SMA Expanded Dataset

Annual Report: Year 2

June 2021

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Executive Summary

This report is provided to the project funders (Biogen) to summarise and discuss the progress made during the second year of the TREAT-NMD Expanded SMA Dataset Implementation Project, and to lay out key plans for its final year starting June 2021.

Ten registries were prioritised for support during year 2, and at the end of the reporting period 9 registries had started collecting the expanded dataset for new or follow-up patients. Dataset compliance is at 86% for mandatory items and 80% for non-mandatory items across all registries.

Confirmation of remaining TGDOC registries to take part in year 3 is still underway however some have already started work on implementing the dataset. Year 3 participation was always anticipated to be more challenging, as most registries with sufficient resource and motivation to adopt the dataset will have already engaged in previous years.

1. Introduction

In September 2018, following a pilot study, TREAT-NMD expanded its core SMA dataset for collection by its global network of SMA Registries. The purpose of the expansion was to better inform on the natural history of SMA, provide context to understand the safety and effectiveness of new treatments, and support post marketing surveillance (PMS) for those new treatments.

The results from the pilot study informed the final contents of the dataset as well as a plan for a 3-year phased implementation project. During year 2 (June 2020 – May 2021) we worked with and supported 10 registries in the TREAT-NMD network to adopt the expanded SMA dataset in their data collection activities.

This project report summarises and discusses the progress made in year 2, the status and challenges of the individual registries which have participated since the pilot project, key themes such as therapy availability and outcome measures, and outlines plans for year 3.

2. Deliverables

Table 1: Year 2 deliverables

Deliverable	Due	Completion date
D7: Financial bursaries available for year 2 registries not receiving direct Biogen funding	M13 (June 2020)	30-06-2021
D8: Year 2 workshop for dataset implementation support/harmonisation	M16 (Sept 2020)	27-10-2020
D9: Year 2 Project Report	M24 (May 2021)	02-07-2021 (extension)

D7: Financial Bursaries

SMA registries in the TREAT-NMD network are being asked to significantly increase their data collection activities in order to comply with the expanded SMA Dataset. Work of this nature often has considerable time and/or cost implications. There is therefore a financial bursary available for any registries who are not already receiving direct financial support from Biogen for their data collection activities.

Bursary amount
Up to €8,000 (EURO) per registry is available, in 2 parts (part A and part B) of €4,000 each.
(Both parts may be claimed together if all Part B conditions can already be met.)

Bursary timelines
Part A: 50% (€4,000) is available when the registry starts work on implementing the expanded SMA Dataset (available immediately if work has already begun)

Part B: 50% (€4,000) is available when the registry provides:
1. Evidence that data collection has begun for all relevant mandatory data items (e.g. a copy of the new registry questionnaire or case report form).
2. Feedback (provided in Part B of the Bursary Request Form) on:
    a. Benefits of / issues with the expanded dataset
    b. Suggested improvements for the expanded dataset
    c. The process of implementation and support received.

To date, 23 registries (10 Pilot, 3 year 1 and 10 year 2) have been offered a dataset bursary as part of the pilot and implementation projects. Year 2 registries were invited to apply on 30 June 2020, however changes in the TGDOC membership process delayed some applications until membership renewal was completed. Additionally, one registry from year 1 was provided with an unplanned bursary at the request of Biogen. To date we have received applications from 9 of the 13 eligible year 1 and 2 registries, for at least part A of the bursary.

Of the applications received so far, all have indicated that the true cost of implementation will be greater than €8000. Consistently, registries have reported that a substantial proportion of the bursary will be allocated to staff time for data entry and software development. Many have also indicated that a proportion will be needed for the training of staff, including physiotherapists and clinicians.

