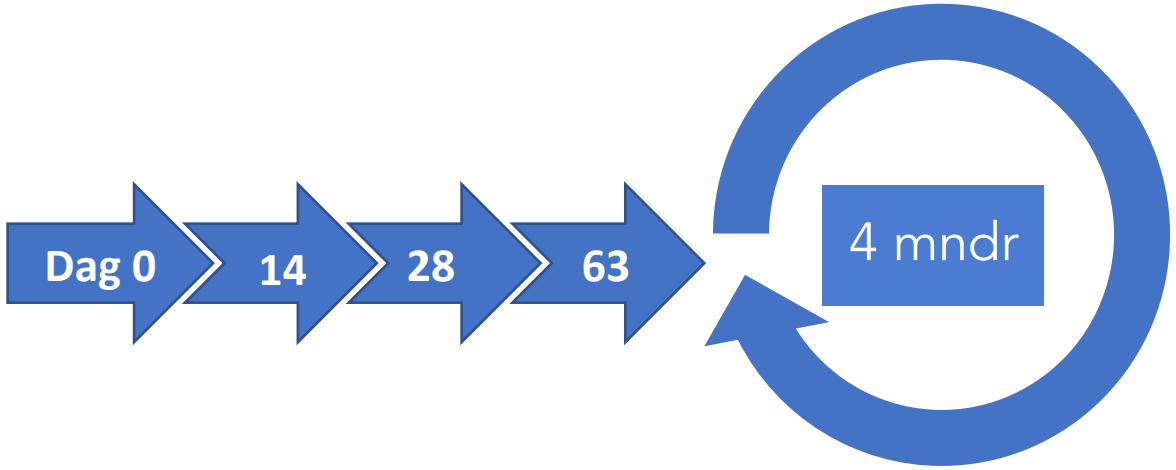
Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics

Oppfølging:

- Innleggelse for behandling
- Tverrfaglig vurdering ved barnehabilitering



Motor - Ortopedi

Rehabilitation assessment and intervention.

	Assessment	Intervention	Care considerations
Non-sitters	Postural control Scoliosis Hip dislocation Sitting tolerance Chest deformities	*Positioning and Bracing* Daily use of seating systems, postural and positioning supports, thoracic bracing and cervical bracing for head support. Static thoracic bracing should have incorporated modifications for respiratory support including abdominal cutouts.	To be effective, orthoses should be applied for more than 60 minutes to overnight. Session duration for effective stretching and range of motion depends on specific patient needs, joints, and rehabilitation aims.
	Contractures (ROM, goniometry)	*Stretching* Daily use of orthoses for upper lower limb orthoses for stretching and to promote function and range of motion. Static orthoses Knee immobilizers and hand splints are recommended for positioning and stretching. AFOs and KAFOs can be used for stretching and positioning. TLSOs are used for positioning. Supported standing	The minimal frequency for stretching and range of motion is 3–5 times per week The minimal frequency for bracing to be effective is 5 times per week.
	Muscle weakness (Antigravity movements) Functional scales (CHOP INTEND) Motor development (HINE)	*Promote function and mobility* Use of seating and mobility systems Mobile arm supports to assist upper extremity function.	Recommend toys with switches, light weight rattles, Bath equipment, adapted beds, upper extremity assistive devices, as well as hoists (lifts), Environmental controls, and eye tracking devices for computers and communication, Strollers with recline and the ability to lay flat, power wheelchairs should have recline/tilt, adapted seating systems

Table 1
Rehabilitation assessment and intervention.

