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CLINICAL RESEARCH ARTICLE

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Assessment of the upper limb function, strength, and mobility in treatment-naive children with spinal muscular atrophy Types 2 and 3

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Abstract

Introduction/Aims: Current upper limb assessments in pediatric spinal muscular atrophy (SMA) may not adequately capture change with disease progression. Our aim was to examine the relationship between motor function, strength, and hand/finger mobility of the upper limb in treatment-naïve children with SMA Types 2 and 3 to assess new methods to supplement current outcomes.

Methods: The Revised Upper Limb Module (RULM), grip and pinch strength, and hand/finger mobility data were collected from 19 children with SMA Types 2 and 3 aged 5.2–16.9 years over a year.

Results: A median loss between 0.5 and 2.5 points in the RULM was seen across all SMA subgroups with the biggest median loss recorded between 10 and 14 years of age. The grip strength loss was −0.06 kg (−4.69 to 3.49; IQR, 1.21); pinch improvement of 0.05 (−0.65 to 1.27; IQR, 0.48); hand/finger mobility test improvement of 4 points (−24 to 14; IQR, 6.75) for the whole cohort. Significant correlations were found between the RULM and grip strength ($p < .001$), RULM and pinch strength ($p < .001$), RULM and revised Brooke ($p < .001$), grip strength and pinch strength ($p < .001$).

Discussion: The combined use of the RULM, dynamometry, and hand mobility provide insight about correlations between function and strength in children with SMA.

Abbreviations: HFMS, Hammersmith Functional Motor Scale; HFMSE, Hammersmith Functional Motor Scale Extended; IQR, interquartile ranges; MAA, Managed Access Agreement; MFM, Motor Function Measure; RULM, Revised Upper Limb Function; SMA, spinal muscular atrophy; SMN, survival motor neuron; UK, United Kingdom.

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The RULM and grip strength assessments captured a significant decline in upper limb function, whereas the pinch and finger/hand mobility showed an improvement over the course of 1 year and these results should be considered for future studies.

KEYWORDS
SMA, strength, upper limb function

1 | INTRODUCTION

Upper limb function assessments in children with spinal muscular atrophy (SMA) have been used by clinicians to monitor changes caused by disease progression.[1] The Revised Upper Limb Module (RULM)[2,3] was designed to specifically investigate upper limb function in SMA. However, recent studies have shown that both the RULM and the Motor Function Measure (MFM),[4] which also captures information on upper limb function, are limited when trying to capture decline in the stronger, ambulant SMA Type 3 patients.[5,6]

SMA in children is classified into three main disease subtypes, characterized by the age of onset and highest motor milestone achieved.[1,7] SMA Type 1 children never achieve independent sitting, Type 2 achieve sitting but never walk independently, and Type 3 have a later onset and achieve unaided walking, but often lose ambulation over time.[8,9] The RULM has been used in numerous longitudinal natural history studies in combination with other disease-specific outcome measures to monitor symptom progression in all types of SMA. These studies demonstrate the upper limb function negative slope of change starts at 5.8 years for Type 2 and 7.3 years for Type 3.[10–12] Muscle strength also declines with age in SMA.[13] Recent studies have shown a good correlation between the MFM and hand grip, pinch strength, and hand/finger mobility.[6,14]

Because treatments are changing the natural history trajectories of patients with SMA,[15–18] there is a need for a more holistic approach to help clinicians better understand the progression of upper limb symptoms in this population. This study investigated the relationship between upper limb function, strength, and finger mobility in a group of treatment-naïve children with SMA Types 2 and 3. We aimed to provide methods to supplement currently used outcome measures in the assessment of children with SMA and address some of the limitations of those scales.

2 | METHODS

Patients were recruited among those attending SMA clinic at Great Ormond Street Hospital for Children in London, UK, if they had 5q SMA Types 2 or 3 and were aged between 5 and 18 years. Children were classified as Type 2 or Type 3 dependant on their motor milestone achievement of independent sitting or walking, respectively. The assessments took place between July 2016 and April 2021. Patients treated with any experimental or approved SMN modifying drugs were excluded. All participants were receiving the recommended standards of clinical care during the study.[1,19] Ethical approval was granted by the joint UCL and Great Ormond Street Hospital R&D department (REC# 13/LO/1748). Written informed consent/assent was obtained from parents or legal guardians of all participants.

