

## RESEARCH PAPER

# The applicability of four clinical methods to evaluate arm and hand function in all stages of spinal muscular atrophy type II

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### Abstract

**Aim:** To evaluate the ability of four clinical methods to reflect arm and hand function at impairment and activity level and to determine their ability to discriminate among SMA II patients of all ages and in all stages of the disease. **Methods:** Fifty-two patients with SMA II (age range: 8–73 years) were assessed by means of the Egen Klassifikation 2 (EK2 scale), the Motor Function Measure Scale (MFM D3), the Manual Muscle Test (MMT) and Hand-Held Dynamometry (HHD) in full fist grip and lateral pinch grip. Patients were classified into six levels of upper limb function by means of the Brooke Upper Limb Scale, and the four methods' ability to differentiate among patients within these levels was calculated. Modified versions of the EK2 scale (EK Upper Limb) and the MFM D3 (MFM D3 Upper Limb) were assessed in the same manner. **Results:** The patients' physical abilities were best described by the MMT and EK2 while the "EK Upper Limb", MFM D3 and MMT were best at discriminating among patients across the range of upper limb function. Quantitative muscle tests as measured by Citec™ HHD were less applicable to weak patients; full fist grip could discriminate among patients at Brooke levels 3–5, and lateral pinch grip among the strongest patients. **Conclusion:** At the impairment level, MMT is the superior measure of muscle function in very weak patients in whom HHD cannot reflect capacity. At the activity level, the EK 2 represents daily activities whereas the MFM D3 measures motor functions. In differentiating among SMA II patients of all ages and in all stages of the disease, the ability of abbreviated versions of scales targeting upper limb function is superior to unabridged versions of these scales.

### ► Implications for Rehabilitation

Evaluation of upper limb function in spinal muscular atrophy II

- Even very weak patients with SMA II have some residual upper limb function that is measurable if the right method is chosen.
- The Manual muscle test is applicable to all patients with SMA II and is useful to determine possible interventions – such as methods to drive a wheelchair or operate a computer.
- Abbreviated versions of the EK2 scale and the MFM are useful as methods to evaluate subtle changes in upper limb function resulting from disease progression or interventions.

### Introduction

Spinal muscular atrophy (SMA) is caused by a mutation in the SMN1 gene. The disease is divided into three phenotypes according to age at onset and maximum motor milestones achieved [1]. The onset of SMA II is between 7 and 18 months. The child can sit independently, but cannot stand or walk independently. The ability to sit independently may be lost within the first year of life or may persist into adulthood, resulting in broad variation in motor ability among these patients [2]. In general, the disease is characterized by a profound impairment of physical functions; upper limbs are stronger than lower limbs [3],

with best preserved muscle strength in flexion of the elbow and in hands and fingers [4,5]. A gradual loss of muscle strength and physical functions in the upper limbs has been demonstrated [6,7].

There is no curative treatment for SMA; because patients with SMA II have never been able to walk or stand unaided, their physical abilities and independence are highly contingent upon their ability to move their arms and hands and concerns about their disease focus especially on loss of functionality in the upper limbs, e.g. reduced ability to write, to operate their wheelchair and to eat unaided [8].

The fact that SMA II is a relatively stable disorder, both deteriorating slowly over time and encompassing a wide range of functional abilities, from the patient who cannot feed himself to the patient who has preserved most of his or her upper extremity functions, makes it difficult to find a uniform method to monitor natural history or responses to treatment. Since rehabilitation of SMA II patients can take place at any time during the patient's

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life, it requires methods that are applicable to all stages, at all ages of the disorder and sufficiently sensitive to capture small differences in motor function among patients and over time in the individual patient. To ensure that assessment methods are clinically relevant and pertinent to the patients, these methods must be able to assess function both in the impairment domain such as physical capacity (e.g. muscle strength) and the activity and participation domain such as capability (e.g. the ability to eat) of the individual patient, including very weak patients [9]. A method that can discriminate among patients with a wide range of upper limb-function could also potentially act as an outcome measure that can identify small changes over time, which is a prerequisite for clinical trials or evaluation of rehabilitation interventions [10].

