Revised Hammersmith Scale for Spinal Muscular Atrophy (RHS)

D. Ramsey[1], M.Scoto[1], A. Mayhew[2], M. Main[1], I. Wilson[1], E. Mazzone[3], J. Montes[4], S. Dunaway[4], A. Pasternak[6], R. Salazar[4], A.M. Glanzman[7], T. Duong[8], R. Gee[8], M. Civitello[5], K. Bushby[2], R. Finkel[5], E. Mercuri[1,3], F. Muntoni[1]

[1]Dubowitz Neuromuscular Centre, UCL & Great Ormond Street Hospital, London, UK, [2]Institute of Human Genetics, Newcastle University, UK, [3]Universita' Cattolica Roma, Italy, [4]Department of Neurology, Columbia University Medical Center, New York, USA, [5]Nemours Children's Hospital, University of Central Florida College of Medicine, Florida, USA, [6]Boston Children's Hospital, Boston, USA, [7]The Children's Hospital of Philadelphia, Philadelphia, USA, [8]Stanford University, Palo Alto, California, USA

BACKGROUND:

- Outcome measures which meet standards set by modern psychometric analysis as well as classical measures of reliability are viewed more favourably as robust tools of choice for use in clinical trials. Recent psychometric analysis identified shortcomings in the clinically reported outcome measures currently used to assess motor function in SMA[1].

- An international collaboration between SMA REACH UK, the Italian SMA Network and the PNCRN SMA network (USA) have been working to address the shortcomings observed in functional outcome measures currently used for SMA type 2 and 3 to ensure that functional scales used in SMA are robust and 'fit for purpose'.

AIM: To develop a robust functional clinician rated outcome measure to be used clinically and in clinical trials for use in ambulant and non-ambulant SMA type 2 and 3.

METHODS:

- Physiotherapists and Clinicians from SMA REACH UK, the Italian SMA Network and the PNCR SMA USA undertook an iterative process to revise the Hammersmith Functional Motor Scale Expanded (HFMSE) using item response theory via the Rasch Measurement Method, expert panels and three international pilots.

- Scale development:

  - The expert group meticulously discussed each item of the HFMSE, scoring criteria, psychometric properties and the experience of use in clinical trials. This process highlighted item repetition, the need to adjust/refine scoring criteria and additional items.

  - Two draft revised scales were piloted internationally: Exploratory HFMSE piloted January – May 2014 (n = 52), Revised Hammersmith Scale (Draft) June to December 2014 (n=70), and the above process repeated until agreement was achieved on the final version of the scale, the Revised Hammersmith Scale for SMA (RHS), in March 2015.

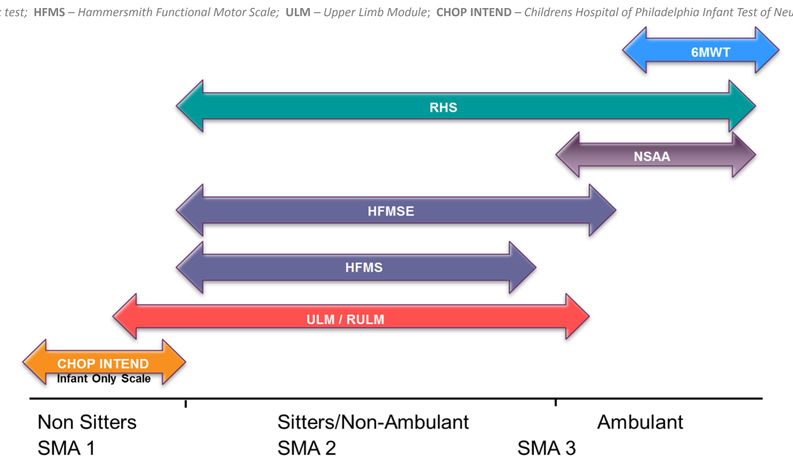
  - The RHS consists of 36 items to measure weak type 2 SMA through to strong type 3 SMA. Each item is graded on an ordinal scale of 0, 1, 2 except 3 items which are scored 0, 1. It incorporates items from the North Star Ambulatory Assessment (NSAA) and additional WHO developmental milestones.

