applied sciences

MDPI

Review

Physical and Respiratory Rehabilitation in Spinal Muscular Atrophy: A Critical Narrative Review

Serena Cammarano [1], Vincenzo Alessio Chirico [1], Benedetto Giardulli [2], Giovanna Mazzuoccolo [1], Carlo Ruosi [1] and Bruno Corrado [1,*]

[1] Department of Public Health, University of Naples Federico II, 80131 Naples, Italy; se.cammarano@studenti.unina.it (S.C.); vincenzoalessio.chirico@unina.it (V.A.C.); giovanna.mazzuoccolo@unina.it (G.M.); caruosi@unina.it (C.R.)
[2] Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health, University of Genova, Campus of Savona, 17100 Savona, Italy; benedetto.giardulli@edu.unige.it
* Correspondence: bruno.corrado@unina.it; Tel.: +39-0817462796

Abstract: Spinal muscular atrophy (SMA) is a genetic disorder causing motor neuron loss and progressive muscle weakness, significantly affecting daily activities and breathing in severe cases. While rehabilitation is a crucial component of SMA management, no standardised rehabilitation guidelines currently exist. This review synthesised physiotherapy and respiratory interventions for SMA patients based on a comprehensive literature search from 1990 to 2024. Eighteen studies were analysed: eleven on physiotherapy and seven on respiratory rehabilitation. Five physiotherapy approaches were reported: electrical stimulation, electrotherapy with cycling, strengthening exercises, aerobic training, and hydrotherapy-based rehabilitation. Respiratory interventions, such as non-invasive ventilation and cough assistance, were mainly studied in SMA Type I, reporting prolonged survival and improved respiratory function. A few studies found that combining pharmacotherapy with intensive physiotherapy led to significantly better motor improvements than drugs alone. Despite these promising reported results, the lack of standardised methodologies and long-term clinical trials prevents definitive conclusions. Research should prioritise randomised controlled trial studies with standardised methodologies and larger sample sizes to investigate the efficacy of physiotherapy and respiratory interventions and, secondly, inform evidence-based rehabilitation protocols and clinical guidelines.

Keywords: muscular atrophy; spinal; complications; rehabilitation

Academic Editor: Arkady Voloshin

Received: 5 March 2025
Revised: 10 April 2025
Accepted: 12 April 2025
Published: 16 April 2025

Citation: Cammarano, S.; Chirico, V.A.; Giardulli, B.; Mazzuoccolo, G.; Ruosi, C.; Corrado, B. Physical and Respiratory Rehabilitation in Spinal Muscular Atrophy: A Critical Narrative Review. *Appl. Sci.* **2025**, *15*, 4398. https://doi.org/10.3390/app15084398

1. Introduction

Spinal muscular atrophy (SMA) is a group of genetic diseases characterised by the loss of motor neurons in the brain and spinal cord, causing skeletal muscles to become increasingly weak [1,2]. The incidence of SMA is 1/11,000 live births, while prevalence is approximately 1/54 [3,4]. The most common forms of spinal muscular atrophy (SMA), ranging from type I to type IV, are caused by a mutated or absent gene known as the survival motor neuron gene 1 (SMN1). The SMN1 gene, located on chromosome 5q, encodes the survival motor neuron (SMN) protein, which is essential for maintaining the health and normal function of motor neurons. Loss of SMN1 can be partially balanced by the presence of neighbouring SMN2 genes, which are 99% like SMN1 genes. The number of SMN2 gene copies varies from person to person and determines the clinical severity of SMA; the greater the number of SMN2 gene copies a person has, the more functional SMN protein is available, and thus, the later the onset of disease symptoms and the milder

the disease course. New research studies have highlighted the role of microRNA as a potential biomarker to monitor disease progression and treatment efficacy [5]. SMA usually affects the performance of activities of daily living such as crawling, sitting, standing, and neck and head control, but even swallowing and breathing in the worst cases [6]. Hence, respiratory failure is the main cause of death and morbidity; meanwhile, musculoskeletal pain, contractures, limited mobility, fatigue and spinal deformities are the main factors that affect the quality of life of people with SMA [7–13]. To date, SMA requires prompt treatment and has no cure if not diagnosed early; therefore, healthcare management focuses on early diagnosis and on conservative treatments involving different healthcare professionals, among which the physiotherapist, to preserve the quality of life [14–31].

All neuromuscular disorders require a multidisciplinary approach. Physiotherapy represents a key factor in improving patients' function and quality of life [32–40]. The purpose of rehabilitation is to preserve motor and respiratory functions, reducing symptoms and comorbidities. Concerning SMA, in a recent paper by Eugenio Mercuri and collaborators, some recommendations about rehabilitation have been proposed; stretching, positioning, mobility exercises, and chest physiotherapy gained a moderate level of evidence [32]. However, no instructions about how to perform them were added. In consideration of the above, the objective of this narrative review is to summarise the available evidence on physiotherapy and respiratory interventions in people with SMA and to give technical specifications about how to perform them to improve patients' function and quality of life as much as possible.

2. Materials and Methods

A critical narrative review was conducted. The primary aim was to investigate which rehabilitation interventions have been proposed for patients with SMA and to search for those with better evidence. The secondary aim was to give physiotherapists some technical tips about how to operate in the best way possible. The narrative review was carried out following the Scale for the Quality Assessment of Narrative Review Articles (SANRA) [41]. A comprehensive search using MEDLINE via PubMed and the PEDro databases was conducted from January 1990 to December 2023, as an arbitrary limit (e.g., last five years) may lead to potential loss of data. Papers were considered only if written in English. Case series, single-case studies, randomised controlled trials (RCTs), and prospective non-randomised studies were included. Abstracts, reports, and systematic reviews were excluded. Concerning the clinical phenotypes of SMA and the age of patients, no restrictions were set. All physiotherapeutic interventions were admitted. Studies that involved pharmacological or non-rehabilitative treatments were rejected. The outcomes included were biomarkers related to physical exercise (e.g., CK, LDH), motor function scales (e.g., Modified Hammersmith Functional Motor Scale-Extend), and physical properties tests (e.g., Time Up and Go, Six Minutes Walking Tests). The adopted search strategy involved the use of relevant "Keywords" and "Boolean Operators" (Table 1). The snowball technique was not adopted [42]. Articles were identified for potential inclusion during three stages of assessment by a single reviewer without peer evaluation: title, abstract and full text. The reviewer collected data such as the title, authors, study design, number of participants, intervention and controls, outcomes, and the main results reported by the authors.

Table 1. Databases research strategies.

PubMed Medline Research Strategy		
Search	**Query**	**Items Found**
#1	(spinal muscular atrophy) AND (electrical stimulation)	133
#2	(spinal muscular atrophy) AND (whole body vibration training)	5
#3	(spinal muscular atrophy) AND (strength training exercise)	36
#4	(spinal muscular atrophy) AND (aerobic training)	72
#5	(spinal muscular atrophy) AND (hydrotherapy)	3
#6	(spinal muscular atrophy) AND (scoliosis)	243
#7	(spinal muscular atrophy) AND ("Respiratory Insufficiency/therapy")	55
#8	(spinal muscular atrophy) AND (Positive-Pressure Respiration)	46
#9	((spinal muscular atrophy) AND (rehabilitation)) AND (orthoses)	15
#10	((spinal muscular atrophy) AND (contractures)) AND (range of motion)	10
#11	(spinal muscular atrophy) AND (Wheelchairs)	62
PEDro research strategy		
#1	"Simple research" with "spinal muscular atrophy" as keyword	12

3. Results

The search strategy gave 692 potential studies. After the removal of duplicates, they were reduced to 686. Then, the titles and abstracts of these remaining studies were evaluated, excluding further studies that did not meet the inclusion criteria. The title and abstract screening excluded 644 records, ending with 46 studies.

Of the 46 remaining studies, the full-text version was evaluated. Of these, 28 studies were excluded because they did not meet the inclusion criteria, while the remaining 18 were considered eligible. Figure 1 shows the entire process represented in the PRISMA 2020 Flow Diagram. The selected studies are classified as follows: two randomised controlled trials, one non-randomised controlled trial, two prospective cohort studies, two retrospective cohort studies, one retrospective analysis, two case–control studies, three case series, two multi-case studies, and three case reports.

Among the 18 studies included, 11 investigated the role of physiotherapy, and 7 investigated respiratory interventions.

After a detailed analysis of the articles, five physiotherapy approaches to patients with SMA were identified: electric stimulation, electrotherapy combined with cycling exercise, a combination of strengthening exercises and whole-body vibration, strengthening training, aerobic exercises, and hydrotherapy combined with a rehabilitation program.

Regarding the studies that investigated respiratory rehabilitation, seven were included. The adopted interventions were non-invasive ventilation care (Bilevel Positive Airways Pressure—BiPAP), eventually combined with cough assistance (manual or Mechanical Insufflation–Exsufflation—MIE), compared in terms of survival and hospitalisation for respiratory failure, to tracheostomy or supportive care, and noninvasive ventilation used to improve respiratory and sleep parameters. The studies' characteristics are described in Table 2.