Arm function in SMA II is often evaluated by means of the Brooke Upper Limb Scale [11] which is an ordinal scale representing impairment stage in the upper limbs based on the patients' ability to raise the hand, forearm and arm against gravity. The scale reflects the natural history of functional deterioration with age in SMA II; since its development in the early 1980s, the scale has been widely used both in the clinic and in studies. The scale is reliable [7,12] and is often used to validate other functional scales [13–17]. Although it is easily administered and gives a quick impression of the patient's upper-limb capabilities, it does not cover capabilities of all SMA II patients because it has a ceiling effect among very weak patients and is too crude to register changes over time in strong patients [5,7]. While this makes the Brooke scale useful in classifying and illustrating range of upper-limb function, it is inappropriate as an evaluation tool in SMA II. Other assessment methods used to evaluate patients with SMA II could be more precise but their applicability to the evaluation of arm and hand function has not been studied.

## Aim

In this study, we wanted to investigate the ability of four standard assessment methods to reflect physical capacity and capability across the range of upper limb function in SMA II and to study the individual methods' ability to differentiate patients within various levels of upper limb function as classified by the Brooke Upper Limb Scale.

## Methods

All patients who were registered by the Danish SMA registry ( $n = 65$ ) aged  $\geq 5$  years as of September 2010 with a clinical and genetically confirmed diagnosis of SMA II, were invited to participate in this study. The Danish registry contains the total Danish SMA II population. Patients who accepted the invitation signed an informed consent. If the patient was  $< 18$  years, parents signed the consent. The Danish local ethics committee approved the study without notification.

The sitting position is the patient's habitual position in which daily activities are performed and best controlled, and transferring to and from the wheelchair can be time-consuming and troublesome for the more disabled patients. For this reason, we found it most appropriate to evaluate the patients' activities in their wheelchairs.

## Classification of upper limb function

The Brooke scale was used to illustrate and classify the patients' range of upper-limb function. The scale has six levels that are ranked according to the level of difficulty. Level 1 represents highest function; level 6 represents lowest function (Table 1). No elbow support (from armrest, thigh, etc.) was allowed if the patient was placed in levels 3 or 4. Patients who did not meet the

Table 1. Brooke Upper Limb Scale.

Item	
1	Starting with the arms at the sides the patient can abduct arms in full circle until they touch above head.
2	Can raise arms above head only by flexing the elbow.
3	Cannot raise arms above head but can raise 8 oz glass of water to mouth.
4	Can raise hands to mouth but cannot raise 8 oz glass of water to mouth.
5	Cannot raise hands to mouth but can use hands to pick up pennies from table.
6	Cannot raise hands to mouth and has no useful function of hands.

The scale was used to categorize patients according to level of arm function.

criteria for item 5: "hold pen or pick up pennies from table" were placed in level 6: "no useful function of hands".

## Muscle tests—measurement at impairment level

### Manual muscle test (MMT)

Manual muscle test (MMT) recorded as MRC% score [18]: seven muscle groups were tested bilaterally (elbow flexion/extension, wrist flexion/extension, finger flexion, thumb opposition/adduction). The scores were estimated from the joint motion available also in the presence of contractures. MMT scores were transformed to an 11-point rating scale (0–10) [11]. Total score for each arm was calculated as a percentage of highest possible score [(sum of graded scores)/(number of muscle tested  $\times$  10)  $\times$  100]. The strongest arm was used for analysis [19].

### Quantitative muscle test

Quantitative muscle test performed as a maximal voluntary isometric contraction with a hand-held dynamometer (Citec™, C.I.T. Technics BV, Groningen, the Netherlands) and expressed in Newton (N): The reliability of the hand-held dynamometer for use in patients with SMA has been established in several studies [20–22].

"Full fist grip" and "lateral pinch grip" were tested bilaterally in a standardized sitting position with elbow and forearm on the armrest and the dynamometer held in a vertical position by the evaluator. If the tests could not be performed with the dynamometer in a vertical position (e.g. due to contractures), the test score was excluded. For each measurement, best value out of three was recorded and used for analysis. In accordance with the manufacturer's instruction, the "full fist grip" score was multiplied with 2.