- The RHS was piloted in the 3 international networks across 7 sites from March – September 2015.

- Psychometric properties of the scale were analysed using Rumm2030 software, additional scale analysis was conducted using SPSS version 22.

Figure 1: Continuum of SMA Specific Functional Outcome Measures Related to Functional Ability/Classification

KEY: **6MWT** - *6 minute walk test;* **HFMS** – *Hammersmith Functional Motor Scale;* **ULM** – *Upper Limb Module;* **CHOP INTEND** – *Childrens Hospital of Philadelphia Infant Test of Neuromuscular Disorders*



RESULTS:

- **Subjects:** n = 140, please refer to table 3 for more detail on subject demographics. Rasch analysis 3 invalid results, 2 extreme scores

- **Psychometric properties – Item response theory utilising RASCH Measurement Method:**

  - Very good fit of all 36 items to the construct of motor performance in SMA, table 1. No items with a fit residual outside of ±2.5, and only one item had a significant v^2 probability (p = 0.001, table 2).

  - Good reliability as demonstrated by a high Person Separation Index - PSI (0.97), table 1.

  - Logical and hierarchical individual item scores for 27/36 items, figure 3.

  - Targeting excellent with minimal ceiling, figure 2. Weaker non-ambulant patients had fewer items which measured their ability.

  - Dependency was noted between items which assess left and right and similar items such as rolling from prone to supine and supine to prone.

- **Groups Validity:**

  - The RHS differentiates between clinically different groups: SMA type ($p < 0.01$), WHO categories ($p < 0.01$), ambulation status ($p < 0.01$) and Salbutamol use ($p < 0.05$), table 3 and figures 4 to 7.

  - The RHS has a strong significant positive correlation with the WHO motor milestones $r = 0.860$, $p < 0.01$.

- **Type 3 Subgroup Analysis RHS vs RHS Timed Tests**

  - A moderate negative correlation was observed between RHS total score and timed rise from the floor (RHS item 25) $r_s = -0.513$, $p = 0.061$, $r^2 = 0.323$, figure 8.

  - A very strong significant negative correlation was observed between the RHS total score and timed 10 metres (RHS item 19) $r_s = -0.939$, $p = 0.00055$, $r^2 = 0.605$, figure 9.

PSYCHOMETRIC ANALYSIS USING RASCH MEASUREMENT METHOD:

Table 1: Results of RHS Rasch Analysis

	Item Fit	SD	Person Fit	SD	PSI	DF
RHS	-0.179	0.665	-0.225	0.336	0.9745	72

Figure 2: RHS item targeting

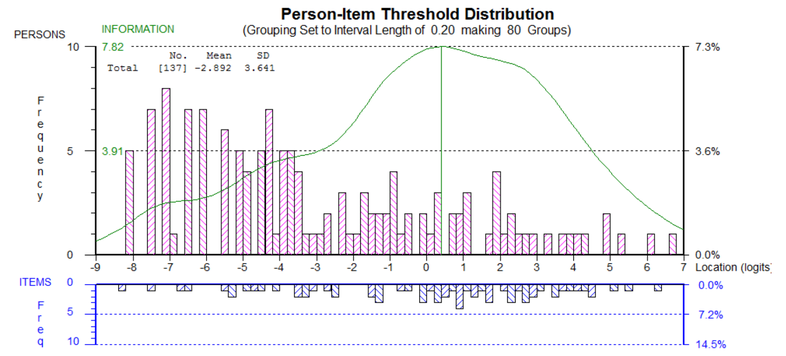


Figure 3: Threshold Map for RHS items in order of difficulty

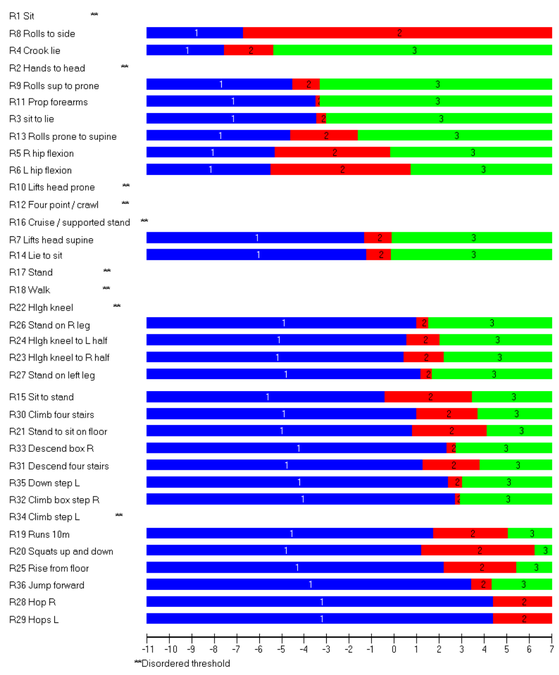


Table 2: Individual Item Fit for RHS (*significant v^2 probability)

Revised Hammersmith Scale for SMA					
Seq	Item	Location	FitResid	ChiSq	Prob
1	Sit	-7.31	-0.038	0.676	0.713179
8	Supine to side lying	-6.721	0.089	21.924	*0.000019
4	Crook lying	-6.463	0.048	9.777	0.007532
2	Hands to head	-4.45	-0.026	2.564	0.277464
9	Rolls supine to prone	-3.905	-0.292	3.574	0.167438
11	Props on forearms	-3.384	-0.434	1.485	0.47596
3	Sit to lie	-3.245	-0.359	0.328	0.848561
13	Rolls prone to supine	-3.1	-0.786	4.364	0.112789
5	R hip flexion	-2.722	1.557	10.616	0.004952
6	L hip flexion	-2.377	2.485	8.295	0.015803
10	Lifts head from prone	-2.016	0.189	4.141	0.126129
12	Four point/ crawl	-1.154	-0.291	0.911	0.63412
16	Cruise / supported stand	-1.108	-0.961	2.171	0.337762
7	Lifts head supine	-0.717	1.115	5.438	0.065955
14	Lie to sit	-0.669	-0.72	0.904	0.636219
17	Standing	-0.226	-0.556	0.18	0.913901
18	Walking	0.127	0.071	2.996	0.223589
22	High kneeling	0.564	-0.337	1.507	0.470763
26	Stand on R leg	1.263	-0.531	0.814	0.665737
24	High kneel to L half	1.306	-0.428	1.775	0.41174
23	High kneel to R half	1.328	-0.587	1.648	0.438583
27	Stand on L leg	1.436	-0.474	0.697	0.705661
15	Sit to stand	1.533	-1.063	3.304	0.191643
30	Climb stairs	2.357	-0.691	0.811	0.666605
21	Stand to sit on floor	2.477	-0.455	0.977	0.613541
33	Down box step R	2.55	-0.256	0.366	0.832741
31	Descend stairs	2.555	-0.317	0.619	0.733785
35	Down box step L	2.716	-0.246	0.462	0.793781
32	Climbs box step R	2.831	-0.265	0.599	0.741157
34	Climbs box step L	2.857	-0.227	0.791	0.673365
19	Runs 10 metres	3.401	-0.416	0.495	0.780808
20	Squat up and down	3.735	-0.5	0.705	0.703071
25	Rise from floor	3.828	-0.277	0.237	0.88814
36	Jumps forward	3.896	-0.131	0.081	0.960477
28	Hops R	4.401	-0.162	0.303	0.859262
29	Hops L	4.407	-0.163	0.304	0.859076

GROUP VALIDITY & SUBGROUP ANALYSIS:

Table 3: Demographics

	N	Mean RHS Score	Group Validity (*significant p < 0.05)
SMA Type			
Type 1	2	2.50	
Type 2	89	8.74	ANOVA
Type 3	49	39.39	p < 0.01*
WHO Groups			ANOVA
No longer sits	21	3.19	p < 0.01*
Sits	72	9.89	
Crawls	4	23.00	Kruskal Wallis
Stands with Assistance	2	25.00	p < 0.01*
Walks with Assistance	1	27.00	
Stands Alone	5	39.60	Pearson Correlation
Walks Alone	31	46.48	r = 0.898 p < 0.01*
Ambulatory Status			
Non- Ambulant	106	10.69	
Ambulant	34	46.47	p < 0.01*
Sex			
Male	73	20.07	
Female	67	18.63	p = 0.647
Salbutamol			
No	52	23.81	
Yes	89	16.76	p = 0.029*
Spinal surgery			
No	127	20.57	
Yes	13	7.69	p = 0.016*
Age			
Mean (95% CI)		10 (8.55 to 11.27)	
SD		8.20	
Range		1 yr 4 mths to 51 yrs 7 mths	

Figure 4: RHS total score vs SMA type

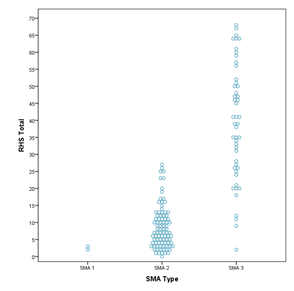


Figure 5: RHS total score vs WHO groups

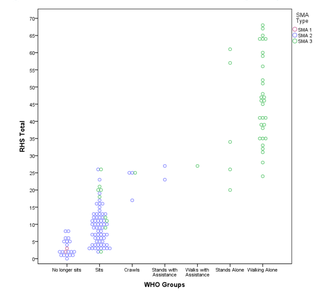


Figure 6: Mean RHS score vs SMA type

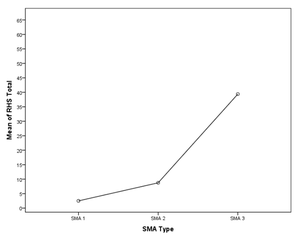


Figure 7: Mean RHS score vs WHO groups

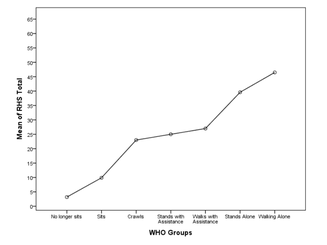


Figure 8: SMA 3 RHS score vs Timed Rise

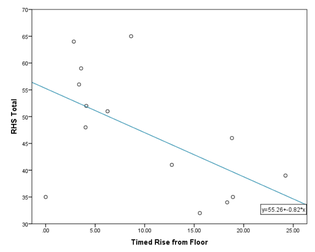
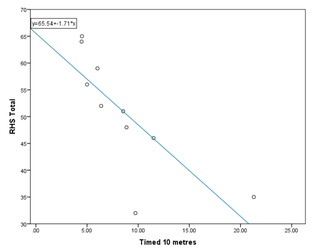


Figure 9: SMA 3 RHS score vs Timed 10 metres



CONCLUSION:

- The RHS is able to test the physical abilities of patients with type 2 and 3 SMA and has improved the psychometric properties of the original scales, the outstanding concerns for a few items will be addressed following discussion with the expert panel to simplify scoring criteria.

- A floor effect is noted with the weaker type 2 patients. Since gross motor assessment becomes less pertinent in the very weak patients the RHS should be used in conjunction with a more sensitive scale such as the CHOP INTEND for infants, Revised Upper Limb Module (RULM) or patient reported outcome measures.

- The RHS is able to differentiate between clinically different SMA groups, and is significantly correlated with WHO developmental milestones thereby demonstrating both construct and concurrent validity.

- We are currently establishing additional validity and reliability properties of the scale. Future work will incorporate defining longitudinal trajectories using the RHS within different sub-groups of patients with SMA.

References:
1. Cano SJ et al (2013) Rasch Analysis Of Clinical Outcome Measures In Spinal Muscular Atrophy. Muscle Nerve

Correspondence: danielle.ramsey.12@ucl.ac.uk www.SMAREACHUK.com

20th International World Muscle Society Congress 30th September – 4th October 2015, Brighton, UK