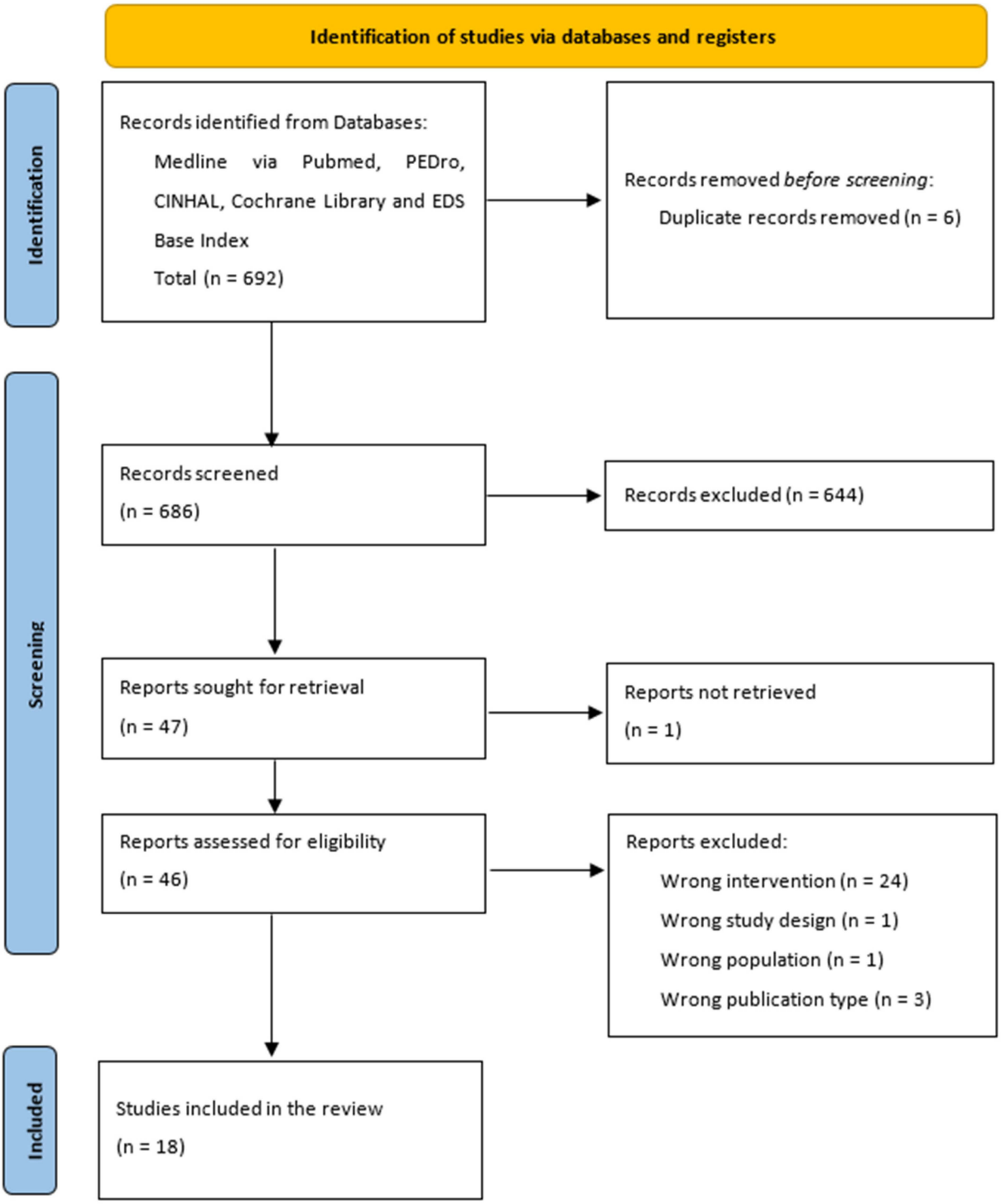

Figure 1. PRISMA Flow Diagram.

Table 2. Characteristics of the studies included.

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Bach et al. (2002) * [43]	Retrospective Analysis	16 patients underwent tracheostomy (group A); 33 used high-pressure PIP + PEEP nocturnal ventilation and were intubated during intercurrent respiratory infections (group B); 7 died from respiratory failure, refusing intubation and tracheostomy (group C).	56 patients with SMA I	Survival, hospitalisation, language, and outcomes related to the need for a respirator in patients with SMA I, using non-invasive ventilation or tracheostomy.	Compared to group B, patients in group A had fewer hospitalisations until the age of 3, but more after 5 years and 15 out of 16 lost all spontaneous respiratory tolerance post-tracheostomy and could not speak. One patient from group A passed away at 16 months of age, and the others were 73.8 +/− 57 months old (the oldest being 19 years old). Two patients from group B passed away at 6 and 13 months, while the remaining 31 were 41.8 +/− 26.0 months old (and up to 8.3 years). Three of the 31 in group B required continuous PIP + PEEP with minimal tolerance for breathing on their own, and 4 could not communicate verbally.
Bach et al. (2000) * [44]	Retrospective Cohort Study	Non-invasive respiratory care (BiPAP, manual and mechanic assistance) versus conventional care.	11 patients with SMA I	Successes and failures of a non-invasive respiratory management protocol vs. conventional respiratory management.	Two children survived for 37 and 66 months and were never intubated despite requiring 24-h nasal ventilation from 5 to 7 months of age. Two children underwent tracheostomy, and one child was lost to follow-up three months after successful extubation. The other six children were managed at home for 15–59 months (average 30.4) using nighttime nasal ventilation after an episode of respiratory failure. Nine children were successfully extubated 23 out of 28 times using the protocol. In contrast, the same children managed conventionally without the protocol were successfully extubated only 2 out of 20 times ($p < 0.001$ from a two-tailed Fisher exact test).
Bulut et al. (2019) [45]	Case report	Ergometric training was performed three times a week for 12 weeks. After a wash-out period of 6 weeks, hydrotherapy was applied twice a week for 12 weeks.	1 child with SMA I	HFMS, GMFM and PedsQL 3.0.	The HFMS and GMFM scores, child's lung function, and quality of life scores of their parents improved with both approaches. The improvements were maintained during the 1-year follow-up.

Table 2. *Cont.*

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Chatwin et al. (2011) * [46]	Case series	Sleep study; non-invasive positive pressure ventilation (NIPPV) for ventilatory support and physiotherapy; use of mechanical insufflation/exsufflation (MI-E).	13 patients with SMA I	Oxygen saturation (SpO2) and transcutaneous carbon dioxide (TcCO2).	NIPPV and MI-E were used for successful extubations guided by the protocol (No. = 9) but not for those not guided by the protocol (No. = 3). NIPPV was essential for home discharge in ventilator-dependent patients (n = 7) and used for palliating respiratory symptoms (n = 4). The chest wall shape improved with NIPPV. The parents of the deceased children (n = 5) were positive about the use of these techniques.
Cunha et al. (1996) [47]	Multi-case study	Individual physiotherapy once a week and hydrotherapy and therapeutic swimming (Halliwick method) for 30 min for children and 45 min for adults, twice a week for 2 years.	50 patients (30 with SMA II and 20 with SMA III)	Deformities in joints, development of scoliosis, Manual Muscular Test, Barthel Ladder, and motorial activities.	The degrees of deformity in the hips, knees, and feet increased in all patients; scoliosis was more pronounced in type II patients compared to type III. Muscle strength stabilised or improved in patients with SMA type III. A total of 93% of type II patients and 100% of type III patients showed improvement in activities of daily living (Barthel Ladder); type II patients improved their motor activities except for ambulation. Type III patients improved all motor activities, including ambulation.
Fehlings et al. (2002) [48]	RCT	Therapeutic electrical stimulation (TES) at low intensity was applied for 6 to 12 months on the deltoid and biceps muscles in the treatment arm. The control arm received placebo stimulation.	13 patients with SMA II and III	Myometry, manual muscle testing, maximum evoked muscle response amplitudes (M waves), and the PEDI.	There was no statistically significant difference between the treatment arm and the control arm at baseline, 6 and 12 months in quantitative myometry, manual muscle testing, M-wave amplitude ($p = 0.12$), and PEDI ($p = 0.11$).

Table 2. *Cont.*

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Gobbo et al. (2019) [49]	Case report	During phase I (weeks 1–8) was provided a home-based program for quadriceps strengthening through neuromuscular electrical stimulation (NMES). During phase II (weeks 9–18), at-home NMES was combined with functional electrical stimulation (FES) assisting volitional cycling for a broader, systemic conditioning.	1 patient with SMA type III	Quadriceps circumference and strength (MIVC), Tinetti scale, Hammersmith scale (HFSME), Heart rate (HR); oxygen consumption (VO2); and metabolic equivalents of task (METs).	By the end of Phase I, quadriceps isometric strength showed a significant increase, rising from 1.7 to 2.2 kg on the right side and from 0.8 to 2.0 kg on the left. Thigh circumference expanded by 7 mm and 3 mm on the right leg and by 5 mm and 3 mm on the left. At the conclusion of Phase II, thigh circumference further increased compared to baseline, reaching 15 mm and 9 mm on the right leg and 12 mm and 6 mm on the left. Maximum voluntary isometric contraction (MVIC) of the right quadriceps rose by 70.6%, while the left quadriceps nearly tripled in strength, increasing from 0.8 to 2.3 kg. Motor function assessments indicated a 7-point improvement on the HFMSE scale. The Tinetti score increased by 4 points for both balance and gait. Energy expenditure during FES-assisted cycling progressively increased from 2.3 METs to a final value of 3.1 standard METs and from 2.6 to 3.4 measured METs. Cycling power also improved, with average power rising from 7 to 9.8 watts and maximum power increasing from 14.4 to 16.8 watts between the first and final sessions.

