TREAT-NMD Neuromuscular Network

SMA Core Dataset Workshop 2020

Agenda:

11:00	**Welcome**	Anna Ambrosini (TGDOC Chair Elect)
11:05	**Introduction**	Jo Bullivant (Project Manager)
11:15	**Work done for this revision**	
11:25	**Patient-focussed work 2021**	
11:30	**V2 Structure: General principles**	Marcel Heidemann (IT/Data Expert)
12:05	**Dataset Appendix**	Joanna Das (Project Coordinator)
12:10	**Questions**	All
12:25	**Comfort break (10 minutes)**	
12:35	**V2 Contents** - **Headline changes** - **Future considerations** - **Research questions**	Miriam Rodrigues and/or Victoria Hodgkinson (TGDOC SMA Subgroup Leads)
12:55	**Discussion groups**	
13:15	**Feedback from groups**	
13:30	**Next steps**	Jo Bullivant (Project Manager)
13:35	**Questions and discussion**	All
13:55	**Close**	Anna Ambrosini (TGDOC Chair Elect)

Welcome

Anna Ambrosini, TGDOC Chair Elect

Introduction

Jo Bullivant (Project Manager)

Joanna Das (Project Coordinator)

Victoria Hodgkinson: TGDOC SMA Subgroup Lead

Dr Hodgkinson is the National Program Manager for the Canadian Neuromuscular Disease Registry, where she oversees the scientific management and coordination of national patient registries in neuromuscular disease. Her work involves management of the registry network, development and review of registry datasets, and research project design and scientific analyses. She is actively engaged in global collaborative projects to share data for common purposes, and improve registry design and utility worldwide.

Miriam Rodrigues: TGDOC SMA Subgroup Lead

Miriam Rodrigues is a genetic counsellor whose dedication to rare neuromuscular disorders began when she was appointed Membership Services Manager at the Muscular Dystrophy Association of New Zealand (MDA NZ) in 2006. She is the Coordinator of the New Zealand Neuromuscular Disease Registry and Neuromuscular Disease Research Associate at Auckland District Health Board.

Marcel Heidemann: IT consultant

Marcel Heidemann is an IT consultant and software developer who has been involved with neuromuscular registries since 2008. He developed the patient registry platform for the LMU Munich hospital which is now used for 12 neuromuscular registries based in Munich and Newcastle. Marcel holds a Master's degree from LMU Munich in philosophy, biology and political science.

Introduction

Context

- Expanded core dataset released in Sept 2018, following extensive pilot study.
- Currently in year 2 of a 3-year implementation plan (June 2019 to May 2022) to support the phased adoption of the expanded dataset across the TGDOC registry network. Year 1 Report is available on project web page.
- Implementation plan includes a Formal Revision Process to reflect our commitment to continuous improvement, harmonisation with other initiatives, and responsiveness to the needs of the SMA community.
- First revision: consultation launched in March, draft v2 circulated for review start of September, and v2 released 2 weeks ago.
- The content of the dataset (what data we are asking you to collect) has not drastically changed
- V2 is structured, presented and described in a very different way than v1, so this year's workshop is focussed on providing an overview of these key changes, and guidance on how to interpret/adopt them in your registry.
- Please save questions for the dedicated sessions, or type them into the chat.

Introduction

v2 Data item count

	v1	v2
Mandatory CR	113	117
Mandatory PR	92	91
Not mandatory	50	37
TOTAL	**167**	**154**

v1	v2
7.00 Holding head up without support. Specify: Never able; Gained (age YY-MM); Gained & lost (age gained YY-MM & age lost YY-MM) *And:* Observed in clinic; Reported by Patient/Caregiver	**Motor ability:** Holding head up without support **Motor ability status:** Currently, Previously, Never **Motor ability observed in clinic:** Yes/No **Motor ability episode:** Start/stop/ongoing dates

The v1 to v2 revision

"The purpose of expanding the core dataset of the TREAT-NMD SMA registries should be to collect robust longitudinal data that (a) captures natural history, (b) measures the effectiveness of interventions and (c) informs standards of care for patients"

v1 areas for improvement

- ✗ Worded and structured like a data collection form – items were represented by questions (too specific).
- ✗ Focussed only on what to collect – not how to collect it (not specific enough).
- ✗ Mixed data types (not specific enough and not FAIR)
- ✗ Items were numbered – neither stable nor unique (not FAIR)
- ✗ Free text – useless for central analysis (not specific enough)
- ✗ Strayed into areas that are not within TREAT-NMD remit, e.g. which contact details to collect for your patients, name of main healthcare centre, upload of genetic report etc. Can be part of guidance provided, but should not be part of the core dataset (too specific)