2.1 | Revised Upper Limb Module

This scale evaluates 20 tasks of typical daily life such as raising arms above the head and lifting weighted objects.[3] An entry item is used to establish the functional level and 19 subsequent items assessing distal to proximal upper limb function are tested. The revised Brooke scale, used as the entry item on the RULM, was only collected as a guide for functional status and does not contribute toward the total score. All items are tested without any orthotic devices. The RULM total score ranges from 0 to 37, with higher scores indicating better function. As per the standard protocol, the same side used for baseline assessment was also used at the follow-up visit and patients were allowed two attempts per item. For the purposes of the study, only the total score and revised Brooke score were used for analysis. The physiotherapists collecting the data completed face-to-face RULM training and complied with inter- and intra-reliability criteria. An annual refresher training for the RULM was completed for each evaluator throughout the study period.

2.2 | Grip and pinch strength assessment

Grip and pinch strength were measured using highly sensitive dynamometers (respectively, MyoGrip and MyoPinch, Ateliers Laumonier, Nesles-la-Vallée, France).[20] The measurements were recorded in kg units. The MyoGrip device measures forces between 0 and 90 kg with a resolution of 10 g and an accuracy of 50 g. The handle width is adjustable. The MyoPinch device measures forces between 0 and 18 kg with a resolution of 1 g and an accuracy of 10 g. Children in the study performed three trials with each dynamometer using their dominant hand. An average of the three was used for analysis with the aim of demonstrating a maximal isometric grip and pinch strength.

2.3 | Hand/finger mobility assessment

The MoviPlate (ValoTec, Villejuif, France) was designed to evaluate hand/finger mobility using repeated back-and-forth movements (tapping two circle platforms with fingers) performed as fast as possible

for 30 s.[20] This test was developed for non-ambulant patients as an endurance test for upper limbs. It evaluates strength, speed, coordination, and endurance capacities. Normal values range from 40 to 70 for children below 12 years and from 60 to over 100 for adolescents and adults. The MoviPlate test was performed twice, with a minute rest between, on each participant and only the higher score was used for the analysis.

All physiotherapists were trained to the use of the MyoTools by specialist physiotherapists at the Institute of Myology in Paris.

2.4 | Statistical methods

Motor functional assessments were performed at baseline and 12-month follow-up. To analyze the age factor, three age subcategories were reviewed: "5 to 9 years," "10 to 14 years," and "15 years and above." All analyses are presented as median, range, and interquartile ranges (IQR). Median values were used due to small sample size and non-normally distributed data. To interpret a relationship between two variables, a correlation coefficient was used where strong or very strong correlations were defined as those with coefficients of 0.70–1.00, moderate correlations as 0.40–0.69, and weak as 0.10–0.39.[21] The relationship between variables were examined using Spearman's correlation coefficients. Non-parametric correlation analysis between the RULM, revised Brooke score and grip strength, pinch strength, and hand/finger mobility was performed to look at the relationship between all upper limb measurements.

Analyses were performed using SPSS Statistics version 25 software (IBM, Armonk, NY). The limit of statistical significance was set to 0.05.

3 | RESULTS

3.1 | Cohort characteristics

Thirty-eight assessments from 19 patients (11 females, 8 males; median age at baseline 11.2 years, range: 5.2–16.9) were included (Table 1). Ten patients had a diagnosis of SMA Type 2 and nine of SMA Type 3 (of which four remained independently ambulant throughout the study). Six patients (four SMA Type 2 and two SMA Type 3 non-ambulant) had undergone spinal surgery prior to their baseline assessment. Fifteen patients were right-handed and four patients were left-handed.

3.2 | One-year change in functional scales

A median decline of two points in the RULM scale was seen across all participants (Table 2). The 10–14 years and the 15 years and above groups recorded the largest median decline on the RULM. The youngest participants, between 5 and 9 years, declined by 1 point (Table 2) and this was the group with the highest score in RULM at both baseline and 12-month follow-up.