Table 2. *Cont.*

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Lemoine et al. (2012) * [50]	Retrospective Cohort Study	Proactive respiratory care with BiPAP during sleep and cough assistance twice a day in the first group; respiratory support care through suction, with or without supplemental oxygen in the second group.	44 children with SMA I	The primary outcome was time of death comparing the children who received proactive respiratory care versus supportive care.	Children treated with early proactive respiratory care had statistically longer survival compared to support therapy (log rank 0.047); however, the hazard ratio for adjusted survival concerning confounding variables was not statistically different (2.44 [95% confidence interval 0.84–7.1]). Children in the proactive group were more likely to be hospitalised for respiratory failure (83% vs. 46%), and the time from diagnosis to the first hospitalisation for respiratory failure was reduced (median 118 vs. 979 days).
Lewelt et al. (2015) [51]	Prospective cohort study	Supervised resistance exercise program performed at home, 3 times a week for 12 weeks.	9 patients with SMA II and SMA III	Feasibility, safety, QMA, HHD, MMT, and MHFMS-Extend.	The average amount of weight lifted by the participants as a group increased significantly ($p < 0.001$) by 0.27 (0.05) kg; the perceived exertion level remained unchanged ($p = 0.76$). Pain was perceived as absent 99.5% of the time on the FACES scale. For strength, there was a significant change in the total composite MMT score ($p = 0.01$), a non-significant increase in QMA, and no change in HHD. MHFMS-Extend scores for motor function significantly improved ($p = 0.04$).
Madsen et al. (2015) [52]	Non-randomised control trial	A 12-week training program with a cycle ergometer, consisting of 42 sessions of 30 min at 65–70% of VO2max, performed 2 to 4 times a week.	6 patients with SMA III and 9 healthy people of the same age and gender	VO2max, ADL, changes in Wmax, isometric leg muscle strength (hand-held-dynamometer), body composition, and performance in functional tests (6MWT; 6SST, TUG; 5STST).	The training improved VO2max in patients with SMA III by 27 ± 3% ($p < 0.001$). There was no change or increase in fatigue in all subjects. The maximum workload capacity (Wmax) remained unchanged in half of the patients and increased in the other half. There were no significant changes in muscle strength, 6MWT, 6SST, TUG, and 5STST in any patient.

Table 2. *Cont.*

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Markström et al. (2010) * [53]	Cohort Study	Nightly BiPAP use for more than 12 months (median 32 months, min. 14, max. 72 months) and comparison with parameters in the absence of support.	10 patients with SMA II	Oxygen saturation (SpO2), transcutaneous partial pressure of carbon dioxide (TcPaCO2) and oxygen (TcPaO2), phase angle between chest and abdominal movements, and electrocardiogram (HR, PTT, PTT range).	The HR and PTT parameters between breathing without support and with optimal Bi-PAP were comparable (p = 0.85 and 0.79, respectively), as were the blood gases (SaO2, TcO2, TcCO2 p = 0.79, 0.88, 0.79, respectively). Respiratory efficiency improved when Bi-PAP was optimal (reduction in phase angle from 42 to 22). Suboptimal Bi-PAP due to mask air leakage was associated with significant increases in breath-to-breath variability in HR, PTT, and phase angle.
Mellies et al. (2004) * [54]	Case–ontrol Study	Non-invasive ventilation use for 7–12 h at night in SMA patients with sleep disturbances; Supportive treatment in SMA patients without sleep disturbances.	12 patients with SMA I and II	Inspiratory vital capacity (IVC), PIP, PEEP, complete polysomnography with transcutaneous carbon dioxide partial pressure (PtcCO2), respiratory disturbance index (RDI), and a visual analogue scale.	The non-invasive ventilation during sleep eliminated disordered breathing, normalised sleep architecture, and improved symptoms ($p < 0.05$ for all).
Mirea et al. (2022) [55]	Retrospective observational study	Correction of posture, reduced stiffness, increased range of motion and muscle strengthening at least 5 times per week.	55 patients with SMA I, II, III	CHOP INTEND was performed in SMA type I patients, while HFMSE in type II and III patients.	Motor skill improvements were statistically significantly ($p < 0.001$) higher in the study group, being almost four times better (12.66%), effect size, in comparison to the control group (3.18%).

Table 2. *Cont.*

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Montes et al. (2015) [56]	RCT	A muscle strengthening program (3 times per week for 30 min/day), combined with a home-based aerobic exercise program using a cycle ergometer (5 times per week for 30 min/day), for 19 months in the experimental group and 12 months in the control group.	14 patients with SMA IIIa and IIIb	6MWT, HFMSE, TUG, FVC, PedsQL Generic Quality of Life Inventory, Multidimensional Fatigue Scale and Fatigue Severity Scale.	At baseline, the two groups were similar in all clinical variables. There were no significant changes in the experimental group after 6 months in the primary outcome measure (6MWT walking distance), or in measures of strength or motor function. VO2 max improved by 4.9% in all participants at 6 months (p = 0.036) (n = 10).
Novikov et al. (2023) [57]	Case series	Spinal cord stimulation was applied alongside physical therapy. The therapy included both passive and active stretching of the upper and lower joints, positioning techniques, weight movements, exercises to prevent scoliosis, stepping and kicking actions, as well as breathing exercises. Stimulation targeted one or two spinal cord regions, either above the cervical or lumbar enlargements, or above the cauda equina.	5 patients with SMA II or III	RULM, HFMSE, FVC and goniometry.	Testing of HFMSF of participants' sitters showed an increase of 0, 2 and 1 points, respectively. The length of sitting independently of one participant increased from 20 s to 3 min; another participant learned to move from the couch to the wheelchair, from the wheelchair to the floor and back to the couch, and managed to pull himself to a standing position while holding on to the bars of the Swedish Wall. FVC increased by 7%, 1% and 3% of predicted values based on height and age in three participants.

Table 2. *Cont.*

Author and Year	Study Design	Intervention	N. of Participants	Outcomes	Main Results
Petrone et al. (2007)* [58]	Case series	Baseline sleep study (polysomnography) and use of BiPAP for 20 min, 2/3 times a day.	9 patients with SMA I and II	Assessment of the sleep apnea/hypopnea index (AHI), mean oxygen haemoglobin saturation (SpO2), oxygen desaturation index, transcutaneous carbon dioxide tension (tcpCO2), and the mean phase angle during sleep as a measure of thoracoabdominal coordination.	Comparing the baseline sleep studies with those conducted after non-invasive ventilation, a significant improvement was observed in the oxygen desaturation index (p 0.010), mean tcpCO2 (p 0.001), and phase angle (p 0.001). For five patients, the improvement in thoracoabdominal phase angle became significant when using high-pressure biphasic airway pressure (PAP) at two levels.
Salem et al. (2010) [59]	Case report	Hydrotherapy for 45 min per session, 2 times a week for 14 weeks.	1 patient with SMA III	GMFM, PDMS-2 and GAITRite system.	There was an improvement in muscle strength of the lower limbs, pelvic movements, hip flexion, knee flexion, and ankle flexion during the swing phase. The GMFM improved by 11%. The gross motor quotient for PDMS-2 improved from 66 to 74. Additionally, spatial and temporal gait measures (walking speed, stride length, etc.) showed improvement.
Vry et al. (2014) [60]	Multi-case study	8 weeks of whole-body vibration training (15–18 Hz) at home using an alternating side-to-side platform (3 sets x 3 min, twice a day, 5 days a week).	22 patients (8 SMA and 14 with DMD)	Serum creatine kinase levels, function tests, muscle strength and angular degree of dorsiflexion of the ankles.	In patients with SMA, laboratory parameters (CK, PCR, electrolytes) were unchanged. Secondary outcomes on training effectiveness (muscle strength, ankle dorsiflexion, temporal functional testing) showed mild, but not significant, improvements, except for the 6-min walk test (6MWT) ($p < 0.01$).

N, number; *, respiratory studies; RCT, randomised controlled trial; SMA, spinal muscular atrophy; DMD, Duchenne muscular dystrophy; GMFM, gross motor function measure; HFMS, Hammersmith motor function scale; MHFMS-Extend, modified Hammersmith motor function scale-extend; PEDI, paediatric evaluation of disability inventory; BiPAP, bi-level non-invasive ventilation; PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; PedsQL, paediatric quality of life inventory; RULM; revised upper limb module for spinal muscular atrophy; QMA, quantitative muscle analysis; HHD, hand-held dynamometery; MMT, manual muscle testing; VO2max, maximum oxygen consumption; ADL, activities of daily life; PDMS-2, Peabody developmental motor scales, second edition; 6MWT, 6 min walking test; 6SST, six sit-to-stand test; TUG, timed up and go; FVC, forced expiratory vital capacity; 5STST, five times sit to stand test; CHOP INTEND, the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; FES, functional electrical stimulation; METs, metabolic equivalents of task.

3.1. Motor Rehabilitation

3.1.1. Hydrotherapy

In three of the selected studies, hydrotherapy (alone or in combination with physiotherapy) was applied to improve trunk and limb motor functions and ambulatory ability.

