TREAT-NMD SMA Dataset Manual

Version 1

13-Dec-2019

This document has been prepared by the TREAT-NMD SMA Dataset project team on behalf of the TGDOC (TREAT-NMD Global Database Oversight Committee), to support patient registries in the TREAT-NMD network with the collection of the Core SMA Dataset.

The SMA Dataset (and this dataset manual), will be subject to an annual revision process, and feedback is welcome from stakeholders or other interested groups or individuals. Feedback for the 2020 dataset revision (v2) should be submitted before 13 March 2020, by sending an email or an annotated version of the document to Project Manager joanne.bullivant@newcastle.ac.uk.

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Introduction

TREAT-NMD is a network for the neuromuscular field that provides an infrastructure to ensure that the most promising new therapies reach patients as quickly as possible. Since its launch in January 2007 the network's focus has been on the development of tools that industry, clinicians and scientists need to bring novel therapeutic approaches through preclinical development and into the clinic, and on establishing best-practice care for neuromuscular patients worldwide.

The TREAT-NMD global network of SMA Registries feed into a central hub called the TREAT-NMD Global SMA Registry, which can receive requests from third parties in order to answer research questions. National registries that are part of the Global Registry must collect as a minimum, a standardized core dataset from their patients.

The TREAT-NMD Global SMA Registry is governed by a Charter* and by the TREAT-NMD Global Database Oversight Committee (TGDOC). The TGDOC is responsible for reviewing the requests for data from the Global Registry and it votes on whether the request is in line with the Charter and is in patients' best interests.

In May 2017, TGDOC initiated a project to review and expand the core dataset for the TREAT-NMD network of SMA Registries, and the new dataset (version 1) was confirmed in September 2018. This dataset manual is intended to support the expanded dataset.

** The TGDOC Charter is currently under review*

Important notes: please read before using dataset

This manual is written to support healthcare professionals (HCPs) and Registry Curators/Data Managers in the collection of the TREAT-NMD SMA Registries Core Dataset. It provides:

- Background and context information on the Expanded SMA Dataset
- Data Dictionary (definitions of all data items and guidance on collection and reporting)
- Suggested standard wording/templates for consent information and ethical approval applications

To further support registries, an Outcome Measure Toolkit (to support the selection and collection of motor measures and patient-reported outcomes) will be developed by May 2020.

The following documents are also available which present the Dataset in a more simplified way than in this manual:

- **High level overview of the Expanded SMA Core Dataset**
- **Full Expanded SMA Core Dataset**

Any comments or questions about the dataset, or anticipated training or support requirements should be reported to joanne.bullivant@newcastle.ac.uk (Project Manager) or joanna.das@newcastle.ac.uk (Project Coordinator).

Identifiable data

Identifiable personal data such as name, date of birth, address or contact details **will never be requested by TREAT-NMD for central submission**. These items are included in the core dataset as guidance to individual registries about which demographic fields may prove useful in the local management of the registry.

Data submissions

Schedule: Currently, registries who are part of the TGDOC global registry model are asked to submit data centrally on an ad-hoc basis; when needed to respond to a 3rd party enquiry into the global registry.

Method: Currently, registries are asked to provide the requested data by emailing it in an excel spreadsheet.

Data: Currently, registries are only asked to provide aggregate data (e.g. patient numbers, often stratified, against a specified number of data items).

Dataset compliance

Mandatory items: Registries are required to include all these items (where applicable) in their case report forms (as either mandatory or conditional fields). If this is not possible, Curators should discuss with the Dataset Project Team and agree actions to work towards inclusion if feasible.

Highly Encouraged items: Registries are encouraged to include these items in their case report forms, however this is optional.

Additional items: Registries in the TREAT-NMD network are independent and as such are free to collect additional data within their registries according to their needs and/or priorities.

Data entries: As best practise, registries should ensure that all data entries and updates are date-stamped (and time-stamped if possible).

Date formats: When the exact date is requested in the dataset, it should be reported in the DD-MM-YYYY format. For example, 1st July 2018 would be recorded as 01-07-2018. Where only the month and year is requested, it should be reported in the MM-YYYY format. For example, July 2018 would be recorded as 07-2018.

Dataset key

Items in black = mandatory

Items in blue = highly encouraged

CR = mandatory only for clinician-reported registries

PR = mandatory only for patient-reported registries (an adapted dataset with different wording will be developed for these registries)

◊ = in patient-reported registries, these data items should be reported by the Registry Curator, following review of the patient's genetic report.

^ = items which support PPRL functionality (Privacy Preserving Record Linkage)

Response options

Unknown / Don't know

If the 'Unknown' option for any given item is not appropriate for your registry, you may choose not to include it. If you wish to encourage your registry users to return and complete any missing information as soon as possible, you may choose to use 'To be confirmed' instead of 'Unknown', where you feel this is appropriate.

Patient-reported registries may wish to include an "I don't want to disclose" option for potentially sensitive questions.

Feedback, Harmonisation & Revisions

The TREAT-NMD Global SMA Registry is one of several notable data collection initiatives in operation across the world. Harmonisation and comparability across these different data repositories is vital to ensure that the collected data meets the current and future needs of the SMA community.

Considerable work has gone into ensuring that the data collected by the TREAT-NMD registries, through this first iteration of the expanded core dataset, will be comparable with the data collected by other initiatives. However, many of these initiatives are still in development, and in addition to this, global consensus on the most appropriate and relevant data to collect is expected to continue to evolve over the coming years.

An annual Dataset Revision Process has been developed to reflect TREAT-NMD's commitment to ensuring that the core SMA dataset remains appropriate, feasible, collaborative, harmonised with other initiatives, and responsive to the needs of the SMA community. Please note, we do not anticipate that these changes will be significant; we are equally keen to limit the burden on the registries who will need to implement any changes made.

The Revision Process is described in full in the SMA Dataset Revision Process document which is available from the SMA Dataset Project team and will also be made available on the SMA Dataset webpage.

Data Sharing & Publications

Data Sharing

Third parties may request a report on data held in the TREAT-NMD Global SMA Registry, by submitting a global enquiry to the TREAT-NMD Secretariat. Only de-identified, aggregate data is included in enquiry reports.

If an enquiry is approved (via vote) by the TGDOC, the relevant SMA registries are asked to provide the relevant data. More information on the voting process can be found in the TGDOC Membership and Voting SOP which is available from the TREAT-NMD Secretariat. The data that the registries provide is always de-identified. When the national registries submit data to the central TREAT-NMD secretariat team, it is cleaned and compiled into an aggregated data report for the third party.