## Functional scales—measurements at activity level

### Egen Klassifikation

Egen Klassifikation (EK) [13] is an ordinal scale based on functional abilities of daily living in non ambulatory persons with Duchenne muscular dystrophy or SMA II. An extended version, EK2, primarily designed for patients with SMA II, has recently been developed and tested for validity and reliability in a multinational study [23]; EK2 has 17 items, each of which are scored in four categories from 0 to 3, based on an interview of the patient. EK-sum score is calculated as the sum of all items. Maximum EK-sum score (51) represents lowest function, minimum EK-sum score (0) represents highest function.

Five of the 17 EK-items assess arm and hand function. These items were scored by observation where patients were asked to perform the task associated with the individual items.

Table 2. EK Upper Limb; 5/17 EK2 items measure upper limb function.

Item	Score	
1. Ability to use wheelchair. How do you get around indoors and outdoors?	0	Able to use a manual wheelchair on flat ground, 10 m < 1 min.
	1	Able to use a manual wheelchair on flat ground, 10 m > 1 min.
	2	Unable to use manual wheelchair, requires power wheelchair.
	3	Uses power wheelchair, but occasionally has difficulty steering.
5. Ability to move the arms. Can you move your fingers, hands and arms against gravity?	0	Able to raise the arms above the head with or without compensatory movements.
	1	Unable to lift the arms above the head, but able to raise the forearms against gravity, i.e. hand to mouth with/without elbow support.
	2	Unable to lift the forearms against gravity, but able to use the hands against gravity when the forearm is supported.
	3	Unable to move the hands against gravity but able to use the fingers.
6. Ability to use the hands and arms for eating. Can you describe how you eat?	0	Able to eat and drink without elbow support.
	1	Eats or drinks with support at elbow.
	2	Eats and drinks with elbow support; with reinforcement of the opposite hand + or – aids.
	3	Has to be fed.
13. Ability to control joystick How do you operate your wheelchair?	0	Uses a standard joystick without special adaptation.
	1	Uses an adapted joystick.
	2	Uses other techniques for steering than joystick.
	3	Unable to operate wheelchair.
17. Hand function. Which of these activities can you do?	0	Can unscrew the lid of a water of fizzy drink bottle and break the seal.
	1	Can write two lines or use computer keyboard.
	2	Can write signature or send text or use remote control.
	3	Cannot use hands.

Each item is scored from 0 to 3 with higher score representing lower function. Item number refers to the number on the EK2 scale.

The sum of scores was calculated as ‘‘EK Upper Limb’’ with maximum score (15) representing lowest function and minimum score (0) representing highest function (Table 2).

#### Motor function measure

Motor function measure (MFM) [14], an ordinal scale constructed for use in patients with neuromuscular disorders: This scale comprises 32 items that evaluate physical function in three dimensions. Each item has four levels scored from 0 to 3 representing the ability to perform the/a task; the higher the score, the higher the function. Dimension 1 (13 items) evaluates functions related to standing and transfer. Dimension 2 (12 items) evaluates axial and proximal function in supine and sitting position on mat and chair (3/12 items evaluate arm function with the patient seated on a chair).

We used dimension 3 (MFM D3) which evaluates distal capacity by means of seven items (Table 3); maximum score is 21, minimum score is 0. Six of the seven items measure motor function in forearm and hand and are assessed with the patient sitting in front of a table. If the patient was not able to sit in front of the examination table, a detachable desktop was placed on his/her wheelchair. The seventh item (item 4) measures the ability to dorsi-flex the ankle and should be measured in supine position, but because we wanted to assess the patients sitting in their wheelchairs, this item was measured with the wheelchair-seat maximally tilted, with the patient’s leg supported by the examiner. The MFM D3 score is calculated as the percentage of highest possible scores [14]. Since our aim was to study arm and hand function, we also calculated the score of ‘‘MFM D3 Upper Limb’’ without item 4. This score was calculated as a percentage of the maximum possible score of six items.

#### Statistics

SAS 9.2 software package (SAS Institute Inc., Cary, NC) was used for statistics. Significance levels were set at  $p < 0.05$ . As not all data were normally distributed, descriptive statistics (median and

Table 3. MFM D3 distal dimension.