Children with SMA Type 2 (median age, 10.2; 5.2–16.6) and non-ambulant SMA Type 3 demonstrated a decrease in the RULM scale of two points over 12 months (Table 2). Within the SMA Type 2 group, the 10–14 year-old group declined the most. The RULM for ambulant SMA 3 children (median age, 9.6; 8.4–10.8) improved slightly. Within that group, the 5–9 year-old group showed improved, although the 10–14 year-old group declined. All three subgroups in the non-ambulant SMA Type 3 showed a decline, with the largest negative change in score presented in the youngest (5–9 years) (Table 2).

Grip strength declined in median value over the 12-month period in this patient cohort (Table 2). The 5–9 and 10–14 year groups showed reduced grip strength, but the above 15 years group showed improvement. When different SMA subtypes were compared, all three showed a decline in median value, with the biggest reduction recorded in the ambulant Type 3 (Figure 1).

Pinch strength results showed an overall increase (Table 2). An improvement in score was recorded in the 5–9 years group, while we detected a decline in pinch strength in the 10–14 years and 15 years and above age subgroups.

Children with Type 2 SMA demonstrated a small positive percentage change in pinch strength over 1 year (Table 2). Both 5–9 years and 15 years and above showed an improvement, whereas the 10–14 years group showed a decline. The difference in overall positive change comes from the bigger range improvement in the 5–9 years patient group (Table 2).

The Type 3 non-ambulant group showed better pinch strength result at 12 months compared to baseline (Table 2). The Type 3, 5–9, and 10–14 year groups showed an improvement in pinch strength, whereas the 15 years and above showed a decline. The Type 3 ambulant subgroup demonstrated a small gain in percentage change when comparing pinch strength in this population (Table 2).

The hand/finger mobility assessment showed a median four-point improvement in 1-year follow-up across the three SMA subtypes. The largest change was observed in the ambulant Type 3 group, followed by the Type 3 non-ambulant and Type 2 groups. Only the 10–14 years SMA Type 2 age subgroup (which scored a median of 55 at baseline and 50 at 12-months follow-up) showed a decline in score across all age subgroups in both Types 2 and 3 (Table 2).

The difference in grip strength, pinch strength, and hand/finger mobility scores between SMA Type 2, SMA 3 ambulant, and SMA 3 non-ambulant were statistically significant ($p < .05$).

3.3 | Relationship between RULM and muscle strength and hand/fingers mobility

A strong correlation was found between the RULM and grip strength, and between RULM and pinch strength (Figure 2). A strong correlation was also observed between the grip and the pinch strength but weak correlations between grip strength and hand mobility score and pinch strength and hand mobility score (Figure 2). A weak correlation was found between the RULM and the hand mobility score (Figure 2).

TABLE 1 Baseline characteristics for each individual patient in the study.

Patient	Age (years)	Gender	Ambulant (Y/N)	SMA type	Spinal surgery (Y/N)	Salbutamol (Y/N)	Dominant hand (right/left)	Myogrip average of 3 (kg)	Myopinch average of 3 (kg)	Finger/hand mobility	RULM score	Brooke score
1	8.3	F	N	2	N	Y	R	3.38	2.096	46	26	5
2	10.0	M	Y	3	N	Y	R	4.79	2.066	54	36	6
3	10.9	M	N	2	Y	Y	R	0.63	0.276	46	8	3
4	5.2	M	N	2	N	Y	L	1.17	0.495	35	22	5
5	10.8	F	Y	3	N	Y	R	7.41	2.632	59	37	6
6	8.4	F	Y	3	N	N	R	3.60	1.22	57	30	6
7	6.0	F	N	2	N	Y	R	0.43	0.060	37	18	5
8	11.3	F	N	2	Y	Y	R	1.08	0.512	57	14	3
9	13.6	F	N	3	N	Y	R	0.58	1.310	63	23	5
10	9.2	M	Y	3	N	N	R	9.06	3.936	63	37	6
11	10.4	M	N	3	N	Y	R	2.35	1.153	38	19	3
12	16.9	F	N	3	Y	Y	L	3.69	1.523	63	24	4
13	13.2	F	N	3	Y	Y	R	1.72	0.542	46	17	3
14	9.6	F	N	2	N	Y	R	1.81	1.508	44	23	5
15	7.5	F	N	2	N	Y	L	1.26	0.675	40	21	5
16	15.9	M	N	2	Y	Y	R	3.23	0.656	61	17	3
17	8.4	F	N	3	N	Y	R	7.87	2.630	35	33	5
18	16.6	M	N	2	N	N	R	1.22	0.551	44	7	3
19	10.5	M	N	2	Y	Y	L	1.58	1.437	55	11	3