Publications

TREAT-NMD and the TGDOC acknowledge that a great deal of hard work, resource and expertise goes into the collection of high quality patient data by its affiliated registries, and we are committed to ensuring that contributions towards the TREAT-NMD Global SMA Registry are appropriately acknowledged wherever and whenever relevant. To this end, TGDOC have formed a Publications Committee who have a priority task to develop and have ratified a TREAT-NMD Global Registries Publications Policy.

If you would like to be involved in the Publications Committee, please contact the Committee Chair, Dr Rasha El Sherif (dr.rashaelsherif@gmail.com).

Standard text for consent and ethics

Patient Information text

[*Registry name*] is part of an international network called TREAT-NMD. The TREAT-NMD network has created a global SMA database called the Global SMA Registry, which collects information from SMA registries across the world, including [*registry name*]. The Global SMA Registry ensures that patients from all over the world can be contacted if their profile fits a clinical trial. In addition, it can help researchers, companies and regulators to answer important questions about SMA, provide information to help monitor how well different treatments are working, and support other activities to improve patient care, such as the assessment of standards of care in different countries.

If you give us permission to share your data with the TREAT-NMD Global SMA Database, we will never transfer any of your personal identifiable details; your records will only be identifiable by an anonymous code. Researchers using the TREAT-NMD Global SMA Database therefore cannot identify you personally from the information they have access to. Only the person in charge of [*registry name*], [*name of PI*], or a person explicitly appointed by [*him/her*], will ever be able to "de-code" the data to get access to your personal details.

Patient consent statement

"I give permission for my de-identified data to be transferred and stored in the TREAT-NMD Global SMA Registry, where it may be used for research and the planning of clinical trials."

Text for protocol / ethical approval application

[*Registry name*] is part of an international network called TREAT-NMD. The TREAT-NMD network has created a global SMA database called the Global SMA Registry, which collects information from SMA registries across the world and can accept data enquiries from third parties (industry or academic). Only de-identified data will be provided to the TREAT-NMD Global SMA Registry from the [*registry name*].

Third parties wishing to enquire into the data in the TREAT-NMD Global Registry must first have the approval of both the TREAT-NMD Global Database Oversight Committee (TGDOC) and the [*registry name*] Steering Committee. If approval is granted, TREAT-NMD requests the relevant data from the registries in the network, and provides the third party with a report containing anonymous, aggregated data.

Dataset Dictionary

Section 1: ENROLMENT

1.00 Date of enrolment

Mandatory. The date that the patient's details are first entered into the registry, using format DD-MM-YYYY.

1.01 Date of consent (if different from enrolment)

Mandatory. In clinician-reported registries, it is anticipated that this would be the same as the date of enrolment specified in 1.00.

In patient-reported registries, registration (demographic data) is often received online first, and the patient or parent may return at a later date to complete the consent and complete their registration; therefore, the date of consent in 1.01 may be different to the date of enrolment in 1.00.

Use format DD-MM-YYYY

1.02 Date of any re-consents

Mandatory. If the patient is asked to re-consent for any reason (for example a new version of the consent comes into effect, the protocol is changed, or a child reaches the legal age of consent), the date of each re-consent should be recorded using format DD-MM-YYYY.

1.03 Consented to TNMD global registry?

Mandatory. As described in Section 3, bullet point 2 of the TGDOC Charter (TGDOC = TREAT-NMD Global Database Oversight Committee), it is the responsibility of each registry to ensure that each of their participants has provided informed consent for their anonymised data to be shared with the TREAT-NMD Global Database.

Responses: Yes; No

1.04 Local registry ID

Mandatory. It is recommended that registries assign each of their patients a unique local registry ID (identifier), to assist in the anonymisation and internal cross-checking of data. This local ID will never be requested by TREAT-NMD for central submission, however it is mandated as best practise at a local level. The ID must not contain identifiable information such as initials, date of birth or medical record number. For more information about what constitutes personal or identifiable data, please refer to GDPR guidance (https://gdpr.eu/eu-gdpr-personal-data/) and/or the 18 HIPAA identifiers (https://www.hipaajournal.com/considered-phi-hipaa/)

Section 2: DEMOGRAPHICS

Notes:

Identifiable personal data such as name, date of birth, address or contact details would never be requested by TREAT-NMD for central submission.

^ = items which support PPRL functionality (Privacy Preserving Record Linkage)

2.00 Date of birth

Mandatory. Date of birth of the patient, as given on birth certificate or as reported by patient/parent. Format should be DD/MM/YYYY.

2.01 First name

Highly encouraged. The current legal/registered first name of the patient.

2.02 First name given at birth (if different)

Highly encouraged. The first name that the patient was given at birth (as recorded on their birth certificate), if this is different to the name given in 2.01.

2.03 Last name

Highly encouraged. The current legal/registered last name / surname / family name of the patient.

2.04 Last name given at birth (if different)

Highly encouraged. The last name / surname / family name that the patient was given at birth (as recorded on their birth certificate), if this is different to the name given in 2.03.

2.05 Sex

Mandatory. Sex of patient.

Responses: Male; Female; Unspecified

2.06 Sex at birth (if different)

Highly encouraged. The sex that was assigned to the patient at birth (as recorded on their birth certificate), if this is different to the sex reported in 2.05.

Responses: Male; Female; Unspecified

2.10 Address

Highly encouraged. The current residential address of the patient.

2.11 Zip/post code

Highly encouraged. The Zip code, area code, or post code associated with the current residential address given in 2.10.

2.12 Country of residence

Mandatory. The current country of residence, using ISO 3 Standards.

2.13 Country of birth

Highly encouraged. The country in which the patient was born (as stated on the birth certificate), using ISO 3 Standards.

2.14 City/town of birth

Highly encouraged. The place of birth (city/town/municipality), as stated on the birth certificate. If a birth certificate is not available, use as stated on passport or government-issued identity card. Please use place names as specified in the native language of your country. If your country is multi-lingual, we advise to use the language of the patient.

2.15 Email address

Highly encouraged. A current email address for the patient, through which they can be contacted.

2.16 Telephone number

Highly encouraged. A current telephone number for the patient, on which they can be contacted.

2.20 Any other family member affected?

Highly encouraged. Does the patient have any other family member diagnosed with SMA?

Responses: Yes; No

2.21 If Yes, state kinship

Highly encouraged. Record how each family member diagnosed with SMA is related to the patient in question.