Item	
4	From plantar flexion, dorsiflexes the foot to at least 90° in relation to leg. (Supine, leg supported by examiner)
17	10 coins on table—successively picks up and holds 10 coins in hand during 20-s period.
18	One finger placed in center of fixed CD—goes round the edge of CD with one finger without contact of the hand on the table.
19	Pencil on table. Pick up the pencil and draw loops inside frame.
20	Holding sheet of paper: tears the sheet of paper.
21	Tennis ball on table : pick up the ball and turn the hand over completely holding the ball.
22	One finger placed in diagram (nine squares): raise the finger and place it successively on the squares.

Each item is scored from 0 to 3 with higher score representing higher function. Item number refers to the number on the MFM. Item 4 was excluded and the sum of the remaining items was calculated as the ‘‘MFM D3 Upper Limb’’.

range) were used to present data. Kruskal–Wallis’ tests were used to analyze whether the individual method could differentiate among Brooke levels. Mann–Whitney  $U$  tests was then performed as independent comparisons between two adjoining Brooke levels (2/3, 3/4, 4/5, 5/6). As only one person was categorized at Brooke level 1, this person’s scores were noted but were not part of the calculations. Correlations between MRC% score and EK2, ‘‘EK Upper Limb’’, MFM D3, ‘‘MFM D3 Upper Limb’’, respectively, were calculated by means of Spearman’s rho.

#### Results

Data were obtained from 52 patients (22 females, 30 males). Median age was 23 years (8–73). Twelve patients were ventilated via tracheotomy, 22 patients had non-invasive ventilation (BiPAP™) at night. Three patients could propel their manual wheelchairs; 49 patients used a powered wheelchair.

Table 4. Presentation of data from 52 patients.

	Brooke 1 (n = 1)	Brooke 2 (n = 6)	Brooke 3 (n = 10)	Brooke 4 (n = 14)	Brooke 5 (n = 8)	Brooke 6 (n = 13)
Age	30	13 (8–23)	20 (9–33)	22 (8–50)	21 (11–37)	31 (20–73)
EK2 (0–51)	5	9 (5–12)	16 (11–21)	24 (17–34)	31 (26–37)	34 (30–37)
EK UL (0–15)	1	2 (1–3)	4.5 (3–6)	7 (5–9)	9 (8–12)	13 (12–15)
MFM D3%	100	93 (91–100)	83 (71–95)	64 (33–86)	48 (27–52)	5 (0–10)
MFM D3 UL %	100	94 (89–100)	89 (72–100)	67 (33–89)	50 (17–50)	0 (0–1)
MRC%	56	49 (44–73)	39 (33–43)	31 (24–37)	18 (16–31)	11 (1–16)
HHD grip N (n = 19)	42	26 (4–86)	10 (0–18)	4 (0–8)	0 (0–0)	0 (0–0)
HHD pinch N (n = 26)	29	8 (3–38)	4 (1–5)	3 (0–6)	0 (0–2)	0 (0–2)

Distribution of age and scores (median and range) is illustrated according to Brooke level. Scores on EK2 and ‘‘EK Upper Limb’’ are illustrated in raw numbers, (minimum and maximum score). Scores on MFM D3 and ‘‘MFM D3 Upper Limb’’ are illustrated in percentage. MRC% score of seven muscle groups in arm. Hand-Held Dynamometer tests were recorded in Newton, and scored by 19 patients (full fist grip) and 26 patients (lateral pinch grip).

For 31 patients, their minimum function was the ability to lift a hand to their mouth (Brooke levels 1–4); 21 patients could not lift their forearm against gravity (Brooke levels 5 and 6). Patients with the highest level of upper-limb function (corresponding to Brooke level 2) were the youngest patients (median age 13) and patients with the lowest level of upper-limb function (corresponding to Brooke level 6) were the oldest patients (median age 31); patients at Brooke levels 3, 4 and 5 were the same age. Presentation of age, physical functional tests and muscle strength test according to levels of the Brooke Upper Limb Scale is shown in Table 4.

### Brooke levels and muscle tests

Muscle strength was measured by MMT in all patients. All patients achieved an MRC% score  $\geq 1$  (1–73). The weakest person – a 29-year-old woman at Brooke level 6, had only a flicker of movement in her index finger, corresponding to grade 1. MRC% score could differentiate among patients at all Brooke levels (Table 5).