TABLE 2 Study cohort: 12-month change in all three SMA subtypes, divided by age groups (median score [range and IQR]; grip and pinch values measured in kilograms, RULM, and finger/hand mobility in raw scores).

Outcome measure / SMA type	RULM (median/ range, IQR)	Percentage change %	Grip (median/range in kg, IQR)	%	Pinch (median/ range in kilograms)	% Median (range)	Hand/finger mobility (median/range)	%
All ($n = 19$)	−2 (−5 to 3, IQR, 3)	−9% (−50% to 12%, IQR, 18)	−0.06 (−4.69 to 3.49, IQR, 1.21)	−11% (−63% to 51%, IQR, 39.5)	0.05 (−0.65 to 1.27, IQR, 0.46)	7.5% (−47% to 61%, IQR, 36.25)	4 (−24 to 14, IQR, 12)	8% (−52% to 30%, IQR, 25)
5–9 years ($n = 8$)	−1 (−5 to 3, IQR 4.25)	−4.5% (−15% to 12%, IQR 18.25)	−0.25 (−1.1 to 0.93, IQR 1.53)	−11% (−37% to 51%, IQR 53.75)	0.35 (−0.23 to 1.27, IQR 0.4)	15% (−47% to 61%, IQR 25)	8.5 (−1 to 13, IQR 8.25)	17.5% (−3% to 30%, IQR 21)
10–14 years ($n = 8$)	−2.5 (−4 to 0, IQR 1.75)	−14.5% (−50% to 0, IQR 21)	−0.21 (−4.69 to 3.49, IQR 1.86)	−15% (−63% to 42%, IQR 57)	−0.035 (−0.58 to 0.31, IQR 0.24)	0 (−40% to 27%, IQR 36.3)	3 (−24 to 14, IQR 15.75)	6.5% (−52% to 28%, IQR 28.8)
≥15 years ($n = 3$)	−2 (−2 to 0)	−8% (−29% to 0)	0.12 (−0.03 to 0.16)	5% (−1% to 10%)	−0.07 (−0.65 to 0.13)	−13% (−42% to 20%)	4 (−1 to 4)	6% (−2% to 7%)
SMA 2 ($n = 10$)	−2 (−4 to 3, IQR 2.25)	−10.5% (−50% to 12%, IQR 24,5)	−0.005 (−1.1 to 0.93, IQR 0.73)	−4.5% (−48% to 51%, IQR 48)	0.05 (−0.58 to 1.27, IQR 0.47)	6% (−47% to 61%, IQR 53)	3.5 (−24 to 13, IQR 11.5)	6% (−52% to 30%, IQR 28.75)