Responses: Mother; Father; Daughter; Son; Brother; Half Brother; Sister; Half Sister; Niece; Nephew; Maternal Uncle; Paternal Uncle; Maternal Aunt; Paternal Aunt; Maternal Cousin; Paternal Cousin; Maternal Grandfather; Paternal Grandfather; Maternal Grandmother; Paternal Grandmother; Granddaughter; Grandson (Can add multiple)

Section 3: LIVING STATUS

3.00 Is the patient alive?

Mandatory. In patient-reported registries this field should ideally be hidden from the participant and the answer defaulted to 'Yes'. If the Curator is informed of the death of a patient they would then edit this field and complete 3.01 and 3.02 where known.

Responses: Yes; No; Loss of follow-up

3.01 Date of death

Highly encouraged. Date of death of the patient, as given on death certificate or as reported by parent/carer/next of kin. Format should be DD/MM/YYYY.

3.02 Cause of death

Highly encouraged. Registries are advised to use the full ICD-10 Classification system as best-practice. Where this is not yet possible, the options below represent the highest-level ICD-10 Classifications.

Alternative responses if full ICD-10 Classification not possible: Certain infectious and parasitic diseases; Neoplasms; Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; Endocrine, nutritional and metabolic diseases; Mental, Behavioural and Neurodevelopmental disorders; Diseases of the nervous system; Diseases of the eye and adnexa; Diseases of the ear and mastoid process; Diseases of the circulatory system; Diseases of the respiratory system; Diseases of the digestive system; Diseases of the skin and subcutaneous tissue; Diseases of the musculoskeletal system and connective tissue; Diseases of the genitourinary system; Pregnancy, childbirth and the puerperium; Certain conditions originating in the perinatal period; Congenital malformations, deformations and chromosomal abnormalities; Other - Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (Specify, free text)

Section 4: GENETIC DIAGNOSIS

Notes:

◊ = in patient-reported registries, data items marked with ◊ should be reported by the Registry Curator, following review of the patient's genetic report.

4.00 Has the patient had genetic confirmation of SMA?

Mandatory. If the genetic test results are pending, select 'No'

Responses: Yes; No

4.01 ◊ If yes to 4.00, was it through screening?

Highly encouraged. Was the genetic diagnosis made as part of a screening programme?

Responses: Unknown; No; Yes, Family Screening; Yes, Newborn Screening Programme; Yes, Prenatal Screening.

4.02 If 'Yes' to 4.00: Send/upload copy of genetic report (patient-reported only)

Mandatory. The registry should ask the participant to upload (if the registry's platform supports this) or send a copy of their genetic report to confirm their diagnosis.

4.03 If 'Yes' to 4.00: Name/location of genetic testing centre

Mandatory. This will allow curators to request a copy of the genetic report if it is not immediately available or to request further clarification or information if needed (permission to do this should be sought within the consent process where applicable).

4.04 ◊ If 'Yes' to 4.00: Date of genetic diagnosis

Mandatory. The date recorded on the genetic report. Format should be DD/MM/YYYY.

4.05 ◊ If 'Yes' to 4.00: Mutation name in SMN1 gene

Mandatory. This information should be extracted from the genetic report and confirmed with a geneticist if necessary.

Responses: SMN1 homozygous deletion of exon 7 (&8); SMN1 heterozygous deletion of exon 7 (&8) and compound heterozygous to a point mutation in SMN1; Compound heterozygous (or homozygous) for two (or one) point mutation(s) in SMN1)

4.06 ◊ If 'Yes' to 4.00: Method of SMN1 testing

Highly encouraged. This information should be extracted from the genetic report and confirmed with a geneticist if necessary.

Responses: RFLP (Restriction Fragment Length Polymorphism); HRM (High Resolution Melting); MLPA (Multiplex Ligation-dependent Probe Amplification); Luminex Genotyping / DNA Sequencing; qrtPCR (Quantitative Real-Time PCR); ddPCR (Droplet Digital PCR); Other (specify); Unknown

4.07 ◊ If 'Yes' to 4.00: Was SMN2 Copy number tested?

Mandatory. This information should be extracted from the genetic report.

Responses: Yes; No

4.08 ◊ If 'Yes' to 4.07: Method of SMN2 testing

Highly encouraged. This information should be extracted from the genetic report and confirmed with a geneticist if necessary.

Responses: RFLP (Restriction Fragment Length Polymorphism); HRM (High Resolution Melting); MLPA (Multiplex Ligation-dependent Probe Amplification); Luminex Genotyping / DNA Sequencing; qrtPCR (Quantitative Real-Time PCR); ddPCR (Droplet Digital PCR); Other (specify); Unknown

4.09 ◊ If 'Yes' to 4.07: SMN2 copy number

Mandatory. This information should be extracted from the genetic report and confirmed with a geneticist if necessary.

Responses: 1; 2; 3; 4+

Section 5: CLINICAL OBSERVATIONS

5.00 Age of symptom onset

Mandatory. At what age was it suspected that something might be different?

Responses: Prenatal; at birth; age YY-MM (from 0.5M)

5.01 Spinal Muscular Atrophy type

Mandatory. Clinical diagnosis given by clinician in charge of the patient's care.

Responses: 0; 1; 2; 3; 4

SMA type	Usual age of symptoms onset	Impact of muscle weakness on sitting / walking
Type 1	Younger than 6 months	Unable to sit or roll independently
Type 2	7 months – 18 months	Able to sit but not walk independently
Type 3a	18 months – 36 months	Able to walk, though may lose this ability over time
Type 3b	3 years – 18 years	Able to walk, though may lose this ability over time
Type 4	Over 18 years	Mild walking (motor) difficulties

Table taken from the SMA Family Guide[1]

5.02 Height/length (cm)

Highly encouraged. Height or length of the patient, given in centimetres

5.03 Method of height measurement[2]

Highly encouraged. Report method used to measure patient's height/length.

Responses: Standing height; Recumbent length; Arm span; Ulnar length; Other (specify, free text)

Please note: Standing and Recumbent methods will not give accurate results where contractures and/or significant scoliosis exist. Arm span method will not give accurate results where arm contractures exist. In these cases, the Ulnar length method should be used.