Table 2: Planned use of Bursary Funds (€) by implementation project (yr1 & yr2) registries

	Registry 14	Registry 17	Registry 18	Registry 20	Registry 22	Registry 24	Registry 25	Registry 26	Registry 27
Software	1500	2000	8000	3000	3000	7000	3500	100	3000
Staff Time	13000	6000	15300	3000	2000	4000	2000	1000	2000
Training	3000	1000	0	1000	1000	0	1000	1000	1000
PM/Comms	1500	400	4200	3000	1000	3500	500	500	3000
Other	1000	1,000	2000	0	1000	5300	2,000	850000	0
Totals	20000	10400	29500	10000	8000	19800	9000	852600	9000

D8: Year 2 Workshop

The second annual TREAT-NMD SMA Dataset workshop was held on Tuesday 27th October 2020 and repeated on Friday 30th October 2020, virtually due to COVID-19. The main focus of the workshop was to provide a detailed introduction to version 2 of the TREAT-NMD SMA Core Dataset, including new guidelines around data structure, for registry curators participating in the project.

The workshop report provides a summary of the key discussion points, questions raised and any agreed next steps.

D9: Year 2 Report

As defined in the Contract for Research, this report includes, for Year 2 of the Implementation Project:

a. Summary of activities and progress made.
b. Individual reports for each registry targeted or supported:
    i. Dataset implementation status (which data items are now included in the registry CRFs)
    ii. Patient enrolment (number of patients included in registry and % covered by expanded dataset)
    iii. Data completeness (identifying any notable gaps or problems with data collection)
c. "Proof of concept" analyses demonstrating annual progress towards collection of quality data among increasing numbers of SMA patients (with discussion of problematic data items, national considerations)
d. Confirmation of target registries for the coming year.

In preparation for this report, we also consulted Biogen for any particular areas of interest or focus, in addition to those already agreed. They highlighted:

e. A clear picture of completeness and quality of the expanded dataset in the Year 1 registries.
f. Information about which validated motor measures are collected by which registries, or how they are otherwise tracking motor function.
g. Which registries are collecting data on hospitalisations, comorbidities and SAEs.
h. Qualitative information such as reasons behind problematic or missing data items, interpretation of questions etc.

To inform this project report, we conducted individual telephone interviews with each year 2 (n8), year 1 (n8) and pilot year (n10) registry curators, to confirm progress, discuss issues, and collect information on dataset compliance. An online survey (appendix 1) was circulated in advance to collect the underlying information, and the follow-up interviews were used to check assumptions, query gaps or inconsistencies, and discuss context. Information collected through the online survey included patient numbers, expanded dataset coverage, outcome measures and therapy availability. Following each call, we prepared an individual summary document for each registry (appendix 2) which was approved by the Curator before inclusion in this report.

Updates to other Deliverables from Year 1:

D1: Dataset manual

As part of the formal revision and release of version 2 of the core dataset, much of the content of the v1 dataset manual was incorporated into the main core dataset specification. This served to bring all relevant information on the core dataset into a central place and avoid duplication of content across separate documents or locations. The remaining supplementary content was updated and moved into a Dataset Appendix which covers:

- Core dataset context and background information
- Information on feedback, harmonisation, and revisions
- Data sharing and publications information
- Suggested wording for consent and ethics
- Data items not included in v2 but recommended to be collected locally as best practice

D4: Revision Process

To ensure the TREAT-NMD SMA Core Dataset remains appropriate, feasible, collaborative, harmonised with other initiatives, and responsive to the needs of the whole SMA community, a formal Dataset Revision Process (hereafter the Revision Process) was conducted between March 2020 and October 2020. This culminated in the publication of version 2 of the SMA Core Dataset in October 2020.

Delays to the original time line were experienced which were outlined in the Year 1 Annual Report. Improvements included:

- Restructuring into a machine-readable format
- Standardised and clarified response options
- Properly defined data model and data types
- Stable and unique identifier for each data item
- A single source file (JSON) for the dataset containing all relevant information for each data item (descriptions, definitions, response options, applicability, implementation notes, conditional logic, suggested wording for CRFs and example data representations) supported by:
    - A web-based editing tool for the project team to use for future revisions
    - The ability to quickly generate different views of the dataset according to need, for example mandatory items only, patient-reported items only, high level view or full detail, example CRF view and so on.