Hand strength was tested in 42 patients using a dynamometer. For various reasons (dynamometer in disrepair, time schedule), six patients were not tested. Four patients were excluded from the test, as their arm could not be placed in the proper position.

A full-fist grip score  $>0$  was attained by 19 patients. None of the patients at Brooke levels 6 and 5 were able to overcome the dynamometer threshold and not until Brooke level 2 were all patients able to achieve a score  $>0$ . The fist-grip score could differentiate patients at Brooke level 3 and level 4 and level 4 and 5, respectively.

A lateral pinch-grip score  $>0$  was attained by 26 patients. Only one patient at Brooke level 6 and two at Brooke level 5 were able to overcome the dynamometer threshold. All patients at Brooke level 3 achieved a score  $>0$ .

Lateral pinch-grip could differentiate patients at Brooke level 2 and level 3, but not among patients at other Brooke levels (Table 5).

### Brooke levels and EK2

The EK2 scale was scored by all patients. None of the patients attained the minimum score (0), corresponding to highest function or maximum score (51), corresponding to lowest function. When sum of the five upper limb items was calculated, no patient attained the maximum score (15 = lowest function), but one patient scored zero (0 = highest physical function). EK upper limb % score according to Brooke levels is illustrated in Figure 1(A).

The EK2 sum score could differentiate patients at Brooke level 2/3, 3/4 and 4/5 but could not differentiate between the weakest patients at Brooke level 5 and level 6. The ‘‘EK Upper Limb’’ could discriminate among patients at all Brooke levels (Table 5).

Table 5. The clinical method’s ability to differentiate among patients at two adjacent Brooke levels illustrated as *p* values.

	Brooke 5/6	Brooke 4/5	Brooke 3/4	Brooke 2/3
EK 2	0.142	0.006 <sup>a</sup>	0.003 <sup>a</sup>	0.007 <sup>a</sup>
EK UL	0.002 <sup>a</sup>	0.004 <sup>a</sup>	0.001 <sup>a</sup>	0.005 <sup>a</sup>
MFM D3%	0.001 <sup>a</sup>	0.003 <sup>a</sup>	0.012 <sup>a</sup>	0.032 <sup>a</sup>
MFM D3 UL%	0.001 <sup>a</sup>	0.001 <sup>a</sup>	0.009 <sup>a</sup>	0.097
MRC%	0.002 <sup>a</sup>	0.003 <sup>a</sup>	0.012 <sup>a</sup>	0.005 <sup>a</sup>
HHD grip N	0.202	0.040 <sup>a</sup>	0.006 <sup>a</sup>	0.059
HHD pinch grip N	0.127	0.127	0.312	0.050 <sup>a</sup>

EK–upper limb module, MFM D3 and MRC% could discriminate among patients at all Brooke levels.

<sup>a</sup>Significance at 0.05 level.

### Brooke levels and MFM D3

All patients were tested by means of the MFM D3. The maximum score (100% – highest function) was scored by three patients; the minimum score (0% – lowest function) was also scored by three patients. When calculated as ‘‘MFM D3 Upper Limb’’, maximum score (18) was attained by five patients; minimum score (0) by six patients. MFM D3 upper limb score according to Brooke levels is illustrated in Figure 1(B).

The MFM D3 score could differentiate among patients at all Brooke levels; without item 4 (the foot item), the ‘‘MFM D3 Upper Limb’’ could not discriminate between the strongest patients at Brooke level 2 and level 3.

### MRC% and correlation with functional tests

MRC% of forearm and hand was strongly correlated with EK2 sum (–0.917), ‘‘EK Upper Limb’’ (–0.958), MFM D3 (0.925) and ‘‘MFM D3 Upper Limb’’ (0.925).