The v1 to v2 revision

V2 improvements

- ✓ Presented as a technical dataset specification – not a data collection form
- ✓ Provided *example* questions for data collection forms for complex areas, to demonstrate best practice.
- ✓ Defined the data model and different data types
- ✓ Stable and unique identifier for each data item
- ✓ Standardised and defined values (response options) and removed free text fields wherever possible

Resulting in

- ≈ Clearly defined and structured dataset to support (a) accurate and standardised data collection locally and (b) efficient central data aggregation and analysis
- ≈ Clearer guidance on *how* to collect the required data (not just which data to collect)
- ≈ FAIRification of data within our registries
- ≈ Single machine-readable source file, viewable online or as Excel/PDF - instead of multiple text documents
- ≈ Repository of high quality well described data items which can be re-used across other TREAT-NMD dataset projects
- ≈ Online portal for stakeholders to submit feedback and suggestions for future revisions.

Patient-focussed plans

Priority work for 2021

Patient-reported data AND patient-centricity of clinician-reported data in the TREAT-NMD SMA Core Dataset:

- Are we asking the right questions in the right way?
- Is it meaningful for patients and fit for purpose?
- No! Real question = what do we do to improve?

PROMS

- Which, if any, existing PROMs for SMA (or beyond) feel most relevant to patient community?
- Can we help to establish or encourage their use?
- If none, could we partner to develop a patient-driven and patient-centric scale, validated through joint networks?

Uniting pharma efforts with powerful combined voice (using registries for PMS, involving patients, selecting PROMS in clinical trial design)

Training

- How to embed patient involvement more solidly in our work? Practically it is often unclear to all stakeholders (especially patients) how this can and should happen.
- Joint workshop on the role of patients in registries and PROMs development. Main target audience patients but could be helpful for many stakeholders; in SMA and other disease areas.

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V2 Structure: General Principles

Marcel Heidemann

V2 Dataset Appendix

Joanna Das

Dataset Manual in v2.

Any information connected to defining/describing the dataset → Embedded into v2 Dataset

Any supplementary information → SMA Dataset v2 Appendix

Dataset v1 Manual

- 30+ pages
- Background and context information
- Data Dictionary
- Consent and Ethics suggested standard/templates

SMA Dataset v2 Appendix

Any important information not contained within v2 specification

- Background and context information
- Feedback, Harmonisation and Revisions
- Data sharing and Publications
- Consent and Ethics suggestions
- Patient enrolment and demographics

Data that should still be collected locally

Enrolment

Important for registries/curators to know:

- Date of enrolment
- Date of consent
- Date of any re-consents
- Consented to TREAT-NMD Global Registry
- Know the Local registry ID

Demographics

Registries should collect:

- First Name
- Surname
- Address
- Email Address
- Telephone number

PPRL items now mandatory

- PPRL = a way of identifying / linking probable duplicate patient records in different data repositories (registries, studies, databases etc.) without exposing identifiable personal data.
- Relevant for TREAT-NMD on different levels: within URP only, across all TGDOC registries, or externally with other groups or registries such as iSMAC, RESTORE, MDA etc.)
- Each data repository collects a standardised set of demographic data which is **stable** (will not change throughout the person's life), e.g. date of birth, given name at birth, country of birth, gender assigned at birth. **This data always remains within the local registry.**
- Each data repository uses a common PPRL tool to generate a PPRL key for each of their patients, using the standardised data collected. The keys can be shared with other data providers/hubs without exposing any personal data.
- If the same data are collected and the same tool is used, the same patient should always generate the same key, regardless of which repository they are in. So records pertaining to the same individual can be identified and linked safely. Already used successfully in some networks (e.g. cancer).

Patient A ☹	**Patient B** ☺
• Had a muscle biopsy for diagnosis, consented for tissue to be stored in the Newcastle biobank • Took part in a clinical trial in Manchester for 6 months • Attends GOSH for routine care so is part of their clinical database • Joined the UK SMA patient registry	• Born in Ukraine and registered in the PR registry there • Moved to Germany 6 months later to be seen/treated so is in a clinical registry at treatment centre. • Joined the German PR registry coordinated at Munich • All of these registries contribute data to the CDW
Powerful combined data but no way of linking without the data providers sharing personal data with each other. Moreover, anyone interrogating the different data sources would have no way of knowing that these 5 records represent only 1 person.	If registries are all affiliated to TNMD, they collect a standardised set of demographic data items. TNMD selects/provides the appropriate tool for registries to use locally to generate a PPRL key for each patient. Registries include the PPRL key for each **de-identified** patient record when submitting data to us and we can identify or link duplicate patient records.