This work has resulted in:

- A more clearly defined and well-structured version 2 dataset to support accurate and standardised data collection and improve efficiency of future data analysis.
- Example CRF questions for each data item and example data representations to demonstrate best practise.
- A repository of high-quality data items and groups which can be shared or re-used in other areas as needed.
- Links and references to international coding standards where relevant.
- Improved FAIRification of the registries collecting SMA dataset (FAIR = Findable, Accessible, Interoperable, Reusable)
- Reduced duplication and capacity for error due to multiple dataset-related documents
- A usable blueprint for other TREAT-NMD Core dataset projects to follow

Lessons learnt
The existing revision process (appendix 4) will be reviewed for the following reasons:

- The feedback review process was overly labour-intensive and time-consuming due the unexpected amount of feedback received during both consultation rounds.
- Feedback was often provided without sufficient justification or context, nor understanding of the scope of the core dataset. This made review and decision-making difficult.
- Decision-making channels were overly burdensome on a small group of very busy individuals which created bottlenecks.

- Other TREAT-NMD Core Datasets (DMD and LGMD) have been updated or developed and it is essential to agree a standardised revision approach and timeline; not least because many data items appear in all datasets, and many TGDOC registries collect data across all disease areas.

3. Proof of concept

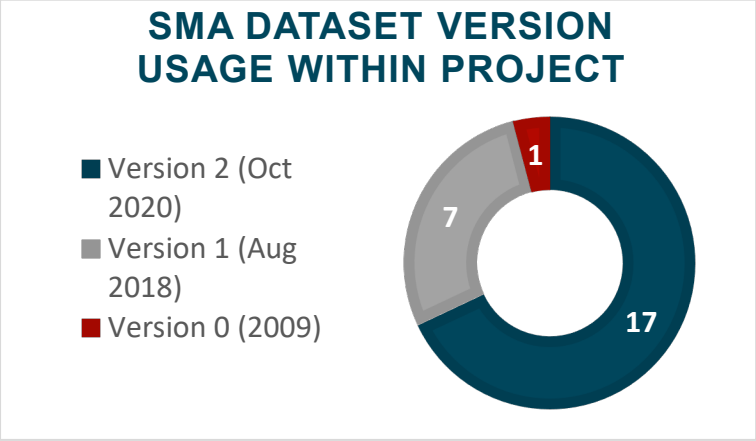
Please note the information in this section was correct on the date of the individual telephone interviews completed as
This information represents 26 registries who responded to our request for an update call (10 from the pilot study, 8 from year 1 and 8 from year 2).

From the 10 registries targeted for support in year 2, one did not respond and one was obliged to withdraw from the project because their capacity to undertake the work was affected by Covid-19. They do however remain committed to implementing the SMA Core Dataset in the future.

Theme 1: General overview of registries

To date 30 registries have formally engaged in the expanded SMA core dataset implementation project (12 in the pilot study, 8 in Year 1 and 10 in year 2). We are currently in active contact with 26 of these. Registry 21 from year 2 was unable to continue their participation, and we have been unable to obtain responses from registries 6 and 7 f (pilot phase) and registry 28 from year 2.