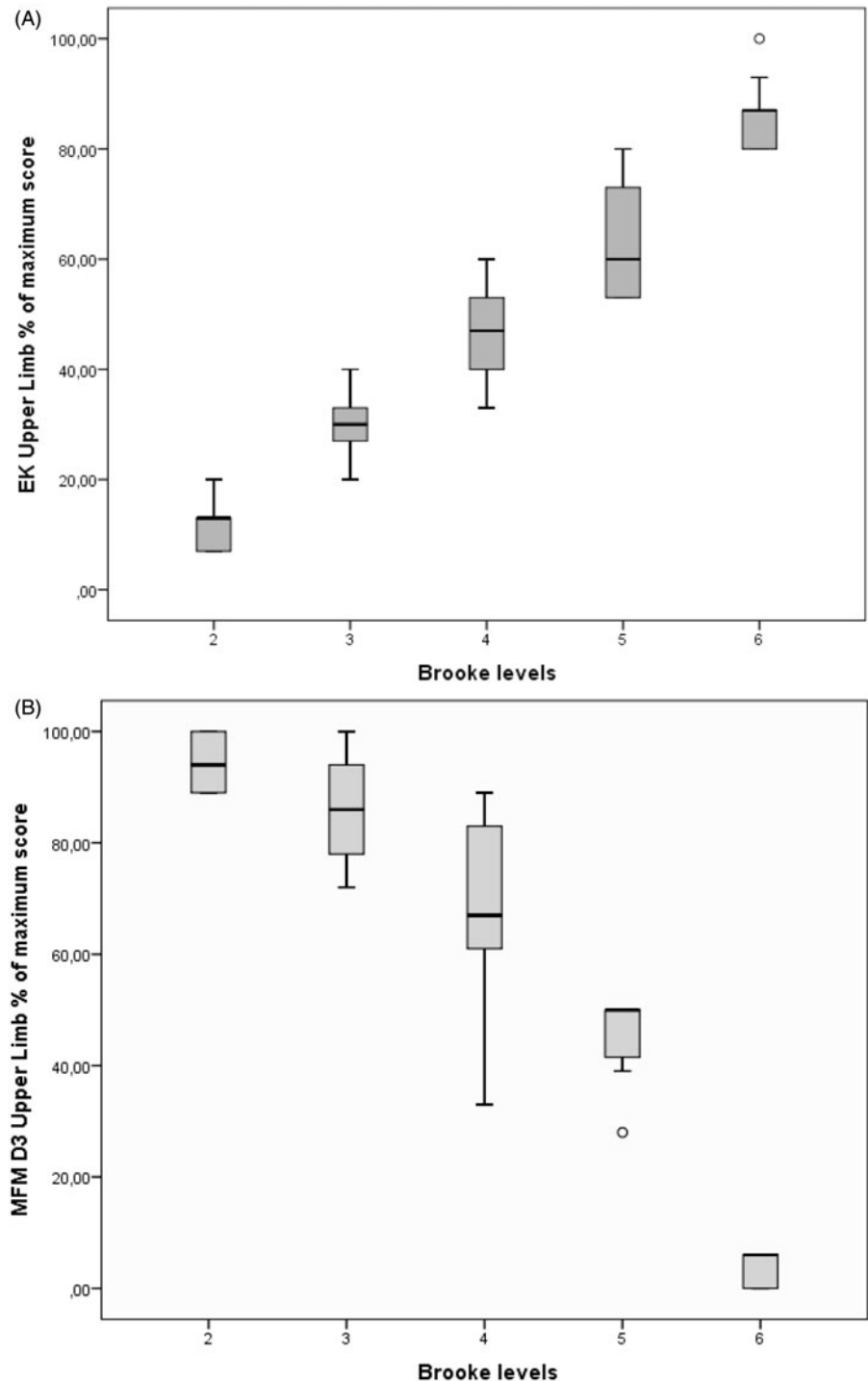
### Discussion

In this study, we demonstrated the ability of some of the most widely used scales to measure upper-limb function in SMA II, a patient group with a diverse range of upper-limb function. Physical capacity at the impairment level was best reflected by the MMT. This testing method was applicable to all patients and could discriminate among patients at all Brooke levels. HHD as measured by the Citec™ dynamometer could not reflect all patients’ capacity, since more than one third of the patients could not overcome the dynamometer’s threshold and the method could only discriminate between patients at a few adjoining Brooke levels.