5–9 years ($n = 5$)	−1 (−2 to 3, IQR 3.75)	−4.5% (−10% to 12%, IQR 16.75)	−0.35 (−1.1 to 0.93, IQR 1.73)	−1.5% (−37% to 51%, IQR 81. 8)	0.17 (−0.23 to 1.27, IQR 1.19)	13% (−47% to 61%, IQR 84.5)	8.5 (−1 to 13, IQR 10.75)	20.5% (−3% to 28%, IQR 24.5)
10–14 years ($n = 3$)	−3 (−4 to −3)	−27% (−50% to −21%)	−0.17 (−0.76 to 0.05)	−15% (−48% to 9%)	−0.14 (−0.58 to 0.05)	−26% (−40% to 17%)	−5 (−24 to 3)	−9% (−52% to 5%)
≥15 years ($n = 2$)	−1 (−2 to 0)	−14.5% (−29% to 0)	0.14 (0.12 to 0.16)	7.5% (5% to 10%)	0.03 (−0.07 to 0.13)	3.5% (−13% to 20%)	1.5 (−1 to 4)	2.5% (−2% to 7%)
SMA 3 non-ambulant ($n = 5$)	−2 (−5 to −2, IQR 2)	−11% (−18% to −8%, IQR 8)	−0.03 (−0.84 to 3.49, IQR 2.78)	−6% (−15% to 42%, IQR 45.25)	0.08 (−0.65 to 0.38, IQR 0.65)	9% (−42% to 27%, IQR 39)	3 (−3 to 13, IQR 9.5)	6% (−5% to 28%, IQR 19)
5–9 years ($n = 1$)	−5	−15%	−0.84	−11%	0.38	15%	1	3%
10–14 years ($n = 3$)	−2 (−3 to −2)	−11% (−18% to −9%)	0.37 (−0.25 to 0.98)	13.5% (−15% to 42%)	0.18 (0.05 to 0.31)	18% (9% to 27%)	8 (3 to 13)	18% (8% to 28%)
≥15 years ($n = 1$)	−2	−8%	−0.03	−1%	−0.65	−42%	4	6%
SMA 3 ambulant ($n = 4$)	0,5 (−1 to 3, IQR 3)	0.5% (−3% to 10%, IQR 9.75)	−1.1 (−4.69 to 0.65, IQR 4.07)	−18.5% (−63% to 18%, IQR 64.5)	0.13 (−0.18 to 0.54, IQR 0.67)	4% (−7% to 31%, IQR 33.5)	9.5 (6 to 14, IQR 6.75)	15.5% (11% to 24%, IQR 10.5)
5–9 years ($n = 2$)	1.5 (0 to 3)	5% (0 to 10%)	−0.17 (−0.98 to 0.65)	−3.5% (−11% to 18%)	0.46 (0.38 to 0.54)	22.5% (14% to 31%)	9.5 (8 to 11)	15.5% (14% to 17%)
10–14 years ($n = 2$)	−0.5 (−1 to 0)	−1.5% (−3% to 0)	−2.96 (−4.69 to −1.23)	−44.5% (−63% to −26%)	−0.15 (−0.18 to −0.12)	−6.5% (−7% to −6%)	10 (6 to 14)	17.5% (11% to 24%)