Standing height[14]	Person length (height) is measured using a vertical length scale. The person would stand with footwear removed over a fixed platform or the floor and an unfixed headboard would be adjusted to the top of the head. Record the measurement to the nearest cm mark.
Recumbent length[14]	Employment of a horizontal length scale (or bench with steel ruler or tape). The person is placed flat on the horizontal measuring board, with footwear removed. The head should be placed against the fixed headboard, and the footboard adjusted so that it is against the base of the feet. Record the measurement to the nearest 1/2 inch / 1 cm.
Arm span	Measure using a flexible tape, from the tip of the middle finger of one hand to the tip of the middle finger of the other hand. The person stands

	with their back to the wall, with both arms abducted to 90°, the elbows and wrists extended and the palms facing directly forward.
Ulnar length[14]	Measure between the point of the elbow (olecranon process) and the midpoint of the prominent bone of the wrist (styloid process) (left side if possible).

5.04 Weight

Highly encouraged. Current body weight of patient, given in kilograms.

5.05 Head circumference (for infants <24 months old)

Highly encouraged. This measurement should be taken with a device that cannot be stretched. Wrap the tape snugly around the widest possible circumference - from the most prominent part of the forehead (often 1-2 fingers above the eyebrow) around to the widest part of the back of the head. Try to find the widest way around the head. [14]

5.06 Chest circumference at full expiration (for infants <24 months old)

Highly encouraged. This measurement should be taken with a device that cannot be stretched. Place one end of the tape measure at the fullest part of the bust, wrap it around (under the armpits, around the shoulder blades, and back to the front) to get the measurement. [14]

5.07 Chest circumference at full inspiration (for infants <24 months old)

Highly encouraged. See 5.06

5.08 – 5.14 Does the patient suffer from contractures

Highly encouraged. Provide a response for each contracture type

5.08 Shoulder contractures
5.09 Elbow contractures
5.10 Wrist contractures
5.11 Finger contractures
5.12 Hip contractures
5.13 Knee contractures
5.14 Ankle contractures

Responses: Yes; No

5.20 Name of the neuromuscular specialist or main doctor in charge of your care (patient-reported only)

Mandatory. In some cases this may be a family doctor such as a GP. Not applicable for clinician-reported registries as this information would typically be known by default.

5.21 Name/location of your main healthcare centre (patient-reported only)

Mandatory. Not applicable for clinician-reported registries as this information would typically be known by default.

Section 6: SCOLIOSIS

6.00 Has the patient been diagnosed with scoliosis?

Mandatory. Has the patient had a confirmed diagnosis of scoliosis?

Responses: Yes; No; Unknown

6.01 If 'Yes' to 6.00: Cobb angle according to radiology results

Highly encouraged. Results should be entered as they appear on the radiology results. Unit is degrees.

6.02 If 'Yes' to 6.00: has the patient had surgery for the scoliosis?

Mandatory. Has the patient had surgery specifically to try and correct the scoliosis?

Responses: Yes; No

6.03 If 'Yes' to 6.02: Surgery technique

Highly encouraged. Which technique was used for the patient's surgery?

Responses: Arthrodesis; Growing Rods; Other (specify); Unknown

6.04 If 'Yes' to 6.02; date (month & year) of first surgery

Highly encouraged. Give the month and year of the first surgery for scoliosis, using format MM/YYYY

Section 7: MOTOR FUNCTION

All items mandatory. This section is intended to be feasible for all registries (both clinician and patient-reported) to collect.

Responses for each motor function listed:

- Never able
- Gained (and record age gained using format YY-MM)
- Gained and lost (and record both age gained and age lost using format YY-MM)

Clinician-reported registries should also record whether each motor function was:

- Observed in clinic
- Reported in clinic by patient/caregiver

7.00 Holding head up without support

Able to support weight of own head without assistance or resting head against an object.

7.01 Rolling onto side

From a supine position, able to roll onto (either left or right) side without assistance.

7.02 Sitting without support [WHO[3]]

Sits up straight with the head erect for at least 10 seconds. Does not use arms or hands to balance body or support position.

7.03 Crawling on hands and knees [WHO[3]]

Alternately moves forward or backward on hands and knees. The stomach does not touch the supporting surface. There are continuous and consecutive movements, at least three in a row.

7.04 Standing with assistance [WHO[3]]

Stands in upright position on both feet, holding onto a stable object (e.g. furniture) with both hands without leaning on it. The body does not touch the stable object, and the legs support most of the body weight. Thus stands with assistance for at least 10 seconds.

7.05 Standing alone (without assistance) WHO[3]

Stands in upright position on both feet (not on the toes) with the back straight. The legs support 100% of the body weight. There is no contact with a person or object. Stands alone for at least 10 seconds.

7.06 Walking with assistance WHO[3]

Upright position with the back straight. Makes sideways or forward steps by holding onto a stable object (e.g. furniture) with one or both hands. One leg moves forward while the other supports part of the body weight. Takes at least 5 steps in this manner.

7.07 Walking alone (without assistance) WHO[3]

Takes at least 5 steps independently in upright position with the back straight. One leg moves forward while the other supports most of the body weight. There is no contact with a person or object.

7.08 Able to walk 10 meters unaided

See 7.07 but walks in this manner for at least 10 meters.

7.09 Climbing stairs

Climbs at least 4 stairs independently. Contact with a railing is permitted but there is no additional help from a person or other object.

7.10 Useful function of hands RULM[4]

Can use hands to hold pencil or pick up a token or drive a powered chair, use phone key pad

7.11 Reaching overhead in a sitting position RULM

Can raise both arms simultaneously above head whilst in a sitting position

7.12 Raising hands to mouth in a sitting position RULM

Can raise one or two hands to mouth whilst in a sitting position

Section 8: WHEELCHAIR USE

8.00 Does the patient use a wheelchair? (For patients ≥ 2 years old)

Mandatory. If the patient is less than 2 years old this item is not applicable

Responses: No (able to walk independently); Part-time (age began YY-MM); Full-time (age began YY-MM)

Part-time: able to spend short periods of time getting around without a wheelchair

Full-time: unable to get around at all without a wheelchair

Section 9: NUTRITION

9.00 Has the patient ever used a gastric or nasal feeding tube?

Mandatory. A Gastric tube or G tube or Gastrostomy is a surgical opening into the stomach, in this case to insert a flexible feeding tube through the abdominal wall and into the stomach to allow direct delivery of adequate nutrition. Sometimes referred to as a PEG (Percutaneuos endoscopic gastrostomy).[1]

Responses: Never; Previously exclusively fed by tube (start and end date MM-YYYY); Previously supplementary e.g. for fluids (start and end date MM-YYYY); Currently exclusively fed by tube (start date MM-YYYY); Currently supplementary e.g. for fluids (start date MM-YYYY); Unknown

Section 10: PULMONARY FUNCTION

10.00 Has the patient ever used invasive ventilation?

Mandatory. Invasive ventilation (IV) is surgery that creates an opening in the windpipe that allows breathing through a tracheostomy tube rather than through the nose and mouth.