While both the EK 2 scale and the MFM D3 were applicable and could express physical capability in patients in all stages at



Figure 1. (A) Scores on ‘‘EK Upper Limb’’ according to Brooke levels. EK scores (0–15) are illustrated as percentage of maximum score; note that maximum score (100%) corresponds to lowest function. Brooke level 1 is not represented since only one patient was categorized at this level. (B) Scores on ‘‘MFM D3 Upper Limb’’ (0–18) according to Brooke levels. Note that maximum score (100%) corresponds to highest function. Brooke level 1 is not represented since only one patient was categorized at this level.



the activity level, they were not equally suited to discriminate among patients. The EK2 scale could discriminate between all adjoining Brooke levels, except for the weakest patients at levels 5 and 6, a result that was improved when the scale was reduced to an upper-limb sub scale and calculated as ‘‘EK2 Upper Limb’’ score. The MFM D3 could discriminate among patients at all Brooke levels, but when calculated as ‘‘MFM D3 Upper Limb’’ this ability was lost in the strongest patients at Brooke levels 2 and 3; furthermore, a possible floor and ceiling effect was indicated (Figure 1B).

In SMA II, a certain level of arm and hand function is needed to maintain some autonomy in everyday activities. Clinical approaches must be able to reflect this in order to plan and evaluate rehabilitation management. New modules are being developed to create a measurement that can meet these

demands [16]. In our study, we wanted to address the applicability of methods already employed in clinical practice.

Patients with SMA II have a diverse range of upper-limb function and we used the Brooke Upper Limb Scale to illustrate this. The scale is widely used, but technological strides have created a huge gap between levels 5 and 6; the latter is now somewhat redundant, as only very few patients in a modern society with access to technical aids will have ‘‘no useful function of hands’’.

In this study, MMT assessed strength in the forearm. This was based on our findings from a previous study in SMA II [5], where we found that the MRC% score of muscles with more physical capability better reflected variation among patients than a total muscle test and in accordance with our criteria patients should be assessed in their wheelchair. We chose to include thumb

adduction and thumb opposition, as we had found that these movements were easier for some patients with SMA II to perform. Corresponding to earlier findings [3], we found that elbow extensors were weak regardless of Brooke level. Finger muscles, and especially thumb muscles, were the strongest muscles across the various Brooke levels. Thumb adduction was the strongest muscle in the patients with inferior muscle strength, and thus vital to the ability to operate a wheelchair and computer by hand. MRC% score was able to differentiate among patients at all Brooke levels, and muscle function was observable – also in the weakest patients. MMT is used worldwide in clinical practice and has been a superior registration of muscle function in very weak patients because it can score even almost imperceptible movements. The method's inter-rater reliability is better when testing weak muscles compared to stronger muscles and better when performed by a limited number of experienced evaluators [21,24]. However, being ordinal, the method has been questioned as an outcome measure in clinical trials, where gold standards are imperative. This has made it difficult to enlist patients with very limited muscle strength in clinical trials, as none of the prevailing clinical methods have been able to measure very weak muscles. MRC% correlated strongly with the functional tests, but strongest correlation was found with the "EK Upper Limb".

Scores of quantitative muscle tests as obtained in HHD are recorded at interval-level and the method has good inter- and intra-rater reliability [20,25]. However, the method has a floor effect, since patients with very weak muscles (<3) do not have the strength to overcome the threshold of the dynamometer [5,21,26]. This corresponds to our findings where an arm function corresponding to Brooke  $\leq 3$  was needed if all patients were to attain a score on the dynamometer. The HHD (Citec™) used in our study has one standard applicator for measuring hand fist grip. Corresponding to Mahony et al. [21], we found that this caused some difficulties in adapting small hands to the applicator of the dynamometer, which may influence the results of the grip test in patients with small hands. This corresponds to the fact that only 45% of our patients could overcome the threshold of the dynamometer in contrast to 75% of the patients being able to obtain a score of  $\geq 2$  on the MRC scale when testing finger flexion. In our clinical experience, patients with SMA II are often capable of activating their thumb, which was why we chose to measure pinch-grip, and 62% of the patients could indeed overcome the dynamometer threshold. However, it was not possible to reflect physical capability in the weakest patients, although muscle strength in the thumb could be measured by means of the manual muscle test. Dynamometers with a lower threshold might serve as outcome measures at the impairment level to reflect muscle strength and motor capacity at an interval scale.