Bulut et al. assessed the effects of two different training interventions on lung and motor functions, as well as the quality of life in a person with type I SMA [45]. The aerobic training, supervised by a physiotherapist, involved using an ergometer three times a week for twelve weeks, with exercise intensity set at 60–70% of the participant's maximum heart rate measured with a pulse oximeter. Following a six-week washout, hydrotherapy was performed twice a week for twelve weeks. The hydrotherapy sessions included 5–10 min of warm-up and stretching exercises, followed by 40 min of the Halliwick method in a heated pool at 30–32 degrees Celsius, and finally, 5–10 min of cooling-down exercises. The results suggested that if protracted over time, this combined approach could improve trunk and limb movements, motor function (HFMS and GMFM), lung function, quality of life and patient autonomy (PedsQL 3.0). Cunha et al. conducted a multiple case study to explore the effects of adding hydrotherapy for individuals with type II and III SMA [47]. Fifty participants (thirty with type II SMA and twenty with type III) performed individual physiotherapy once a week for two years, and at the same time, hydrotherapy (Hallwick method) two times a week. Physiotherapy consisted of kinesiotherapy, stretching, and respiratory exercises. The degrees of deformity in the hips, knees, and feet increased in all patients, as well as scoliosis. A total of 93% of type II patients and 100% of type III patients showed improvement in activities of daily living (Barthel Ladder); type II patients improved their motor activities except for ambulation. Type III patients improved all motor activities, including ambulation.

Salem et al. proposed a hydrotherapeutic programme focused on functional movements in a child with type III SMA to monitor the changes in motor functions and gait's spatiotemporal characteristics [59]. Every session consisted of a warm-up period, in-water exercises, and finally, a cooling period. Both warming and cooling periods were performed in water and included low-intensity aerobic exercises (respiratory exercises, flexibility, and walking activities). Activities were adjusted based on the child's capabilities and to allow practice in the form of play. There was an improvement in the muscle strength of the lower limbs and movements during the swing phase. The GMFM improved by 11%. The gross motor quotient for PDMS-2 improved from 66 to 74. Additionally, spatial and temporal gait measures (walking speed, stride length, etc.) showed improvement.

3.1.2. Aerobic Training

Madsen et al., in their non-randomised controlled trial, studied the effect of training aerobic programs lasting twelve weeks in an in-home setting [52]. Participants trained at home using a cycle ergometer and performing aerobic sessions lasting 30 min at 65–70% of VO2max, estimating VO2max through correlation with heart rate. Thus, maintaining the heart rate to an oxygen uptake of 60–75% of VO2max. All subjects monitored and recorded their heart rate during cycling using a Polar Pulse Watch. The patients were instructed to perform 3–5 min of warm-up before each training session, gradually increasing the workload until they reached the heart rate target. The number of sessions progressively augmented from two to four times a week, aiming to reach 42 sessions in 12 weeks. The training improved VO2max in patients with SMA III by 27 $\pm$ 3% ($p < 0.001$), but no significant changes in muscle strength, 6MWT, 6SST, TUG, and 5STST in any patient.

Montes et al. conducted an RCT to examine the effects of a mixed program involving both strengthening and aerobic home-based training sessions in 14 participants with type III SMA [56]. The participants engaged in aerobic training using a cycle ergometer for 30 min,

five times a week, and performed strengthening sessions three times a week, each with a similar duration. This intervention was administered for 19 months in the experimental group and 12 months in the control group. No significant changes in the experimental group after 6 months of exercise in the 6MWT walking distance were reported. Instead, an improvement in VO_2 max was observed in all participants after six months of exercise, with the greatest gains among those who adhered closely to the program. Compliance was defined as completing at least 90% of the recommended weekly exercise and not missing more than two consecutive weeks within three months. Across all participants (n = 10), percent-predicted VO_2 max increased by 4.9% ($p = 0.036$), while the most compliant individuals (n = 5) experienced an even greater improvement of 6.6% ($p = 0.012$).

3.1.3. Electrical Stimulation

Fehlings et al. conducted an RCT to investigate the effects of therapeutic electrical stimulation (TES; NT-2000), administered for 12 months to 13 patients with SMA II and III on the deltoid (shoulder abductor) and bicep (elbow flexor) muscles of a randomly chosen arm [48]. The opposite arm received sham stimulation (placebo), which stopped after fifteen minutes of stimulation. TES was administered using transcutaneous and conductive silicone rubber electrodes. The electric stimulator used a two-channel battery that generated pulses of coupled alternating current. It was turned on when the participant went to bed and turned off in the morning. Stimulation parameters consisted of a pulse amplitude of 300 μs, a pulse frequency between 35 and 45 Hz, a peak intensity of less than 10 mA, and a 1:1 on/off cycle. The results showed no statistically significant difference between the treatment arm and the control arm at baseline, 6 and 12 months in quantitative myometry, manual muscle testing, M-wave amplitude ($p = 0.12$), and PEDI ($p = 0.11$), suggesting poor effectiveness of this treatment on SMA patients.

Gobbo et al. raised awareness of the potential role of electrotherapy in helping improve motor performance in SMA patients [49]. The study focused on a 13-year-old adolescent with SMA type III who participated in an 18-week strengthening program divided into two phases. Phase I (weeks 1–8) involved a home-based quadriceps strengthening regimen using neuromuscular electrical stimulation (NMES). The NMES protocol was administered for 22 min per session, five days per week. It began with a 2 min warm-up phase consisting of single twitches (frequency: 5 Hz; stimulus width: 380 μs), followed by a 20 min strengthening protocol featuring tetanic contractions (duration: 2 s; frequency: 35 Hz; pulse width: 380 μs), interspersed with 9 s recovery periods of single twitches at 3 Hz. During phase II (weeks 9–18), NMES was combined with functional electrical stimulation (FES) and 10 sessions of voluntary cycling exercise (FES-assisted cycling). The protocol lasted 25 min and was conducted at a speed of 30 rpm, with pedal resistance progressively increasing from 5 to 9 Nm. Stimulation amplitude was set at 45 mA for the quadriceps, 30 mA for the hamstrings, and 25 mA for the gluteal muscles. Results indicated that NMES led to an increase in thigh circumference (up to 7 mm by the end of Phase I), suggesting muscle mass gain. Functionally, improvements were observed on the HFMSE scale, particularly in items related to standing performance and lower limb motor abilities. Similarly, the Tinetti scale allowed appreciation of a substantial gain in balance and gait.

Novikov et al. investigated the effects of transcutaneous spinal cord stimulation combined with physical therapy in five children with genetically confirmed SMA II or III [57]. Participants, classified as sitters or non-sitters, had been receiving nusinersen for approximately two years. The intervention aimed to reduce joint contractures, improve endurance, and develop motor skills through individualised rehabilitation plans. Sessions included passive and active stretching, weight-bearing exercises, stepping movements, and breathing exercises, supplemented by additional therapies such as massage. Functional

improvements were observed in four participants, including increased independent sitting time, improved transfers, and enhanced posture control. No adverse events were reported, and participants tolerated the intervention well.

3.1.4. Whole Body Vibration

Vry et al., in their multi-case study, evaluated the safety and effectiveness of strength and motor performance of whole-body vibration training in ambulatory children with Duchenne muscular dystrophy (DMD) and SMA [60]. After a learning phase in the hospital with the help of experienced physiotherapists, 4 children with DMD and 8 with SMA underwent an 8-week vibration training programme on a Galileo MedM at home (3 × 3 min twice a day, 5 days a week). For the first training, a low vibration frequency of 10 Hz was chosen, gradually increasing to 15–18 Hz as the patients felt comfortable with the training. The target frequency of 15–18 Hz was achieved on the first day for all patients. The vibration amplitude was 4 mm. Each training session consisted of three units, each lasting three minutes, with a three-minute rest between each unit. During each unit, the children performed a physical exercise on the vibrating platform: 1) light squatting, 2) stretching of the gastrocnemius muscle, and 3) light alternating weight shift from the right to the left leg for two consecutive days with two and three training sessions per day in the hospital. After the hospital training phase, the patients continued to practice WBVT at home, 3 × 3 min twice a day, with a minimum break of 4 h between the two sessions, on five freely selected weekly days. The intervention was well tolerated clinically. In boys with DMD, creatine kinase levels initially increased by 56% after the first day of training but returned to baseline after eight weeks of continuous whole-body vibration therapy. No significant changes in laboratory parameters were observed in children with SMA. Regarding training effectiveness, secondary outcomes such as muscle strength and ankle dorsiflexion showed mild, non-significant improvements. However, performance on the 6 min walk test (6MWT) significantly increased from 371.3 m to 402.8 m ($p < 0.01$).

3.2. Respiratory Interventions

3.2.1. NIV vs. Tracheostomy/Supportive Care

Bach et al., in the 2000 study, aimed to investigate whether type 1 SMA could be managed without tracheostomy and whether extubation results could be compared using a protocol for respiratory muscle support [44]. Eleven type 1 SMA children were studied during episodes of respiratory failure, and nine of them required multiple intubations. In addition to standard treatments for nutrition and hydration, these children underwent a protocol with manual and mechanically assisted coughing to reverse the decrease in oxygen saturation associated with airway mucus. The pressures used ranged from 25–40 cm H2O to 225–240 cm H2O for up to 10 min, depending on the needs. Abdominal thrusts were applied during expiration. Extubation was not attempted until, primarily, there was no longer a need for oxygen to maintain oxygen saturation above 94%. After extubation, all patients received nasal positive end-expiratory pressure ventilation.