Note: RULM: Revised Upper Limb Scale (maximum score 37); Grip, pinch and hand/finger mobility measured by the MyoTools: MyoGrip, MyoPinch, MoviPlate.

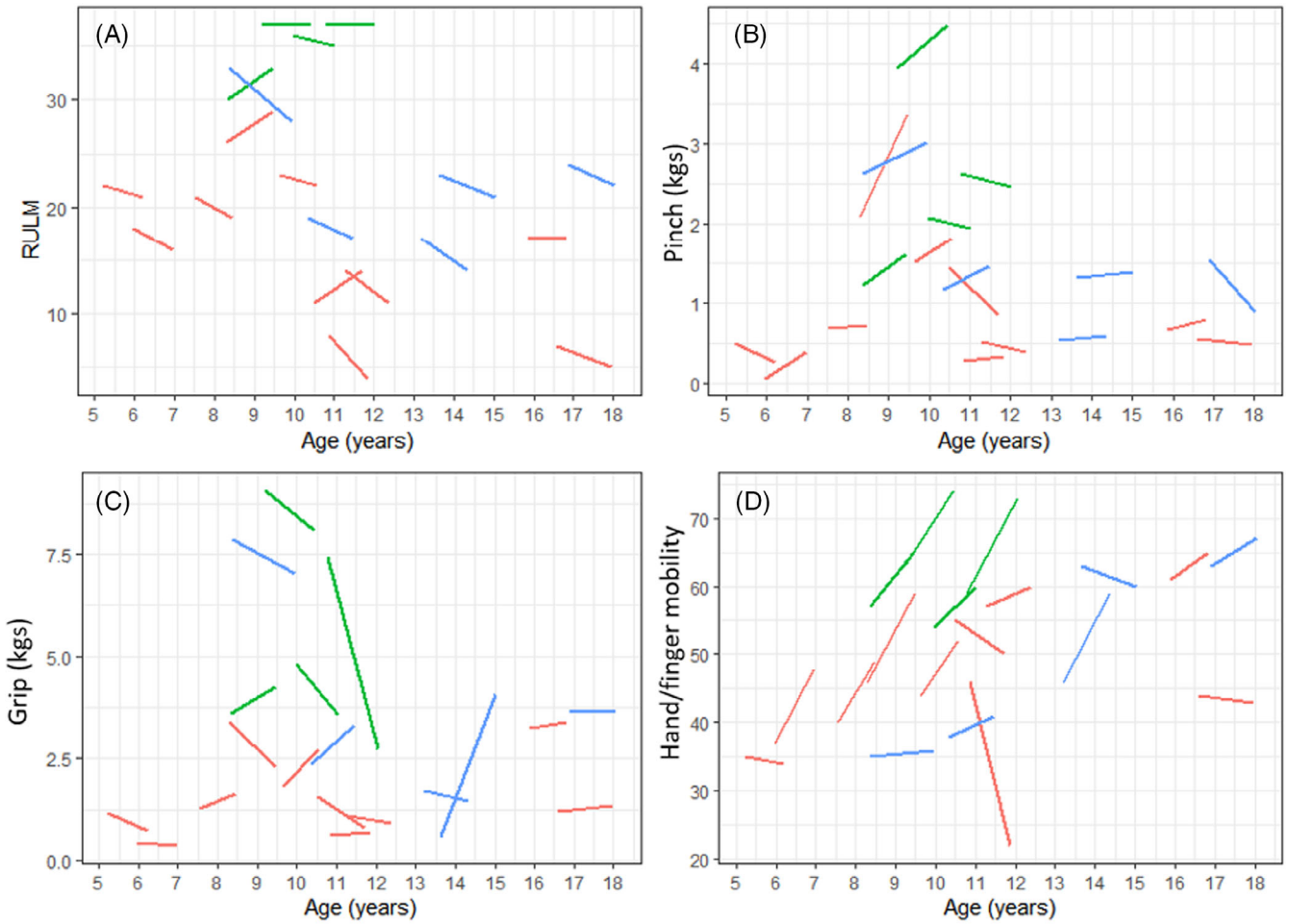

FIGURE 1 Baseline and one-year follow-up scores by SMA type in RULM, grip, pinch, and hand/finger mobility. RULM, Revised Upper Limb Module; SMA, spinal muscular atrophy.