The EK2 scale was developed to assess overall physical functions at the activity/performance level in non-ambulant patients with SMA; it consists of 17 domains representing functional abilities or impairments relevant to the patient's daily activities. The scale is particularly well-suited to daily clinical practice as a means of identifying the need for interventions to preserve functions and to evaluate an intervention. For example, we found that even with an adapted joystick, 22 patients were unable to drive their wheelchairs in cold weather; on the whole, temperature exerts significant influence on motor ability in very weak patients. In our study, the EK2 sum score could discriminate among patients at most Brooke levels with some overlap between patients at Brooke levels 5 and 6, which indicates a lack of sensitivity when measuring very weak patients. This may be because only 5 out of 17 items evaluate upper limb function.

If we want to detect small changes in motor function, we need to focus on the upper limb region since upper-limb functions and their changes over time can be measured in even very weak patients [5,7]. Such changes may be difficult to spot in a score representing overall physical abilities. This opinion was also voiced by Mazzone et al. [16] who found "that upper-limb function may not always strictly follow the overall gross motor function". The calculation of a sub-score of five "upper-limb items" confirmed this and the "EK Upper Limb" could differentiate among patients at all Brooke levels. With this ability, the "EK Upper Limb" could potentially function as an outcome measure in clinical trials on SMA II. However, the module's sensitivity to registering changes in motor function in the individual patient needs to be evaluated in further studies.

The MFM scale measures the physical capability of patients with neuromuscular diseases, including SMA. The MFM D3 subscale assesses the ability to perform activities, but not all are relevant to the patient's daily activities (fingering the edge of a CD, tearing paper, turning a ball). Consequently, the scale has limited relevance in daily clinical practice. Despite this, the scale was able to reflect the capability of the weakest patients at Brooke level 6, as almost half of these patients could slide their finger and point to a single square (item 22) corresponding to a score of "1". Translating this modest activity into daily life practice means that the patients can operate their wheelchairs and computers via remote control – which is of great importance in everyday life. Item 20 (tearing paper) was too difficult for weak patients, and patients did not obtain a score on that item unless they had muscle strength and physical function corresponding to Brooke level 4. The MFM D3 score could discriminate among all patients, but the fact that item 4 (dorsi flexion of the foot) was measured with the patients sitting in their wheelchair could influence the results. Furthermore, we believe that this item is inappropriate when focusing on upper limb function. When item 4 was excluded, the scale lost the ability to discriminate between the strongest patients at Brooke level 2 and level 3. Bartels et al. [27] also used the modified version of MFM D3 to assess upper-limb function in Duchenne muscular dystrophy. Their findings were similar to ours: they found that the "MFM D3 Upper Limb" could differentiate among severely affected individuals with some residual upper limb function, but emphasized "that the score did not identify the last residues of motor function". In our study, six out of 52 patients scored 0 on the "MFM D3 Upper Limb" corresponding to minimal function (cannot initiate task). When scored by the "EK Upper Limb" and the manual muscle test, all six patients possessed identifiable motor function. This suggests that an "MFM D3 Upper Limb" scale must be more sensitive if motor function in patients with very limited muscle strength should be identified.

Although we studied the applicability of "sub-versions" of two frequently utilized scales, our intention was neither to create nor validate new sub-scales but merely to illustrate that a modified version of existing scales has the potential to target an outcome of interest more precisely, and that, in order to provide a holistic picture of the patient, a combination of scales that evaluate both impairment and activity is needed.

## Conclusion

While even very weak SMA II patients have measurable upper limb function, not all methods are equally suited to do this. The manual muscle test and the "EK Upper Limb module" can measure upper limb function across all stages and ages of SMA II. The MFM D3 is also applicable but as upper-limb scale it is limited by its inclusion the item measuring foot function; when this item was excluded the scale became less sensitive.

Thumb muscles and finger flexors seem to be the best preserved muscles in very weak patients. Efforts should be made to make existing instruments more sensitive so that interventions and rehabilitation can also be evaluated in very weak patients.

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### Declaration of interest

The authors declare that there are no conflicts of interest.

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