Bach et al., in the 2002 study, recruited 56 patients with SMA1 who developed respiratory failure before the age of 2 and divided them into three groups based on treatment [43]. The 33 patients in Group B were initially prescribed oximetry, mechanical insufflation–exsufflation (MI-E), and high-flow PIP + PEEP, which was used during sleep and upper respiratory tract infections, with intervals of 13–17 cm H2O and positive inspiratory pressures in the airways up to 20 cm H2O. Positive pressure was applied at 35–40 cm H2O during upper respiratory tract infections to expel airway mucus. For non-cooperative infants, nasal interface placement and initiation of PIP + PEEP during sleep were employed.

Lemoine et al. investigated if the initiation of non-invasive mechanical respiratory interventions in patients with SMA I was associated with longer survival compared to those who received only supportive care [50]. Proactive management of chronic respiration included airway clearance through mobilisation of secretions with manual or mechanical chest physiotherapy and cough assistance, as well as BiPAP ventilatory support during sleep. Supportive care was defined as other respiratory support, such as supplemental oxygen and suctioning.

3.2.2. NIV to Improve Respiratory and Sleep Parameters

Chatwin et al. investigated in a cohort of 13 children with SMA I the role of polysomnography, the provision of non-invasive positive pressure ventilation (NIPPV) for ventilatory support and physiotherapy, and the use of MI-E [46]. Pressures were set low (positive inspiratory airway pressure 12 cm H2O, positive expiratory airway pressure 4 cm H2O with a backup rate between 18 and 35 breaths per minute depending on the child's spontaneous respiratory rate and inspiratory time); settings were then rapidly increased to ensure good chest wall movement and eliminate paradoxical breathing. NIPPV and MI-E were used for protocol-guided successful extubations (n = 9) but not for those not guided by the protocol (n = 3). NIPPV was essential for home discharge in ventilator-dependent patients (n = 7) and was used for palliation of respiratory symptoms (n = 4). The chest wall shape improved with NIPPV. Parents of deceased children (n = 5) were positive about using these techniques.

Markström et al. treated 10 boys with SMA II (aged 8–12 years) with nightly BiPAP for more than 12 months, and all had normal blood gases [53]. All children used BiPAP ventilators set in spontaneous/timed mode. Positive inspiratory/expiratory airway pressures were set at 12–20 cmH2O and 4–7 cmH2O, respectively. The respiratory rate was set slightly below the rate of spontaneous breathing.

Mellies et al., in a cohort of twelve children with SMA I or II, investigated the use of non-invasive ventilation during sleep in six patients with SMA I and one with SMA II, both with sleep disorder, adopting polysomnography and a symptom questionnaire [54]. Five less severely affected patients had no sleep disorders and served as the reference group. In the treatment group, non-invasive ventilation with BiPAP was used for 7–12 h of sleep during the night with the following ventilator settings: positive inspiratory airway pressure range of 8–14 cmH2O, positive end-expiratory pressure range of 3–4 cmH2O, and backup respiratory rate range of 16–24 bpm. Patients in the reference group and their caregivers, on the other hand, were trained in assisted coughing techniques, which they applied daily.

Petrone et al. investigated the effectiveness of non-invasive ventilation in treating thoracoabdominal asynchrony during sleep in children with SMA I and II [58]. After baseline polysomnography, the examination was repeated following nasal BiPAP. BiPAP was introduced by using it for 20 min, two or three times a day, before the sleep study. All patients used high-flow BiPAP (range 14–20 cm H2O) to achieve good chest and alveolar expansion.

4. Discussion

The following narrative review investigated the available evidence in the literature on physiotherapeutic and respiratory interventions in people with SMA. Among the 18 studies included, 11 investigated the role of physiotherapy in this population, including two RCTs, while 7 investigated the role of respiratory interventions, including no RCTs.

Over the past three decades, research on physiotherapy and respiratory interventions in SMA has expanded, with early studies focusing on symptom management and now shifted towards optimising long-term functional outcomes and integrating new therapeutic

approaches [61–69]. Drug treatments, such as nusinersen, rusdiplam and gene therapy, have further shaped rehabilitation approaches.

4.1. Physiotherapy Interventions

Electric stimulation (NMES + FES) did not enhance muscle strength and self-care in people with SMA II and III [48]. This lack of improvement might stem from challenges such as the instability of electrode positioning during sleep and the low stimulation level (10 mAh), which might not be sufficient to recruit partially denervated muscles. However, in the Gobbo et al. study, electrotherapy (NMES + FES) combined with cycling exercise may be well tolerated in an adolescent with SMA III and may improve motor performance in SMA patients [49]. Given its promising role in neuromuscular conditions, electrotherapy could be considered an adjunct to conventional rehabilitation rather than a standalone intervention.

Whole-body mechanical vibrations were safe and well-tolerated, with no notable changes in electrolytes and CK levels [60]. However, objective differences in muscular strength, function, and flexibility were not observed, although participants reported positive subjective outcomes. Considering the potential benefits observed in individuals with spinal injury, where whole-body vibrations increase blood flow and activated muscle mass, it raises the question of whether this therapy could be valuable as a complementary treatment in SMA [70].

Aerobic training sessions using a cycle ergometer, lasting 30 min over multiple weeks, seemed to enhance VO2 max and ultimately improve muscular capacity in people with SMA III, causing no harm [45,52]. Notably, it did not enhance muscle strength or functional mobility, as it was not the primary focus, nor were motor functions and ADL [52]. However, optimal intensity and dosage of aerobic training remain uncertain in this population, especially considering their susceptibility to fatigue [52]. Madsen et al., for example, reported increased fatigue perception following aerobic training in individuals with SMA III [59]. It is worth noting that intermediate grades of SMA, such as type II, have received much attention in the literature.

Hydrotherapy was primarily studied as an adjunctive treatment to conventional physiotherapy or aerobic training, showing benefits in motor and pulmonary functions, ADL, and quality of life for caregivers and people with SMA [45,47,59]. However, studies with more follow-ups and wider samples are needed to investigate the long-term effects of hydrotherapy.

Finally, progressive resistance/strength training in people with SMA II and III was safe and well-tolerated, with high levels of adherence reported by participants (~90%) [51]. Participants in the Lewelt et al. study reported a subjective improvement in pain and perceived fatigue [51], and in muscular strength and function. Not only that, but the use of nusinersen therapy, in conjunction with physical therapy, can result in a more favourable motor outcome [55]. However, the role of strength training is still controversial due to the low level of evidence, as also reported by Bartels B et al. in their review [71].

4.2. Respiratory Interventions

Respiratory interventions primarily targeted people with SMA I, recognising their need for timely pulmonary care to extend their life expectancy. People with SMA commonly exhibit combined inspiratory and expiratory muscle weakness, while the diaphragm is partially spared. This weakness compromises the cough mechanism, leading to recurrent infections and subsequent nocturnal hypoventilation, hypercapnia, desaturation, and paradoxical breathing [46]. In recent years, pulmonary treatments have shifted from a reactive to a proactive approach, particularly with the introduction of early treatments [50]. Chronic proactive respiratory management comprehends various strategies, including airway clearance through manual or mechanical physiotherapy techniques, cough assistance, and NIV (BiPAP) support during sleep. In severe cases, tracheostomy may be necessary [50].

NIV (BiPAP) was associated with improved sleep quality, reduced hypercapnia, and facilitated hospital discharge in SMA I [44,46]. Bach et al. suggested timely and appropriate use of pulmonary aids (among which especially NIV), rather than immediate tracheostomy, can ensure survival, although instances like thoracic infections may lead to temporary periods of intubation and hospitalisation [44]. Polysomnography conducted during BiPAP in people with SMA I and II has revealed differences in thoracic-abdominal movement coordination (measured by phase angle, transcutaneous oximetry, and SpO2 desaturation rate), suggesting that nocturne NIV (BiPAP mode) might normalise various parameters such as AHI, SpO2, and inspiratory muscle synchronisation [56]. Another study on NIV supported its potential role in enhancing muscle synchronisation during sleep and improving sleep quality [46]. Proper facial mask positioning has been highlighted as crucial, as incorrect positioning may negatively affect the hemodynamic status of people with SMA undergoing long-term treatment (14–72 months) [53]. However, further research with long-term follow-ups is recommended to fully understand the effects of BiPAP therapy on hemodynamics, disease progression and motor function.

4.3. Limits and Implications

Several limitations must be addressed. First, the high heterogeneity among included studies in terms of participants, as the most represented were people with SMA I, poses challenges in generalising findings to other SMA types. Moreover, variations in intervention modalities, intensity, and outcomes measured across studies make any direct comparison difficult. Additionally, this review included only studies published in English, which may introduce a potential language bias that future reviews could overcome by setting no limitation to a study's language. Future research with more robust methodologies and broader participant samples is imperative to elucidate the efficacy of physiotherapy and respiratory interventions in people with SMA. Specifically, future studies on aerobic training and hydrotherapy should focus on defining the optimal duration, frequency, and intensity of these interventions and assess their long-term effects on motor function and fatigue management. Regarding respiratory interventions, current research is mainly focused on SMA I, and limited studies have been conducted on SMA II and III. Future research should explore the role of respiratory interventions in preventing respiratory decline and optimising pulmonary function before severe deterioration occurs. Early rehabilitation interventions should also be planned in light of recent evidence that highlights how early interventions prevent the deterioration of motor and respiratory functions, as well as preventing scoliosis onset [72,73]. Finally, individual interventions should be compared to combined approaches to identify the most beneficial rehabilitation strategies, as well as explore the role of assistive technologies such as power mobility [74]. Moreover, recent advances in assistive technologies and digital health solutions could open new pathways for SMA rehabilitation. The development of wearable sensors and AI-assisted rehabilitation programs could enhance the monitoring of functional progress and enable personalised interventions [75,76].