Questions so far?

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Comfort break

SMA Core Dataset V2 Content
What's changed?

Miriam Rodrigues & Victoria Hodgkinson

Genetic Diagnosis & SMA type

Genetic Diagnosis

Have added:

Genetic modifier 859G>C (yes/no/unknown) – not mandatory

- Type 0
- Type 1*
- Type 2*
- Type 3a*
- Type 3b*
- Type 4*
- Undetermined type of 5q SMA

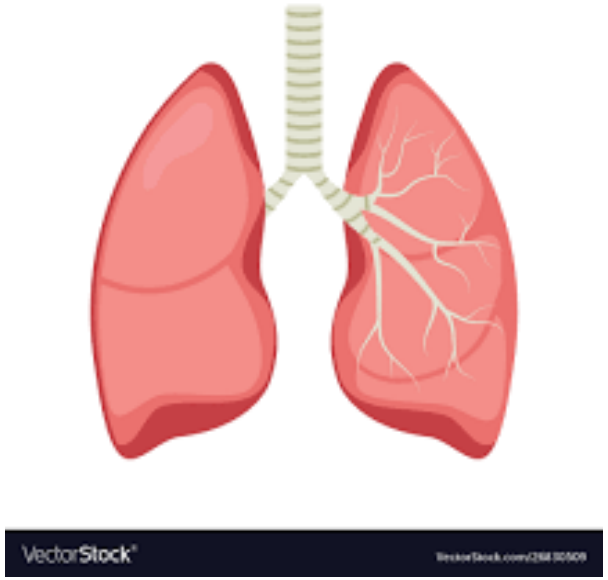
* SMA Standard of Care

Ambulatory status

- 'wheelchair use’

- refers to manual or powered wheelchairs or similar assisted mobility devices, includes devices such as a mobility scooter or a stroller, but exclude devices that assist the user in walking (e.g. a walker or cane) or do not support mobility (e.g. a static standing frame)

Spirometry



- Added Peak Cough Flow (PCF)
- Removed “type of airway clearance”

Disease Modifying Therapies (DMTs)

- Section relabeled

Formerly: Therapies & Medications

Now: SMA Disease Modifying Therapies

- Section restructured for new therapies and mode of delivery
- Allopathic drugs & Therapy Interventions are still included and have moved into the Co-Morbidities Section
- Allopathic drug further defined as managing symptoms rather than disease modifying

Disease Modifying Therapies (DMTs)

- Zolgensma:
- AAV antibody titre incl. date of test & result
- Corticosteroid use & dose
- Weight (kg) at therapy initiation
- Reason for stopping [DMT] also covers reason for switching DMT

SAEs

- Reworded "was this also reported as an SAE?” to “was this also classed as an SAE?”
- Removed "In addition to the hospitalisations, co-morbidities or death already recorded: any other SAEs reported?"

Comorbidities

- Defined start date = date of diagnosis [of co-morbidity]
- Defined end date = last date of symptoms

Outcome Measures Library

- **Motor Outcome Measures can be selected from OM Library**
- **Validated PROMs can be selected from OM Library**

Patient Reported Outcome Measures

- Patient Global Impression of Severity PGI-S (baseline) and Patient Global Impression of Improvement PGI-I (followup) is mandatory
- CGI –S and CGI-I has moved to Clinical Outcomes Section

Future considerations and Research questions

Over 700 suggestions received during v1 and v2_draft consultations

This engagement and input is incredibly valuable but we can't implement every suggestion.

Each one was carefully considered and discussed, results can be separated into broad categories:

1. Applied
2. Applied with modifications
3. Not applied (e.g. judged not in scope or not in line with core dataset objectives)
4. N/A (e.g. item was already changed/removed)

5. **Possibly in scope for future versions, but not v2**

6. **Not in scope for core dataset but could be an interesting research question**

Identify priorities from suggestions in (5) and (6) – work in groups (15 minutes) then feedback to the workshop.

Could lay foundations for further discussions and planning activities at the 2020 TGDOC Curators Meeting (1 & 2 December), and/or the SMA subgroup break-out session (30 November).