	Assessment	Intervention	Care considerations
Sitters	Postural control Foot and chest deformities Scoliosis and pelvic obliquity Hip dislocation	*Positioning and Bracing* Thoracic bracing is recommended for posture and to promote function. Cervical bracing is often used for head support for safety and transportation.	Orthoses should be worn for more than 60 minutes to overnight. The minimal frequency for bracing: 5 times/week.
	Contractures (ROM, goniometry)	*Stretching* Orthoses are used for the upper and lower limbs to promote function and ROM Regular stretching for segments known to be at risk for contractures: hip, knee and ankle, wrist and hand Knee immobilizers, KAFOs, and AFOs are recommended for positioning and standing. RGOs and KAFOs can be used for supported ambulation. TLSOs and hand splints are used for positioning.	Minimal frequency for stretching and ROM: 5–7 times/week When stretching or performing joint mobilization ensure joint segments are aligned throughout the treatment. Supported standing should be up to 60 minutes and minimal frequency is 3–5 times/week, optimal 5–7 times/week.
	Functional scales (HFMSE, RULM, MFM) Muscle weakness (Strength tests)	*Promote function and mobility* Use of seating and mobility systems. Use of gait training devices and mobility devices to promote supported ambulation Mobile arm supports to assist upper extremity function.	Exercise can have an effect on function, strength, ROM, endurance, ADLs, participation, and balance Recommend swimming, hippotherapy, and wheelchair sports. All sitters should have electric/power wheelchairs with custom postural support and seating systems The option to tilt and/or recline and a seat elevator is sometimes necessary in weaker patients. Lightweight manual wheelchairs or power assist wheels are ideal to promote self-propulsion in stronger patients.

2.4.2.2. Positioning. Thoraco-lumbar sacral orthoses are recommended for posture and to promote function. Cervical bracing is often used for safety and transportation. Static, dynamic and functional orthoses are used for positioning and standing and, when possible, for supported ambulation.

Supported standing is important to facilitate lower extremity stretching but also to promote bodily functions and bone health, enable upright participation, and promote spine and trunk posture.

Table 1
Rehabilitation assessment and intervention.

	Assessment	Intervention	Care considerations
Ambulant	Mobility Timed tests Measure of endurance (6MWT) Falls Functional scales (HFMSE, RULM) Muscle weakness (Strength tests)	*Promote function and mobility*	Recommend aerobic and general conditioning exercise for SMA walkers. Options include: Swimming, walking, cycling, yoga, hippotherapy, rowing, elliptical/cross-trainers. Exercise program should be designed and monitored by a physical or occupational therapist, familiar with SMA. Optimal duration for aerobic exercise: at least 30 minutes
	Contractures (ROM, goniometry)	*Stretching*	Minimal frequency: 2–3 times/week, optimal: 3–5 Maintain flexibility through active assisted stretching and include the use of orthoses according to specific needs.
	Postural control	*Positioning and Bracing*	Recommend some form of balance exercise.
	Scoliosis Hip dislocation		Lower limb orthoses are used for posture and function at the ankle and knee, Thoracic bracing may be used to promote posture in sitting

2.5 Ernæring - *non sitters*

- Etter Spinraza…
- *Langtids effekt på svelging*
- Oppfølging
  - mellom dose 5 og 6
- Gastrostomi
  - Til alle ???
- Logoped
  - Når begynner vi ?
  - Munn åpning
- Fasting

Table 2
Nutritional assessment and intervention.

	Assessment	Intervention	Care considerations
Non-sitters	Video Fluoroscopic Swallow Study shortly after diagnosis and when suggested by clinical signs suggestive of dysphagia (weak suck, fatigue, humid voice, pneumonias) Difficulties with feeding (pocketing, jaw contractures, increased mealtimes) Nutritional analysis of food records/feeding regimen Longitudinal anthropometrics Acute care monitoring 25 Hydroxy-vitamin D labs and Body Composition and Bone density Constipation	If swallow study is passed, consider referral to specialist for feeding therapy/modification For failure of a swallow study or for growth failure, for proactive care, place nasojejunal tube until a Gastric-tube can be placed with Nissen fundoplication. A dietitian should adjust caloric, fluid, macronutrient, micronutrient intake and timing of feeds. Nutrition labs may be indicated. Minimize fasting during acute care to less than 6 hours. Provide adequate fluid intake during illness. Monitor electrolyte levels and correct as needed. Monitor glucose levels to correct hypo/hyperglycemia. Provide adequate calcium, vitamin D intakes for bonehealth. Adequate hydration. Use of bowel regulation medications.	Determine appropriate calorie needs based on growth. Standardized growth charts are a good tool to track growth trends, but optimally, should be used with other body composition measurement tools to assess appropriate growth. For optimal care, recommend evaluation by a dietitian every 3–6 months for younger children and annually for older children/adults. Evaluation is especially important for those on specialized diets.