From a clinical perspective, aerobic training and hydrotherapy could be added to rehabilitation programs, but careful monitoring of intensity and duration is essential to prevent excessive fatigue, particularly in individuals with SMA III. Resistance training appears safe and well tolerated, especially in SMA II and III, but its effectiveness may depend on individualised protocols and its integration with pharmacological treatments such as nusinersen. Given the progressive nature of SMA, early and proactive respiratory interventions are crucial, particularly in SMA I, to prevent respiratory decline. NIV should be prioritised whenever possible, with frequent reassessment to ensure optimal parameter settings. Furthermore, a multidisciplinary approach combining physiotherapy, respiratory support, and pharmacological treatment could enhance patient outcomes.

5. Conclusions

This narrative review reports various evidence on physiotherapy and respiratory interventions for SMA. While various approaches like hydrotherapy and aerobic training show promise in improving motor function and quality of life, optimal intensity and dosage remain unclear. Similarly, respiratory interventions, primarily targeting SMA Type I, emphasise proactive management with NIV and cough assistance, but further investigation is needed to refine their application across different SMA subtypes. However, the lack of RCTs and heterogeneity among studies pose limitations, necessitating further research with standardised methodologies and larger sample sizes.

Author Contributions: Conceptualisation, S.C., V.A.C., and B.G.; methodology, S.C. and B.G.; software, S.C. and G.M.; validation, V.A.C. and B.C.; resources, C.R. and B.C.; data curation, S.C. and B.G.; writing—original draft preparation, S.C., V.A.C., B.G., and G.M.; writing—review and editing, B.C. and B.G.; visualisation, B.G.; supervision, C.R. and B.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data supporting reported results can be requested by writing to bruno.corrado@unina.it.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Kolb, S.J.; Kissel, J.T. Spinal Muscular Atrophy. *Neurol. Clin.* **2015**, *33*, 831–846. [CrossRef] [PubMed]
2. Ojala, K.S.; Reedich, E.J.; Didonato, C.J.; Meriney, S.D. In Search of a Cure: The Development of Therapeutics to Alter the Progression of Spinal Muscular Atrophy. *Brain Sci.* **2021**, *11*, 194. [CrossRef] [PubMed]
3. Arkblad, E.; Tulinius, M.; Kroksmark, A.K.; Henricsson, M.; Darin, N. A population-based study of genotypic and phenotypic variability in children with spinal muscular atrophy. *Acta Paediatr.* **2009**, *98*, 865–872. [CrossRef] [PubMed]
4. Norwood, F.L.M.; Harling, C.; Chinnery, P.F.; Eagle, M.; Bushby, K.; Straub, V. Prevalence of genetic muscle disease in Northern England: In-depth analysis of a muscle clinic population. *Brain* **2009**, *132 Pt 11*, 3175–3186. [CrossRef]
5. Barbo, M.; Glavač, D.; Jezernik, G.; Ravnik-Glavač, M. MicroRNAs as Biomarkers in Spinal Muscular Atrophy. *Biomedicines* **2024**, *12*, 2428. [CrossRef] [PubMed] [PubMed Central]
6. Mercuri, E.; Finkel, R.; Montes, J.; Mazzone, E.S.; Sormani, M.P.; Main, M.; Ramsey, D.; Mayhew, A.; Glanzman, A.M.; Dunaway, S.; et al. Patterns of disease progression in type 2 and 3 SMA: Implications for clinical trials. *Neuromuscul. Disord.* **2016**, *26*, 126–131. [CrossRef]
7. Kanner, C.H.; Rodriguez-Torres, R.; Wallach, R.; Bakarania, P.; Montes, J. Therapeutic Scoliosis-Specific Exercises for a Child with Spinal Muscular Atrophy: A Case Report. *Pediatr. Phys. Ther.* **2025**, *37*, 282–287. [CrossRef] [PubMed]
8. Rodriguez-Torres, R.; Montes, J. Fatigue and Fatigability in Spinal Muscular Atrophy; a Proposed Taxonomy to Enhance Assessment and Treatment. *Muscle Nerve* **2025**, *71*, 133–137. [CrossRef] [PubMed]
9. Govoni, A.; Ricci, G.; Bonanno, S.; Bello, L.; Magri, F.; Meneri, M.; Torri, F.; Caponnetto, C.; Passamano, L.; Grandis, M.; et al. Six-minute walk test as outcome measure of fatigability in adults with spinal muscular atrophy treated with nusinersen. *Muscle Nerve* **2024**, *70*, 816–823. [CrossRef] [PubMed]
10. Steiner, L.; Tscherter, A.; Henzi, B.; Branca, M.; Carda, S.; Enzmann, C.; Fluss, J.; Jacquier, D.; Neuwirth, C.; Ripellino, P.; et al. Chronic Pain in Patients with Spinal Muscular Atrophy in Switzerland: A Query to the Spinal Muscular Atrophy Registry. *J. Clin. Med.* **2024**, *13*, 2798. [CrossRef] [PubMed] [PubMed Central]
11. Kahraman, A.; Mutlu, A.; Livanelioğlu, A. General movements in spinal muscular atrophy type 1. *Physiother. Theory Pract.* **2024**, *40*, 1249–1255. [CrossRef] [PubMed]
12. Coratti, G.; Pera, M.C.; Montes, J.; Pasternak, A.; Scoto, M.; Baranello, G.; Messina, S.; Dunaway Young, S.; Glanzman, A.M.; Duong, T.; et al. Different trajectories in upper limb and gross motor function in spinal muscular atrophy. *Muscle Nerve* **2021**, *64*, 552–559. [CrossRef] [PubMed]