Responses: Never; Previously (start and end date MM-YYYY); Currently (start date MM-YYYY); Unknown

10.01 If 'Yes' to 10.00: Frequency of invasive ventilation

Mandatory. How often the patient uses invasive ventilation

Responses: Full-time; part-time; unknown

Full-time: needs ventilation for all (or almost all) of the time (can sometimes go without for +/- 1 hour, e.g. for showering)

Part-time: needs ventilation for several hours a day and/or at night

10.02 If 'Yes' to 10.00: Invasive ventilation start date (month and year)

Mandatory. Record the month and year that the patient started using invasive ventilation, using format MM-YYYY.

10.03 Has the patient ever used non-invasive ventilation?

Mandatory. Non-Invasive Ventilation (NIV) uses airway support that is administered through a nose or face mask.[1]

Responses: Never; Previously (start and end date MM-YYYY); Currently (start date MM-YYYY); Unknown

10.04 If 'Yes' to 10.03: Frequency of non-invasive ventilation

Mandatory. How often the patient uses non-invasive ventilation.

Responses: Full-time; part-time; unknown

Full-time: needs ventilation for all (or almost all) of the time (can sometimes go without for +/- 1 hour, e.g. for showering)

Part-time: needs ventilation for several hours a day and/or at night

10.05 If 'Yes' to 10.03: Non-invasive ventilation start date (month and year)

Mandatory. Record the month and year that the patient started using non-invasive ventilation, using format MM-YYYY.

10.06 Does the patient need assistance in airway clearance and/or secretion mobilisation?

Highly encouraged. Does the patient use any of the chronic respiratory management techniques included in the list in 10.07-10.11?

Responses: Yes; No.

If 'Yes' to 10.06; Type of assistance (select all that apply)

All items highly encouraged.

Responses for each type of assistance used (more than one may be applicable):

- Daily
- Weekly

- Occasionally (less frequently than weekly)

10.07 Suction

10.08 Chest percussion

10.09 Cough Assist device

10.10 IPPV (Intermittent positive-pressure ventilation)

10.11 Other (please specify)

10.12 Has the patient had a Forced Vital Capacity (FVC) Test?

Mandatory. Forced vital capacity (FVC) is the total amount of air exhaled during the FEV (Forced Expiratory Volume) test. Forced expiratory volume and forced vital capacity are lung function tests that are measured during spirometry.[5]

Responses: Yes; No; Unknown

10.13 If 'Yes' to 10.11: Date of most recent FVC test, if known

Mandatory. Record date of most recent FVC test if known, using format DD-MM-YYYY.

10.14 If 'Yes' to 10.11: FVC litre (clinician-reported only)

Mandatory. As reported on FVC test results, unit is litres.

10.15 If 'Yes' to 10.11: FVC predicted %

Mandatory. As calculated in your local laboratory and/or reported on FVC test results. Range 0-150%

Section 11: THERAPIES AND MEDICATIONS

11.00 Has the patient ever received a disease-modifying therapy for SMA? (Clinician-reported only)

Mandatory. Disease modification can be defined as treatments or interventions that affect the underlying pathophysiology of the disease and have a beneficial outcome on its course[6]. Response options will be modified in future if additional therapies receive marketing authorisation.

Responses: Currently; Previously; Never; Don't know

11.01 Are you receiving Spinraza? (Patient-reported only)

Mandatory. The wording of this question will be modified in future if additional therapies receive marketing authorisation.

Responses: Currently; Previously; Never

All items 11.02-11.10 (inclusive) are applicable only to clinician-reported registries (CR)

11.02 If 'Currently' or 'Previously' to 11.00: Name of drug(s) CR

Mandatory. Report name of disease-modifying therapy that is/was taken by patient. Should be able to report multiple.

Responses: Spinraza; Other (specify, free text) (Can add multiple)

11.03 For each drug named in 11.02: Start date CR

Mandatory. For each drug named in 11.02; Report the date the first dosage was administered/taken using format DD-MM-YYYY.

11.04 For each drug named in 11.02: Stop date if not ongoing [CR]

Mandatory. For each drug named in 11.02; If the patient is still receiving the drug, leave this field blank. If the treatment is no longer ongoing, report stop date using format DD-MM-YYYY.

11.05 If stop date given in 11.04: Reason for stopping [CR]

Mandatory. For each drug named in 11.02; if a stop date has been given in 11.04 (i.e. treatment is no longer ongoing), report reason for stopping.

Responses: Insurance coverage/funding; Side effects from the procedure; Side effects from the drug; Lack of apparent benefit; Elective choice of other treatment

11.06 For each drug named in 11.02: Dosage given [CR]

Mandatory. For each drug named in 11.02; report current dosage levels and specify units

11.07 For each drug named in 11.02: Frequency of dosage [CR]

Mandatory. For each drug named in 11.02; report how often the dose is taken, by specifying numerical value followed by either day(s), week(s), or year(s).

11.08 For each drug named in 11.02: Route of administration [CR]

Mandatory. For each drug named in 11.02; report the means by which the drug enters the body. Response options will be modified in future if additional therapies receive marketing authorisation.

Responses: Intrathecal injection; Other (specify, free text)

11.09 For each drug named in 11.02: Is the patient following the current recommended dosing schedule? [CR]

Mandatory. For each drug named in 11.02; report whether the treatment schedule recommended in the prescribing information is being followed.

Responses: Yes; No; Don't know; Not applicable

11.10 If 'No' to 11.09': Reason for not following dosing schedule [CR]

Mandatory. Give reason for recommended dosing schedule not being followed.

Responses: Illness; Access problem; Scoliosis surgery; Other (specify, free text)

11.11 Has the patient taken any prescribed allopathic drugs in the last 12 months (baseline) / since the last registry update (follow-up)?

Mandatory. For the purposes of this dataset, 'allopathic' is defined a drug intended to treat or manage the symptoms of the disease.

Responses: Yes; No; Don't know

11.12 If 'Yes' to 11.10: Name of drug

Mandatory. Select each type of allopathic drug / supplement taken, from the responses provided. Please note; the inclusion of a supplement in this list does not indicate TREAT-NMD endorsement.