For discussion

Future versions of core dataset?

- **Reason for not choosing a therapy** to begin with, e.g. scoliosis, AAV9 antibodies, funding
- One standardised **PROM**?
- More directive on **motor outcome measures**? E.g. smaller group that registries should select from?
- **Sleep study** / overnight capnography / CO2 measure / pO2 / Apnea Hypopnea Index
- **Bulbar function** / swallowing / speech
- **Heart function** - ECG and ultrasound
- **Independence** scale missing - ability to use spoon, knife, to brush teeth, toilet/self-hygiene independence etc.
- **Biomarker** values (before therapy and on follow up) such as NFL, NSE, Tau
- Response options for **rehabilitative interventions**. Have we got the list right? Are we introducing bias by providing it? Or prompting patients to ask “why aren’t I having all of these?” Is there anything important missing? Where do we draw the line? Do we need to do it a different way?
- Are there other items that this applies to?

For discussion

Potential research questions (1 of 2)

- **Psychosocial** data - for families as well as patients and at different trigger points - diagnosis, loss of function, trail enrolment, trial failure/cessation.
- Extent and impact of **contractures**
- **Scoliosis**: Cobb angle measurement technique/date. Surgery techniques. Impact of scoliosis and impact of scoliosis surgery on QoL and functionality.
- **Motor function transitions** and in-between situations not captured in core dataset which have significant impact on patients. E.g. difference between being able sit without assistance, or being able to move from lying to sitting (or sitting to standing) is very significant.
- Endurance, **fatigue** and fatigability.
- **Bulbar function** / swallowing and speech
- Types of **wheelchair use** and influencing factors (socio-economic, access to equipment, national SoC, personal preference, lifestyle, house layout, local terrain, accessibility)
- Forced expiratory volume **FEV1**
- **Respiratory assessment** / surveillance: Pulse-oximetry/polysomnography, MIP / MEP, blood drawn for gas exchange
- **Sleep study** data

For discussion

Potential research questions (2 of 2)

- **Respiratory physiotherapy**: manual / insuflation exuflation with ambu balloon / mechanical, glossopharyngeal breathing advised / or practiced
- Different types of **orthoses**, type of use (functional/resting, day/night), start date, frequency
- Reasons for **therapeutic interventions**
- **Outpatient** / ER visits
- **Care** Level
- **Education and work** status

- For each **DMT**: Who has pushed for the treatment / who decided for treatment.
- DMT funding (e.g. public funding, clinical trial, compassionate use, private, other).
- **Heart** ultrasound and measurement of ejection fraction (important for cardiomyopathies)
- **Pulmology**: vaccinations, breathing aid devices (cough assist device, ventilator, aspirator), type of ventilation (volume gated, pressure gated, sip), night poligraphy, full spirometry testing, blood gas analysis, number of ICU admissions.

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Discussion groups

Group 1	Group 2	Group 3	Group 4
Damjan Osredkar	Victoria Hodgkinson	Marcel Heidemann	Lindsay Murphy
Davit Babikyan	Natella Kostandyan	Marjan Cosyns	Lenka Mokrá
Vana Vukic	Nina Barisic	Jana Haberlová	Sahar Hassanein
Rasha El Sherif	Aya Ahmed	Suresh Sankaran	Simone Thiele
Beatrix Pálmafy	V Viswanathan	Dominique Baumann	Teik-Beng Khoo
Lip Yuen Teng	P Anandakrishnan	Maria Grazia Cattinari	Vesna Brankovic
İpek Gürbüz	Vitaliy Matyushenko	Ben Watling	Numan Bulut

Feedback from groups

(3 minutes each)

Next steps

Allocate some time to get to know the new v2, including the very important introduction. Check that you understand all the requirements and how they apply to your registry.

If your registry is already conforming to the Expanded SMA Dataset v1 (2018):

1. **Implement relevant revisions as soon as possible, but within 6 months of the revision date (April 2021).**
2. **Notify the project team (Jo Bullivant or Joanna Das) as soon as the revision has been implemented**

If your registry has not yet implemented v1, please start working towards adopting v2 instead, to your original timelines if possible.

If you have any concerns or questions please get in touch:

joanne.bullivant@newcastle.ac.uk or joanna.das@newcastle.ac.uk

Or call in to one of our monthly drop-in sessions for a chat

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Questions and Discussion

Close

Anna Ambrosini, TGDOC Chair Elect