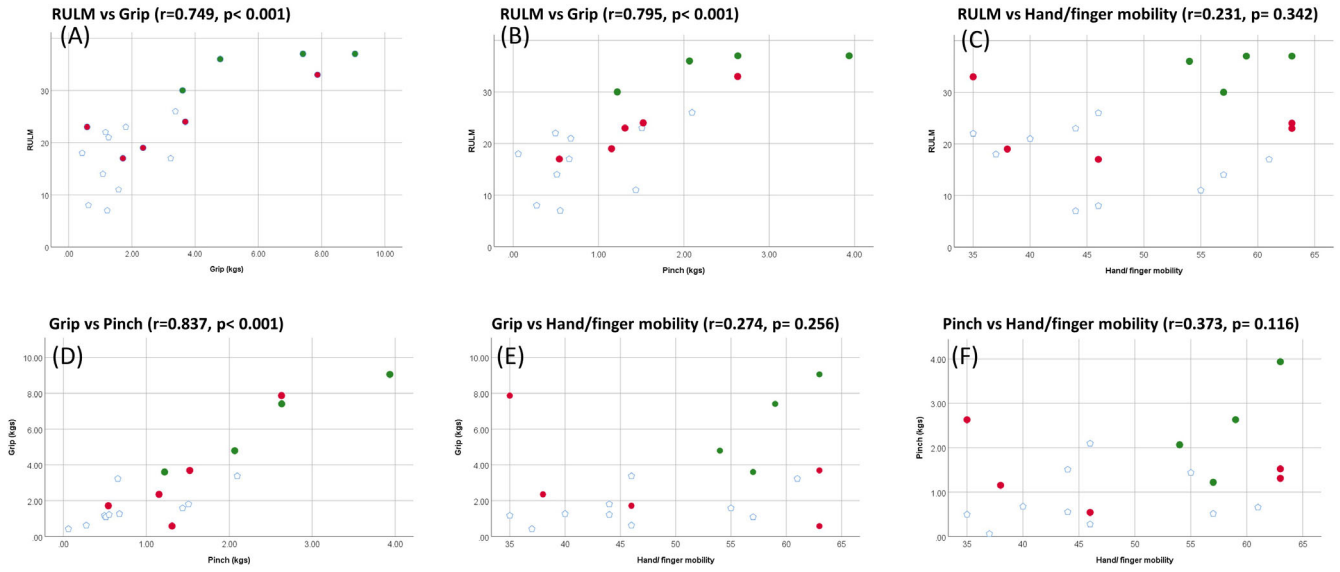

FIGURE 2 Relationships between RULM, strength, and mobility. RULM, Revised Upper Limb Module.

4 | DISCUSSION

Our study demonstrates that the combined use of the RULM, hand dynamometers, and hand/finger mobility provides insight about correlation between function and strength in children with SMA and can help to address the gap where floor and ceiling effect is present in this population. The results showed changes in both Types 2 and 3 SMA patients in function, strength, and mobility of the upper limb over a 12-month period. Although these changes are small, the functional trajectories indicate a decline of upper limb function over time in this group of treatment-naive patients. Stratification of the SMA Type 3 patients into ambulant and non-ambulant allowed for further considerations. SMA Type 3 ambulant children were the strongest at baseline and showed the smallest change in function over the 12-month period (median change difference + 0.5 in RULM score). Both Types 2 and 3 non-ambulant patients showed a decline of ≥2 points in the RULM assessment.

Our results confirmed previous findings in each of the age categories.[5,10] The 5- to 9-year-olds affected by Type 2 and the non-ambulant Type 3 declined but improvement was observed in the Type 3 ambulant group. Coratti et al. have explored the 24-month change in RULM in children with SMA Types 2 and 3, which shows similar changes in upper limb function in our age subgroups.[5] Those results suggest that the most notable negative change in upper limb function occurs during the early teenage years in both SMA Types 2 and 3. Our results confirms the limitations of the RULM scale for the ambulant SMA Type 3 children, where most of the patients showed no change in score over the year. We recognize that a 24-month or longer follow-up period in a larger cohort would be better suited to detect changes in this population as also previously suggested by others.[5,10,22]

While the RULM scale provides an indication of the overall motor function in the upper limbs, high precision dynamometry provides an additional assessment of hand muscle strength allowing more subtle changes to be captured in an interval of time during which RULM changes do not occur. Indeed, in our study, grip strength declined in all three subgroups. The interpretation of the differences in grip strength results in the different subgroups of patients could be due to the timeline of disease progression. The strongest SMA Type 3 cohort in our study showed the largest decline in distal strength, possibly due to their being in the earlier stages of their disease progression. In the more severe SMA Type 2, and non-ambulant Type 3 children, deterioration in these distal muscle groups would already have occurred, causing lower baseline muscle strength.

The distal muscles involved in key pinch showed an improvement across the whole cohort. A previous study of non-ambulant children and adults with SMA found that grip and pinch strength are strongly correlated with age; children demonstrated an upward trajectory prior until reaching puberty, and a decline of muscle strength following this.[14] The three subgroups in our study have similar average ages, but the very small number of patients in the 15 years and above groups in two of the SMA subgroups and none in the ambulant Type 3 patients did not allow us to capture the effect of puberty on strength. We recognize that it would have been ideal to record the pubertal status, and this should be considered when planning future studies in different age groups. Another limitation of our data is that wrist and forearm circumference and hand and palm length can have an effect on grip strength performance,[23] which was not taken into consideration when our study was designed.