Responses: Vitamin D; Calcium; Biphosphonate; Drugs for gastroesophageal reflux; Drugs for constipation; Antibiotics; Anticholinergic drugs; Annual influenza immunizations; Annual pneumococcal immunizations; Creatine; Acetyl-L-carnitine; Phenylbutyrate; Gabapentin; Thyrotropin-releasing hormone; Hydroxyurea; Valproate; Albuterol; Other (specify, free text) (Can add multiple)

11.13 For each drug named in 11.11: Start date (month & year)

Highly encouraged. For each drug named in 11.11; Report the month and year that the drug was first taken, using format MM-YYYY.

11.14 For each drug named in 11.11: Stop date (month & year) if not ongoing

Highly encouraged. For each drug named in 11.11; If the patient is still taking the drug, leave this field blank. If the patient is no longer taking the drug, report the month and year that the drug was stopped, using format MM-YYYY.

11.20 Which of the following therapeutic interventions has this patient received in the last 12 months (baseline) / since the last registry update (follow-up)?

Mandatory. For the purposes of this dataset, 'therapeutic interventions' refers to the management of the patient's condition and quality of life through therapies from allied health professionals such as physiotherapists and speech therapists. Selecting all that apply from the responses provided.

Responses: Physiotherapy sessions (e.g. stretches); Respiratory physiotherapy sessions; Massage; Home programme (e.g. stretches/exercises); Hydrotherapy/water-based activity; Management of contractures using orthotics (e.g. ankle foot orthoses); Brace; Occupational therapy sessions /input for home or equipment; Speech and language therapy sessions; Other (specify, free text)

Section 12: HOSPITALISATIONS AND COMORBIDITIES

12.00 Has the patient been hospitalised in the last 12 months (baseline) / since the last registry update (follow-up)?

Mandatory. If patient has been admitted to hospital for any reason (irrespective of circumstances or connection to their SMA), select 'Yes'.

Responses: Yes; No; Don't know

12.01 If 'Yes' to 12.00: Type of initial hospitalisation

Mandatory. Record type of hospitalisation for each hospitalisation which occurred during the time period specified in 12.00. More than one may be recorded.

Responses: Planned; Acute

Planned: admission was scheduled in advance, e.g. planned surgery / scan / administration of treatment.

Acute: admission was in response to a "sudden, often unexpected, urgent or emergent episode of injury and illness that can lead to death or disability without rapid intervention. The term acute care encompasses a range of clinical health-care functions, including emergency medicine, trauma care, pre-hospital emergency care, acute care surgery, critical care, urgent care and short-term inpatient stabilization."[7]

12.02 For each hospitalisation in 12.01: Admission date (month & year)

Mandatory. For each planned or acute hospitalisation defined in 12.01; Report the month and year of the hospital admission, using format MM-YYYY.

12.03 For each hospitalisation in 12.01: Number of days in hospital

Mandatory. For each planned or acute hospitalisation defined in 12.01; Report the number of days spent in hospital, rounded up to the nearest whole number.

12.04 For each acute hospitalisation: Reason for hospitalisation (clinician-reported only)

Mandatory. For each acute hospitalisation reported in 12.01, the reason for the hospitalisation should be reported using the appropriate MedDRA code.

12.05 For each planned hospitalisation: Reason for hospitalisation (clinician-reported only)

Mandatory. For each planned hospitalisation reported in 12.01, the reason for the hospitalisation should be reported.

Responses: Placement of g-tube; Sleep study; Scoliosis fusion; Hip surgery; Other orthopaedic surgery (specify, free text); Administration of Spinraza; Administration of other disease-modifying treatment for SMA (specify, free text); Other reason (specify, free text)

12.06 For each acute hospitalisation: was this also reported as an SAE? (Clinician-reported only)

Mandatory. PLEASE NOTE: completing this data item does not replace the need to report SAEs immediately via your local reporting mechanisms.

Responses: Yes; No

SAE = Serious Adverse Event. Any untoward medical occurrence that at any dose:[8]

- results in death,
- is life-threatening (NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
- requires inpatient hospitalisation or prolongation of existing hospitalisation,
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly/birth defect.

12.07 If 'Yes' to 12.06: in relation to which medication? (Clinician-reported only)

Mandatory. For each hospitalisation that was also reported as an SAE, which medication was the SAE related to?

Responses: Spinraza; Other (specify, free text)

12.10 In addition to the hospitalisations already reported, has the patient been diagnosed with any other co-morbidities in the last 12 months (*baseline*) / since the last registry update (*follow-up*)?

Mandatory. Co-morbidities are defined as any additional illness or disease occurring alongside the SMA.

Responses: Yes; No; Don't know

12.11 If 'Yes' to 12.10: Co-morbidity details

Mandatory. Record the diagnosis for each co-morbidity, using the appropriate ICD-10 Classification if possible (or selecting from the responses provided if not).

Alternative responses if full ICD-10 classification not possible: Certain infectious and parasitic diseases; Neoplasms; Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; Endocrine, nutritional and metabolic diseases; Mental, Behavioural and Neurodevelopmental disorders; Diseases of the nervous system; Diseases of the eye and adnexa; Diseases of the ear and mastoid process; Diseases of the circulatory system; Diseases of the respiratory system; Diseases of the digestive system; Diseases of the skin and subcutaneous tissue; Diseases of the musculoskeletal system and connective tissue; Diseases of the genitourinary system; Pregnancy, childbirth and the puerperium; Certain conditions originating in the perinatal period; Congenital

malformations, deformations and chromosomal abnormalities; Other - Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (specify, free text) (Can add multiple)

12.12 For each Co-morbidity: Co-morbidity start date (month & year)

Mandatory. For each co-morbidity diagnosis reported in 12.11; Report the month and year of the diagnosis using format MM-YYYY.

12.13 For each Co-morbidity: Co-morbidity end date if not ongoing

Mandatory. For each co-morbidity diagnosis reported in 12.11; Report the month and year of the end of the co-morbidity using format MM-YYYY. If the co-morbidity is ongoing, leave this field blank.

12.14 For each Co-morbidity: Co-morbidity also reported as an SAE? (Clinician-reported only)

Mandatory. PLEASE NOTE: completing this data item does not replace the need to report SAEs immediately via your local reporting mechanisms.

See 12.06 for definition of SAE.

Responses: Yes; No

12.15 If 'Yes' to 12.14: in relation to which medication? (Clinician-reported only)

Mandatory. For each co-morbidity that was also reported as an SAE, which medication was the SAE related to?