13. Oude Lansink, I.L.B.; Gorter, J.W.; van der Pol, W.L.; Bartels, B.; Beelen, A. Impact of contractures on daily functioning in adolescents with spinal muscular atrophy: A qualitative study. *Disabil. Rehabil.* **2024**, *46*, 2593–2599. [CrossRef] [PubMed]
14. Mortenson, P.; Cielecka, J.; Harrison, E.; Zwicker, J.G. Rehabilitation practices for childhood spinal muscular atrophy. *Disabil. Rehabil.* **2025**, 1–10, *epub ahead of print*. [CrossRef] [PubMed]
15. Muni-Lofra, R.; Coratti, G.; Duong, T.; Medina-Cantillo, J.; Civitello, M.; Mayhew, A.; Finkel, R.; Mercuri, E.; Marini-Bettolo, C.; Muntoni, F. Assessing disease progression in spinal muscular atrophy, current gaps, and opportunities: A narrative review. *Neuromuscul. Disord.* **2025**, *49*, 105341. [CrossRef] [PubMed]
16. Corti, S.; Sansone, V.; Bitetti, I.; Brolatti, N.; Gadaleta, G.; Patanella, A.K.; Coratti, G.; Mercuri, E.; SMAkers working group. Italian survey on evolving SMA care with disease-modifying therapies: A consensus workshop on nutrition, swallowing, respiratory and rehabilitation care. *Neuromuscul. Disord.* **2025**, *48*, 105278. [CrossRef]
17. Shin, H.I. shin Strategies for Patients with Spinal Muscular Atrophy in the Era of Disease-Modifying Therapy. *Ann. Rehabil. Med.* **2024**, *48*, 229–238. [CrossRef] [PubMed] [PubMed Central]
18. Wang, D.; Zhang, T.; Li, Y.; Liu, J.; Jia, Y.; Xiao, N. Rehabilitation for spinal muscular atrophy patients in China: A national cross-sectional study. *Orphanet J. Rare Dis.* **2024**, *19*, 279. [CrossRef] [PubMed] [PubMed Central]
19. Ahmed, F.; Islam, A.; Akter, S.; Al Zubayer, M.A.; Mahmud, M.N.; Yeasmin, H.; Mawa, Z. Multidisciplinary physical rehabilitation program of individuals with spinal muscular atrophy in an inclusive school setting. *J. Pediatr. Rehabil. Med.* **2024**, *17*, 247–252. [CrossRef] [PubMed] [PubMed Central]
20. Ippolito, C.; Canthiya, L.; Floreani, A.; Luckhart, K.; Hoffman, A.; McAdam, L. Twice- Weekly Outpatient Rehabilitation Intervention for Young Children with Spinal Muscular Atrophy Treated with Genetic-Based Therapies: Protocol for a Feasibility Study. *JMIR Res. Protoc.* **2023**, *12*, e46363. [CrossRef] [PubMed] [PubMed Central]
21. Sweat, M.; Skalsky, A. The Critical Importance of Early and Combination Treatment for Spinal Muscular Atrophy Type. *Muscle Nerve* **2025**, *71*, 290–292. [CrossRef] [PubMed]
22. Schroth, M.K.; Deans, J.; Bharucha Goebel, D.X.; Burnette, W.B.; Darras, B.T.; Elsheikh, B.H.; Felker, M.V.; Klein, A.; Krueger, J.; Proud, C.M.; et al. Spinal Muscular Atrophy Update in Best Practices: Recommendations for Treatment Considerations. *Neurol. Clin. Pract.* **2025**, *15*, e200374. [CrossRef] [PubMed] [PubMed Central]
23. Bagga, P.; Singh, S.; Ram, G.; Kapil, S.; Singh, A. Diving into progress: A review on current therapeutic advancements in spinal muscular atrophy. *Front. Neurol.* **2024**, *15*, 1368658. [CrossRef] [PubMed] [PubMed Central]
24. Nishio, H.; Niba, E.T.E.; Saito, T.; Okamoto, K.; Takeshima, Y.; Awano, H. Spinal Muscular Atrophy: The Past, Present, and Future of Diagnosis and Treatment. *Int. J. Mol. Sci.* **2023**, *24*, 11939. [CrossRef] [PubMed] [PubMed Central]
25. Walter, M.C.; Laforêt, P.; van der Pol, W.L.; Pegoraro, E.; Attarian, S.; Bartels, B.; Gorni, K.; Goemans, N.; Gusset, N.; Hodgkinson, V.; et al. 254th ENMC international workshop. Formation of a European network to initiate a European data collection, along with development and sharing of treatment guidelines for adult SMA patients. Virtual meeting 28–30 January 2022. *Neuromuscul. Disord.* **2023**, *33*, 511–522. [CrossRef] [PubMed]
26. Leibrock, B.; Landfeldt, E.; Hussong, J.; Huelle, T.; Mattheus, H.; Thiele, S.; Walter, M.C.; Zemlin, M.; Moehler, E.; Dillman, U.; et al. Areas of improvement in the medical care of SMA: Evidence from a nationwide patient registry in Germany. *Orphanet J. Rare Dis.* **2023**, *18*, 32. [CrossRef] [PubMed] [PubMed Central]
27. Krosschell, K.J.; Dunaway Young, S.; Peterson, I.; Curry, M.; Mazzella, A.; Jarecki, J.; Cruz, R. Clinical and Research Readiness for Spinal Muscular Atrophy: The Time Is Now for Knowledge Translation. *Phys Ther.* **2022**, *102*, pzac108. [CrossRef] [PubMed]
28. Pitarch Castellano, I.; Cabrera-Serrano, M.; Calvo Medina, R.; Cattinari, M.G.; Espinosa García, S.; Fernández-Ramos, J.A.; García Campos, O.; Gómez-Andrés, D.; Grimalt Calatayud, M.A.; Gutiérrez Martínez, A.J.; et al. Delphi consensus on recommendations for the treatment of spinal muscular atrophy in Spain (RET-AME consensus). *Neurologia* **2022**, *37*, 216–228. [CrossRef] [PubMed]
29. Rad, N.; Cai, H.; Weiss, M.D. Management of Spinal Muscular Atrophy in the Adult Population. *Muscle Nerve* **2022**, *65*, 498–507. [CrossRef] [PubMed]
30. de Lemus, M.; Cattinari, M.G.; Pascual, S.I.; Medina, J.; García, M.; Magallón, A.; Dumont, M.; Rebollo, P. Identification of the most relevant aspects of spinal muscular atrophy (SMA) with impact on the quality of life of SMA patients and their caregivers: The PROfuture project, a qualitative study. *J. Patient Rep. Outcomes* **2024**, *8*, 78. [CrossRef] [PubMed] [PubMed Central]
31. Poitou, T.; Boyer, F.C.; Benoit, C.; Ferté, J.B.; Pineau, C.; Taiar, R.; Rapin, A. Mobility and quality of life among adults with 5q-spinal muscular atrophy: The influence of individual history. *Ann. Phys. Rehabil. Med.* **2022**, *65*, 101552. [CrossRef] [PubMed]
32. Mercuri, E.; Finkel, R.S.; Muntoni, F.; Wirth, B.; Montes, J.; Main, M.; Mazzone, E.S.; Vitale, M.; Snyder, B.; Quijano-Roy, S.; et al. Diagnosis and management of spinal muscular atrophy: Part 1, Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. *Neuromuscul. Disord.* **2018**, *28*, 103–115. [CrossRef] [PubMed]
33. Gnasso, R.; Corrado, B.; Iommazzo, I.; Migliore, F.; Magliulo, G.; Giardulli, B.; Ruosi, C. Assessment, pharmacological therapy and rehabilitation management of musculoskeletal pain in children with mucopolysaccharidoses: A scoping review. *Orphanet J. Rare Dis.* **2022**, *17*, 255. [CrossRef] [PubMed] [PubMed Central]

34. Sommese, M.; Corrado, B. A Comprehensive Approach to Rehabilitation Interventions in Patients with Angelman Syndrome: A Systematic Review of the Literature. *Neurol. Int.* **2021**, *13*, 359–370. [CrossRef] [PubMed] [PubMed Central]
35. Corrado, B.; Giardulli, B.; Costa, M. Evidence-Based Practice in Rehabilitation of Myasthenia Gravis. A Systematic Review of the Literature. *J. Funct. Morphol. Kinesiol.* **2020**, *5*, 71. [CrossRef] [PubMed] [PubMed Central]
36. Corrado, B.; Ciardi, G.; Lucignano, L. Supervised Physical Therapy and Polymyositis/Dermatomyositis-A Systematic Review of the Literature. *Neurol. Int.* **2020**, *12*, 77–88. [CrossRef] [PubMed] [PubMed Central]
37. Fonzo, M.; Sirico, F.; Corrado, B. Evidence-Based Physical Therapy for Individuals with Rett Syndrome: A Systematic Review. *Brain Sci.* **2020**, *10*, 410. [CrossRef] [PubMed] [PubMed Central]
38. Corrado, B.; Ciardi, G.; Iammarrone, C.S. Rehabilitation management of Pompe disease, from childhood through adulthood: A systematic review of the literature. *Neurol. Int.* **2019**, *11*, 7983. [CrossRef] [PubMed] [PubMed Central]
39. Corrado, B.; Ciardi, G. Hypermobile Ehlers-Danlos syndrome and rehabilitation: Taking stock of evidence based medicine: A systematic review of the literature. *J. Phys. Ther. Sci.* **2018**, *30*, 843–847. [CrossRef] [PubMed] [PubMed Central]
40. Corrado, B.; Ciardi, G.; Bargigli, C. Rehabilitation Management of the Charcot-Marie-Tooth Syndrome: A Systematic Review of the Literature. *Medicine* **2016**, *95*, e3278. [CrossRef] [PubMed] [PubMed Central]
41. Baethge, C.; Goldbeck-Wood, S.; Mertens, S. SANRA—A scale for the quality assessment of narrative review articles. *Res. Integr. Peer Rev.* **2019**, *4*, 5. [CrossRef] [PubMed]
42. Sayers, A. Tips and tricks in performing a systematic review. *Br. J. General. Pract.* **2007**, *57*, 759. [CrossRef] [PubMed]
43. Bach, J.R.; Baird, J.S.; Plosky, D.; Navado, J.; Weaver, B. Spinal muscular atrophy type 1: Management and outcomes. *Pediatr. Pulmonol.* **2002**, *34*, 16–22. [CrossRef] [PubMed]
44. Bach, J.R.; Niranjan, V.; Weaver, B. Spinal muscular atrophy type 1: A noninvasive respiratory management approach. *Chest* **2000**, *117*, 1100–1105. [CrossRef]
45. Bulut, N.; Yardimci, B.N.; Ayvat, E.; Aran, O.T.; Yilmaz, Ö.; Karaduman, A. The effect of two different aerobic training modalities in a child with spinal muscular atrophy type II: A case report. *J. Exerc. Rehabil.* **2019**, *15*, 322. [CrossRef]
46. Chatwin, M.; Bush, A.; Simonds, A.K. Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I. *Arch. Dis. Child* **2011**, *96*, 426–432. [CrossRef]
47. Cunha, M.C.B.; Oliveira, A.S.B.; Labronici, R.H.D.D.; Gabbai, A.A. Spinal muscular atrophy type II (intermediary) and III (Kugel-berg-Welander). Evolution of 50 patients with physiotherapy and hydrotherapy in a swimming pool. *Arq. Neuropsiquiatr.* **1996**, *54*, 402–406. [CrossRef]
48. Fehlings, D.L.; Kirsch, S.; McComas, A.; Campbell, K.; Chipman, M. Evaluation of therapeutic electrical stimulation to improve muscle strength and function in children with types II/III spinal muscular atrophy. *Dev. Med. Child. Neurol.* **2002**, *44*, 741–744. [CrossRef]
49. Gobbo, M.; Lazzarini, S.; Vacchi, L.; Gaffurini, P.; Bissolotti, L.; Padovani, A.; Filosto, M. Exercise Combined with Electrotherapy Enhances Motor Function in an Adolescent with Spinal Muscular Atrophy Type III. *Case Rep. Neurol. Med.* **2019**, *2019*, 4839793. [CrossRef] [PubMed] [PubMed Central]
50. Lemoine, T.J.; Swoboda, K.J.; Bratton, S.L.; Holubkov, R.; Mundorff, M.; Srivastava, R. Spinal muscular atrophy type 1: Are proactive respiratory interventions associated with longer survival? *Pediatr. Crit. Care Med.* **2012**, *13*, e161–e165. [CrossRef]
51. Lewelt, A.; Krosschell, K.J.; Stoddard, G.J.; Weng, C.; Xue, M.; Marcus, R.L.; Gappmaier, E.; Viollet, L.; Johnson, B.A.; White, A.T.; et al. Resistance strength training exercise in children with spinal muscular atrophy. *Muscle Nerve* **2015**, *52*, 559–567. [CrossRef] [PubMed]
52. Madsen, K.L.; Hansen, R.S.; Preisler, N.; Thøgersen, F.; Berthelsen, M.P.; Vissing, J. Training improves oxidative capacity, but not function, in spinal muscular atrophy type III. *Muscle Nerve* **2015**, *52*, 240–244. [CrossRef]
53. Markström, A.; Cohen, G.; Katz-Salamon, M. The effect of long term ventilatory support on hemodynamics in children with spinal muscle atrophy (SMA) type II. *Sleep. Med.* **2010**, *11*, 201–204. [CrossRef] [PubMed]
54. Mellies, U.; Dohna-Schwake, C.; Stehling, F.; Voit, T. Sleep disordered breathing in spinal muscular atrophy. *Neuromuscul. Disord.* **2004**, *14*, 797–803. [CrossRef] [PubMed]
55. Mirea, A.; Leanca, M.C.; Onose, G.; Sporea, C.; Padure, L.; Shelby, E.S.; Dima, V.; Daia, C. Physical Therapy and Nusinersen Impact on Spinal Muscular Atrophy Rehabilitative Outcome. *Front. Biosci.* **2022**, *27*, 179. [CrossRef] [PubMed]
56. Montes, J.; Garber, C.E.; Kramer, S.S.; Montgomery, M.J.; Dunaway, S.; Kamil-Rosenberg, S.; Carr, B.; Cruz, R.; Strauss, N.E.; Sproule, D.; et al. Single-Blind, Randomized, Controlled Clinical Trial of Exercise in Ambulatory Spinal Muscular Atrophy: Why are the Results Negative? *J. Neuromuscul. Dis.* **2015**, *2*, 463–470. [CrossRef]
57. Novikov, A.; Maldova, M.; Shandybina, N.; Shalmiev, I.; Shoshina, E.; Epoyan, N.; Moshonkina, T. First Use of Non-Invasive Spinal Cord Stimulation in Motor Rehabilitation of Children with Spinal Muscular Atrophy. *Life* **2023**, *13*, 449. [CrossRef] [PubMed] [PubMed Central]
58. Petrone, A.; Pavone, M.; Testa, M.B.; Petreschi, F.; Bertini, E.; Cutrera, R. Noninvasive ventilation in children with spinal muscular atrophy types 1 and 2. *Am. J. Phys. Med. Rehabil.* **2007**, *86*, 216–221. [CrossRef] [PubMed]