There was no unanimous consensus but 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 [92]

Consensus is divided on the use of the Amino Acid diet, a diet based on elemental formula [83,93]. Experts agreed that diet type and administration should be based on individual tolerance.

Over the last decade, the approach to treating the pulmonary manifestations of SMA has shifted from a reactive approach, of starting treatment to support airway clearance and ventilation only when there is a clear indication, to a proactive approach of introducing these therapies earlier in the disease process [7].

Pulmonary

Table 1
Pulmonary assessment, intervention and management recommendations.

	Assessment	Intervention	Care considerations
Non-sitters	Physical examination Assessment of hypoventilation (End tidal CO2) Sleep study or pneumograms in all symptomatic patients or to determine if a patient needs to initiate NIV Clinical assessment of gastroesophageal reflux	Support airway clearance Oral suctioning Physiotherapy/respiratory therapy should be implemented immediately: Manual chest therapy Cough insufflator/exsufflator Support ventilation with bilevel NIV in symptomatic patients Nebulized bronchodilators in patients with asthma or a positive bronchodilator response Customary immunizations, palivizumab through 24 months, influenza vaccination annually after 6 months of age	Assessments should be performed at least every 3 months initially, then every 6 months Supporting airway clearance with oronasal suctioning, physiotherapy/respiratory therapy and cough assist is critical to all non-sitters with ineffective cough Ventilation should be started in all symptomatic patients. Some experts recommend using it before documented respiratory failure to palliate dyspnea This should be judged on individual basis NIV should be initiated in observing the patient clinically for adequate gas exchange or during a sleep study. NIV interfaces should be fitted by skilled physiotherapists selecting two interfaces with different skin contact points. Mucolytics should not be used long-term

Table 1
Pulmonary assessment, intervention and management recommendations.

	Assessment	Intervention	Care considerations
Sitters	Physical examination Spirometry (when possible depending on age and cooperation) Sleep study or pneumograms in all patients with even minimal suspicion of symptoms of nocturnal hypoventilation Assessment of gastroesophageal reflux	Support airway clearance Physiotherapy/respiratory therapy should be implemented immediately: Manual chest physiotherapy Cough insufflator/exsufflator Support ventilation with bilevel NIV in symptomatic patients	Assessments should be performed every 6 months Supporting airway clearance is critical to all patients with ineffective cough Ventilation should be started in all symptomatic patients. Some experts recommend using it during acute respiratory illnesses to facilitate discharge. NIV should be initiated during a sleep study or observing the patient clinically for adequate gas exchange. NIV interfaces should be fitted by skilled physiotherapists selecting two interfaces to alternate skin contact points. Mucolytics should not be used long-term
		Nebulized bronchodilators in patients with suspicion of asthma Customary immunizations, annual influenza and pneumococcal vaccination	
Ambulant	Clinical examination with review of cough effectiveness and detailed search for signs of nocturnal hypoventilation	Supportive care when needed Customary immunizations, annual influenza and pneumococcal vaccination	Evidence of weak cough or recurrent infections or suspicion of nocturnal hypoventilation should prompt referral to a pneumologist

3.1 Pulmonary

- Etter Spinraza…
  - *Langtids effekt på respirasjon*
- Pro-aktiv
  - Vurdering dose 1, 4 årlig
  - Tidligere start av NIV
    - ? Økt Resp Frek og Puls
  - Unngå brystkasse malformasjoner
- TOSCA