Responses: Spinraza; Other (specify, free text)

12.20 In addition to the hospitalisations, co-morbidities or death already recorded: any other SAEs reported? (Clinician-reported only)

Mandatory. PLEASE NOTE: completing this data item does not replace the need to report SAEs immediately via your local reporting mechanisms.

See 12.06 for definition of SAE

Responses: Yes; No

12.21 If 'Yes' to 12.20: in relation to which medication? (Clinician-reported only)

Mandatory. For each additional SAE reported in 12.20, which medication was each SAE related to?

Responses: Spinraza; Other (specify, free text)

Section 13: CLINICAL RESEARCH

13.00 Has the patient ever participated in a clinical trial?

Mandatory. In this context, 'participated' means the patient has passed the screening period and has been either randomized (in randomised trial) or dosed (in non-randomized trial). If a patient fails the screening period, or is not randomised/dosed for some other reason (for example consent withdrawal, family relocation), this is not counted as participation.

Responses: Currently; Previously; Never; Don't know

13.01 If 'Currently' or 'Previously' to 13.00: Name of trial(s)

Mandatory. Report the full name(s) of all clinical trials that the patient has participated in (according to the definition given in 13.00) using a free text field.

13.02 For each trial named in 13.01: Name of drug

Mandatory. For each clinical trial named in 13.01, report the full name(s) of the drug that the clinical trial was evaluating using a free text field.

13.10 Is the patient currently part of another registry and/or natural history study?

Highly encouraged. A patient registry can be defined as "an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes."[9]

A natural history study can be defined as "epidemiological studies that focus on describing the frequency, features, and evolution of a disease by collecting real-world data from groups of patients suffering from this disease."[10]

Responses: Yes; No; Don't know

13.11 If 'Yes' to 13.10: Name of registry or natural history study

Highly encouraged. For each other registry or natural history study that the patient is part of, report the full name(s) of the registry or natural history study using a free text field.

Section 14: MOTOR MEASURES (ALL CLINICIAN-REPORTED ONLY)

Mandatory minimum of 1 motor measure. Clinician-reported registries are required to collect a minimum of **1 validated motor measure**, in addition to the mandatory motor function question in Section 7.

Selection of appropriate motor measure(s) is at the discretion of the clinician and/or preference of the patient. Where there is no pre-existing preference, the measures marked with * are suggested by TREAT-NMD, based on current Standards of Care and prior use in Clinical Trials.

An outcome measure toolkit is in development to provide registries with guidance if needed on the selection and collection of appropriate outcome measures for each patient/clinic, and is due for completion by May 2020.

14.00 Was a validated motor measure taken for this patient at this visit?

Mandatory. Report whether a validated motor measure was taken in clinic for this patient, during the visit on which the registry update is based.

Responses: Yes; No

14.01 If 'No' to 14.00: give reason

Mandatory. If no validated motor measure was taken, give reason.

Responses: Unable to attain start position/disease progression; Injury/acute injury/illness (specify, free text); Inability to follow or understand directions; Refusal/attention/behaviour issue; Fatigue; Pain/Muscle cramp; Equipment/software issue; Other (specify, free text)

14.10-14.54 Motor Measure scores and dates

If the answer to 14.00 is 'Yes', use items 14.10-14.54 to report the score and date of any validated motor measure(s) taken.

Outcome measures for infantile onset SMA:

14.10 CHOP-INTEND* score (Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders)
14.11 CHOP-INTEND date (DD-MM-YYYY)

14.12 HFMS* score (Hammersmith Functional Motor Scale)
14.13 HFMS date (DD-MM-YYYY)

14.14 HFMS-E* score (Hammersmith Functional Motor Scale - Expanded)
14.14 HFMS-E date (DD-MM-YYYY)

14.16 HINE Section 2 score (Hammersmith Infant Neurological Exam. Section 2 = motor milestones)
14.17 HINE Section 2 date (DD-MM-YYYY)

14.18 Observed (in clinic) WHO score ((World Health Organisation motor development milestones)
14.19 Observed (in clinic) WHO date (DD-MM-YYYY)

14.20 Other validated motor measure for infantile onset SMA (specify)
14.21 For each measure named in 14.20: score
14.22 For each measure named in 14.20: date (DD-MM-YYYY)

Motor measures for later-onset SMA:

14.30 HFMS-E* score (Hammersmith Functional Motor Scale - Expanded)
14.31 HFMS-E date (DD-MM-YYYY)

14.32 RULM* score (Revised Upper Limb Module)
14.33 RULM date (DD-MM-YYYY)

14.34 Brooke score (Brooke Scale of upper extremity function)
14.35 Brooke date (DD-MM-YYYY)

14.36 Revised Brooke score (Brooke Scale of upper extremity function)
14.37 Revised Brooke date (DD-MM-YYYY)

14.38 MFM score (Motor Function Measure)
14.39 MFM date (DD-MM-YYYY)

14.40 6MWT score (Six-Minute Walk Test)
14.41 6MWT date (DD-MM-YYYY)

14.42 10MWT score (Ten-Metre Walk Test)
14.43 10MWT date (DD-MM-YYYY)

14.44 TUG score (Timed Up and Go Test)
14.45 TUG date (DD-MM-YYYY)

14.46 EK2 score (Egen Klassification)
14.47 EK2 date (DD-MM-YYYY)

14.48 Observed (in clinic) WHO score ((World Health Organisation motor development milestones)
14.49 Observed (in clinic) WHO date (DD-MM-YYYY)

14.50 CHOP-ATEND score (Children's Hospital of Philadelphia Adult Test of Neuromuscular Disorders)
14.51 CHOP-ATEND date (DD-MM-YYYY)

14.52 Other validated motor measure for adult-onset SMA (specify)
14.53 For each measure named in 14.20: score
14.54 For each measure named in 14.20: date (DD-MM-YYYY)

Section 15: PATIENT-REPORTED OUTCOMES (PRO)

15.00 CGI-S (Clinical Global Impression of Severity) (Clinician-reported only)

Mandatory, baseline only. This item should only be captured at baseline and asks the clinician to rate their impression of the current severity of the patient's illness, based on their experience with the relevant patient population.

Responses: 1=Normal, not at all ill; 2=Borderline ill; 3=Mildly ill; 4=Moderately ill; 5=Markedly ill; 6=Severely ill; 7=Among the most extremely ill patients.