59. Salem, Y.; Jaffee Gropack, S. Aquatic therapy for a child with type III spinal muscular atrophy: A case report. *Phys. Occup. Ther. Pediatr.* **2010**, *30*, 313–324. [CrossRef]
60. Vry, J.; Schubert, I.J.; Semler, O.; Haug, V.; Schönau, E.; Kirschner, J. Whole-body vibration training in children with Duchenne muscular dystrophy and spinal muscular atrophy. *Eur. J. Paediatr. Neurol.* **2014**, *18*, 140–149. [CrossRef]
61. Cumplido-Trasmonte, C.; Barquín-Santos, E.; Aneiros-Tarancón, F.; Plaza-Flores, A.; Espinosa-García, S.; Fernández, R.; García-Armada, E. Usability and Safety of the ATLAS 2030 Robotic Gait Device in Children with Cerebral Palsy and Spinal Muscular Atrophy. *Children* **2024**, *11*, 1500. [CrossRef] [PubMed] [PubMed Central]
62. Hirayama, T.; Morioka, H.; Sugisawa, T.; Shibukawa, M.; Ebina, J.; Hanashiro, S.; Nagasawa, J.; Yanagihashi, M.; Okuni, I.; Nakajima, T.; et al. A preliminary study on the effects of long-term robot suit exercise training on gait function and quality of life in patients with spinal and bulbar muscular atrophy. *J. Clin. Neurosci.* **2024**, *128*, 110778. [CrossRef] [PubMed]
63. Urendes, E.; Sanchez, C.; Lerma-Lara, S.; Rojo, A.; Costa, V.; Raya, R. Design, Development, and Functional Validation of a 3D-Printed Passive Upper Limb Exoskeleton. *IEEE Trans. Neural Syst. Rehabil. Eng.* **2024**, *32*, 2503–2512. [CrossRef] [PubMed]
64. Iijima, K.; Watanabe, H.; Nakashiro, Y.; Iida, Y.; Nonaka, M.; Moriwaka, F.; Hamada, S. Long-term effects of the gait treatment using a wearable cyborg hybrid assistive limb in a patient with spinal and bulbar muscular atrophy: A case report with 5 years of follow-up. *Front. Neurol.* **2023**, *14*, 1143820. [CrossRef] [PubMed] [PubMed Central]
65. Nistor-Cseppento, C.D.; Gherle, A.; Negrut, N.; Bungau, S.G.; Sabau, A.M.; Radu, A.F.; Bungau, A.F.; Tit, D.M.; Uivaraseanu, B.; Ghitea, T.C.; et al. The Outcomes of Robotic Rehabilitation Assisted Devices Following Spinal Cord Injury and the Prevention of Secondary Associated Complications. *Medicina* **2022**, *58*, 1447. [CrossRef] [PubMed] [PubMed Central]
66. Secciani, N.; Brogi, C.; Pagliai, M.; Buonamici, F.; Gerli, F.; Vannetti, F.; Bianchini, M.; Volpe, Y.; Ridolfi, A. Wearable Robots: An Original Mechatronic Design of a Hand Exoskeleton for Assistive and Rehabilitative Purposes. *Front. Neurorobot.* **2021**, *15*, 750385. [CrossRef] [PubMed] [PubMed Central]
67. Varela-Aldás, J.; Avila-Armijos, W.; Palacios-Navarro, G. Internet of things (IoT)-based assistive system for patients with spinal muscular atrophy (SMA): A case report. *Disabil. Rehabil. Assist. Technol.* **2024**, *19*, 2498–2505. [CrossRef] [PubMed]
68. Willems, J.; Bablok, I.; Farin-Glattacker, E.; Langer, T. Barriers and facilitating factors of care coordination for children with spinal muscular atrophy type I and II from the caregivers' perspective: An interview study. *Orphanet J. Rare Dis.* **2023**, *18*, 136. [CrossRef] [PubMed] [PubMed Central]
69. Giannotta, G.; Ruggiero, M.; Pirani, G.; Oliva, M.C.; Ferrante, C.; Trabacca, A. Setting multidisciplinary intervention goals for spinal muscular atrophy patients utilizing the international classification of functioning, disability, and health: A pilot study in a small sample sizes. *Acta Neurol Belg.* **2025**. *epub ahead of print*. [CrossRef] [PubMed]
70. Herrero, A.J.; Menéndez, H.; Gil, L.; Martín, J.; Martín, T.; García-López, D.; Gil-Agudo, Á.; Marín, P.J. Effects of whole-body vibration on blood flow and neuromuscular activity in spinal cord injury. *Spinal Cord* **2011**, *49*, 554–559. [CrossRef]
71. Bartels, B.; Montes, J.; Van Der Pol, W.L.; De Groot, J.F. Physical exercise training for type 3 spinal muscular atrophy. *Cochrane Database Syst Rev.* **2019**, *2019*, CD012120. [CrossRef] [PubMed]
72. Sonehara, S.; Bo, R.; Nambu, Y.; Iketani, K.; Lee, T.; Shimomura, H.; Ueda, M.; Takeshima, Y.; Iijima, K.; Nozu, K.; et al. Newborn Screening for Spinal Muscular Atrophy: A 2.5-Year Experience in Hyogo Prefecture, Japan. *Genes* **2023**, *14*, 2211. [CrossRef] [PubMed] [PubMed Central]
73. Ruythooren, F.; Moens, P. Spinal Muscular Atrophy Scoliosis in the Era of Background Therapies-A Review of the Literature. *J. Clin. Med.* **2024**, *13*, 3467. [CrossRef] [PubMed] [PubMed Central]
74. Díaz-López, C.I.; Palomo-Carrión, R.; Romay-Barrero, H.; Pacheco-da-Costa, S.; Coello-Villalón, M.; López-Muñoz, P. Families' experiences and perspectives on the early use of powered mobility in children with spinal muscular atrophy type I in the natural context. *Disabil. Rehabil. Assist. Technol.* **2025**, *12*, 1–9. [CrossRef]
75. Xie, Q.; Meng, Q.; Yu, W.; Wu, Z.; Xu, R.; Zeng, Q.; Zhou, Z.; Yang, T.; Yu, H. Design of a SMA-based soft composite structure for wearable rehabilitation gloves. *Front. Neurorobot.* **2023**, *17*, 1047493, Erratum in *Front. Neurorobot.* **2023**, *17*, 1269432. [CrossRef] [PubMed] [PubMed Central]
76. Tapken, I.; Kuhn, D.; Hoffmann, N.; Detering, N.T.; Schüning, T.; Billaud, J.N.; Tugendreich, S.; Schlüter, N.; Green, J.; Krämer, A.; et al. From data to discovery: AI-guided analysis of disease-relevant molecules in spinal muscular atrophy (SMA). *Hum. Mol. Genet.* **2024**, *33*, 1367–1377. [CrossRef] [PubMed]