The hand/finger mobility score improved across all three subgroups. This indicates that despite progressive weakness SMA patients adopt functional compensatory strategies. Seferian et al. used the same methods for hand/finger mobility evaluation and reported no significant changes over 1-year follow-up or between SMA Types 2 and 3, particularly in the younger (under 14 years) children, suggesting that after the age of 14 years, effects of growth no longer compensate for strength loss.[14] Hand/finger mobility assessments could be subject to a learning effect. This was observed and reported in studies of children with Duchenne muscular dystrophy when performing the same assessment.[24] Growth and maturation effects are factors of improvement in such motor tasks. Although the test for hand and finger mobility combines several aspects of mobility including strength, speed, coordination, and endurance, more studies are needed to verify our findings. Research on mobility and dexterity in the upper limb is needed to address this gap in the literature to better understand how it affects strength and function in this population.

Although statistical significance in the 12-month follow-up was not reached, due to small sample sizes of SMA subtypes and age groups, the 2-point decline may contribute to the understanding of the natural history of individuals with SMA. The RULM evaluation is part of the Managed Access Agreement (MAA) assessment for the use of nusinersen and risdiplam treatments in England and used in many SMA clinical trials.[25] A recent longitudinal study found that many of the SMA 3 patients reach a ceiling effect on the RULM and this was deemed a limitation to further explore upper limb changes in these groups of patients over time.[26] In our study, two of the four ambulant SMA 3 children reached the RULM ceiling. This indicates the need for additional outcome measures to record subtle changes in the upper limb, particularly in this stronger cohort. The dynamometry strength assessments showed that they can detect changes in the weakest and the strongest SMA patients.

5 | CONCLUSION

High precision dynamometry should be considered as an additional upper limb outcome measure in future natural history studies and clinical trials. This is further supported by the strong correlation between the RULM and the tests for grip and pinch strength we report in our study.

With the emergence of new therapies, the importance of capturing changes in all the cohorts of patients becomes essential to assess efficacy in the upper limb. Our results can guide clinicians toward a better interpretation of the changes in the upper limb function and its correlations with strength and hand/finger mobility, before and after treatments. Future research in treated patients is needed to explore our findings.

AUTHOR CONTRIBUTIONS

Evelin Milev: Conceptualization; methodology; data curation; investigation; validation; formal analysis; writing – original draft; writing – review and editing; visualization. **Victoria Selby:** Conceptualization; methodology; writing – original draft; writing – review and editing. **Amy Wolfe:** Writing – original draft; writing – review and editing. **Annemarie Rohwer:** Writing – original draft; writing – review and editing. **Ricarda Tillmann:** Writing – original draft; writing – review and editing. **Danielle Ramsey:** Writing – original draft; writing – review and editing. **Mario Iodice:** Writing – original draft; writing – review and editing. **Jean-Yves Hogrel:** Conceptualization; methodology; writing – original draft; writing – review and editing. **Giovanni Baranello:** Conceptualization; methodology; writing – original draft; writing – review and editing. **Mariacristina Scoto:** Conceptualization; methodology; writing – original draft; writing – review and editing; supervision. **Francesco Muntoni:** Conceptualization; methodology; writing – original draft; writing – review and editing; supervision.

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CONFLICT OF INTEREST STATEMENT

F. M. reports participation to Scientific Advisory boards and teaching initiatives for Novartis, Biogen, Roche; he is involved as an investigator in clinical trials from Novartis, Biogen, and Roche. Both institutions (UCL and GOSH) received funding from Biogen and Roche for the SMAREACH SMA registry. G. B. is PI of clinical trials by Pfizer, NS Pharma, and Reveragen, and has received speaker and/or consulting fees from Sarepta, PTC Therapeutics, Biogen, Novartis Gene Therapies, Inc. (AveXis), and Roche and has worked as principal investigator of SMA studies sponsored by Novartis Gene Therapies, Inc., and Roche. M. S. reports participation to Scientific Advisory boards and teaching initiatives for Avexis, Biogen, Roche; she is involved as an investigator in clinical trials from Avexis, Biogen, and Roche. J.-Y. H. has received consulting fees from Biogen and Roche. Other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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