15.01 Date of Clinician CGI-S score given in 15.00

Mandatory. Using format DD-MM-YYYY

15.02 Total Global Impression (TGI) according to patient or parent

Mandatory. How does the patient/parent feel that the patient's condition has changed in the last 6 months? This can be asked in clinic for clinician-reported registries, or reported directly in patient-reported registries.

Responses: 1=Very much improved; 2=Much improved; 3=Minimally improved; 4=No change; 5=Minimally worse; 6=Much worse; 7=Very much worse

15.03 Date of Patient TGI score given in 15.02

Mandatory. Using format DD-MM-YYYY

15.04 Total Global Impression (TGI) according to clinician

Highly encouraged. How does the clinician feel that the patient's condition has changed in the last 6 months? This item would only be captured from clinicians at follow-up (15.00 is used at baseline) and would enable comparison between the patient's impression of their disease progression (15.02) and the impression of their clinician.

Responses: 1=Very much improved; 2=Much improved; 3=Minimally improved; 4=No change; 5=Minimally worse; 6=Much worse; 7=Very much worse

15.10 Was any other validated PRO taken for this patient at this visit? (Clinician-reported only)

Mandatory. Report whether a validated patient-reported outcome was taken in clinic for this patient, during the visit on which the registry update is based.

Responses: Yes; No

An outcome measure toolkit is in development to provide registries with guidance if needed on the selection and collection of appropriate outcome measures for each patient/clinic, and is due to be completed by May 2020.

15.11-15.25 PRO scores and dates (Clinician-reported only)

If the answer to 15.10 is 'Yes', use items 15.11-15.25 to report the score and date of any validated patient-reported outcome(s) taken.

15.11 PedsQL NM & Fatigue scales score (Paediatric Quality of Life Inventory)
15.12 PedsQL NM & Fatigue scales date (DD-MM-YYYY)

15.13 PEDICAT score (Pediatric Evaluation of Disability Inventory - Computer Adaptive Test)
15.14 PEDICAT date (DD-MM-YYYY)

15.15 SMA FRS score (Spinal Muscular Atrophy Functional Rating Scale)
15.16 SMA FRS date (DD-MM-YYYY)

15.17 ACEND score (Assessment of Caregiver Experience with Neuromuscular Disease)
15.18 ACEND date (DD-MM-YYYY)

15.19 ACTIVLIM score (ACTIVLIM measure of activity limitations)
15.20 ACTIVLIM date (DD-MM-YYYY)

15.21 DISABKIDS score (DISABKIDS measurement of quality of life and level of distress)
15.22 DISABKIDS date (DD-MM-YYYY)

15.23 Other validated patient-reported outcome (specify)
15.24 For each PRO named in 15.23: score
15.25 For each PRO named in 15.23: date (DD-MM-YYYY)

Section 16: ELECTROPHYSIOLOGY AND BIOMARKERS (CLINICIAN-REPORTED ONLY)

16.00 Has the patient had a CMAP (Compound Muscle Action Potential) scan?

Highly encouraged. The CMAP (Compound Muscle Action Potential) scan is a non-invasive electrodiagnostic tool, which provides a quick and visual assessment of motor unit potentials as electrophysiological components that together constitute the CMAP. The CMAP scan records the electrical activity of the muscle (CMAP) in response to transcutaneous stimulation of the motor nerve with gradual changes in stimulus intensity.[11]

Responses: Yes; No; Don’t know

16.01 Has the patient had a DEXA (Dual Energy X-ray Absorptiometry) scan?

Highly encouraged. Bone densitometry, also called dual-energy x-ray absorptiometry, DEXA or DXA, uses a very small dose of ionizing radiation to produce pictures of the inside of the body (usually the lower (or lumbar) spine and hips) to measure bone loss. It is commonly used to diagnose osteoporosis, to assess an individual's risk for developing osteoporotic fractures.[12]

Responses: Yes; No; Don’t know

16.02 Has the patient had any muscle imaging undertaken?

Highly encouraged. Commonly used skeletal muscle imaging techniques include radiography, ultrasound, computed tomography, and MRI. Newer techniques include T2 mapping, blood oxygenation level dependent imaging, diffusion tensor imaging, and magnetic resonance spectroscopy.[13]

Responses: Yes; No; Don’t know

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References

1. UK, S.M.A., et al., *A Guide to the 2017 International Standards of Care for SMA*. 2017. p. 56.
2. Malli, M.S., et al., *Estimation of height of the person by using arm span and hand length measurements.* Gujarat Medical Journal 2015. **70**(1): p. 3.
3. Wijnhoven, T.M.A., et al., *Assessment of gross motor development in the WHO Multicentre Growth Reference Study.* Food and Nutrition Bulletin, 2004. **25**(1): p. 9.
4. Mazzone, E.S., *Revised Upper Limb Module for SMA (RULM for SMA)*. 2014.
5. Michigan, U.o. *Forced Expiratory Volume and Forced Vital Capacity*. 2018 5th September 2018 [cited 2019; Explination of Forced Expiratroy Volume]. Available from: https://www.uofmhealth.org/health-library/aa73564.
6. Cummings, J.L., *Defining and labeling disease-modifying treatments for Alzheimer's disease.* Alzheimer's & Dementia, 2009. **5**(5): p. 406-418.
7. Hirshon, J.M., et al., *Health systems and services: the role of acute care.* Bulletin of thee World Health Organization, 2013. **91**: p. 386 - 388.
8. Agency, E.M., *ICH Topic E 2 A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting*. 1995.
9. Gliklich RE, D.N., Leavy MB,, *Registries for Evaluating Patient Outcomes, 3rd edition*. 3rd ed. 2014.
10. Bevan, A., et al. *Natural History Studies in Rare Diseases and Genetic Biomarkers* 2019; Available from: https://www.evidera.com/natural-history-studies-in-rare-diseases-and-genetic-biomarkers/.
11. Maathuis, E.M., et al., *Optimal stimulation settings for CMAP scan registrations.* Journal of brachial plexus and peripheral nerve injury, 2012. **7**(1): p. 4-4.
12. *Bone Densitometry (DEXA, DXA)* 2019; Available from: https://www.radiologyinfo.org/en/pdf/dexa.pdf.
13. Kuo, G.P. and J.A. Carrino, *Skeletal muscle imaging and inflammatory myopathies.* Curr Opin Rheumatol, 2007. **19**(6): p. 530-5.
14. *The iSMAC group (International SMA Consortium) generously shared their Preliminary Data Dictionary (April 2018) with TGDOC in order to harmonise data definitions wherever possible.*