Fig 1: SMA dataset version usage within project



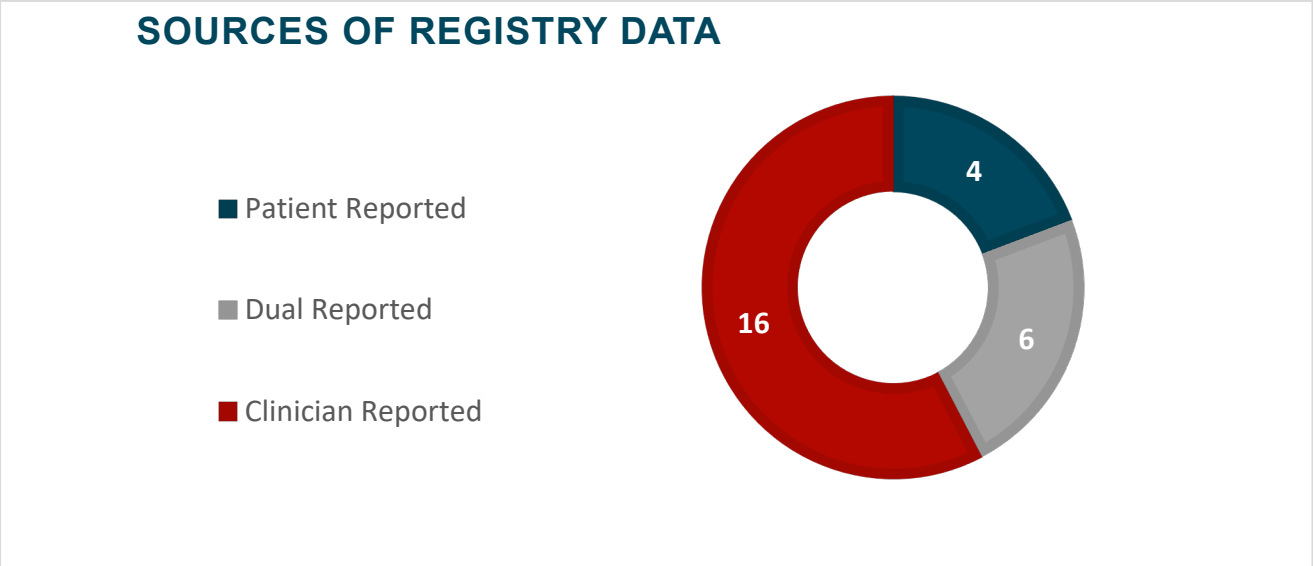
Of those 26, 24 have implemented the expanded dataset (version 1 or 2) for new and follow-up patients. This comprises 7 Year 2 registries, all 8 Year 1 registries, and 9 pilot registries. Of the 26, one year 2 registry has been built using version 2 of the SMA Core Dataset but is yet to officially launch so has been excluded from Fig 1. 17 (68%) of the 25 registries have already implemented version 2 of the SMA Core Dataset in some capacity.

The total number of patients across the 26 registries is 4,806, with the number of patients per registry ranging from 4 to 835. Of the 4,806 patients, 83% are covered by version 1 or 2 of the expanded core dataset at the time of writing this report.

Table 4: Patient numbers

Patient numbers	Number of Registries
Under 50	8
51 – 250	11
251 – 500	5
501 – 750	1
750 - 1000	1

Figure 2: Sources of registry data



Of the 26 registries represented:

- 4 are using a bespoke software platform
- 5 are using REDCap
- 2 are using Clarum provided by Roche
- 10 are using paper forms and/or Excel
- 1 is using Google Docs
- 4 are using other methods, including SQL server in Azure and Compos

The frequency of data updates in each registry varies significantly, ranging from every visit (e.g. every few months for treated patients) to a minimum of once a year.

Table 5: Dataset usage overview for the 28 registries engaged in the dataset project to date

Registry	Participation	Current dataset usage
1. Registry 1	Pilot	Version 2
2. Registry 2	Pilot	Version 1
3. Registry 3	Pilot	Version 1
4. Registry 4	Pilot	Version 2
5. Registry 5	Pilot	Unresponsive
6. Registry 6	Pilot	Unresponsive
7. Registry 7	Pilot	Version 2
8. Registry 8	Pilot	Version 2
9. Registry 9	Pilot	Version 2
10. Registry 10	Pilot	Version 2
11. Registry 11	Pilot	Version 1
12. Registry 12	Pilot	Version 1
13. Registry 13	Year 1	Version 1
14. Registry 14	Year 1	Version 2
15. Registry 15	Year 1	Version 1
16. Registry 16	Year 1	Version 1
17. Registry 17	Year 1	Version 2

18. Registry 18	Year 1	Version 2
19. Registry 19	Year 1	Version 2
20. Registry 20	Year 1	Version 2
21. Registry 21	Year 2	Version 0 (registry development on hold)
22. Registry 22	Year 2	Version 2
23. Registry 23	Year 2	Version 2
24. Registry 24	Year 2	Version 2
25. Registry 25	Year 2	Version 2
26. Registry 26	Year 2	Version 2
27. Registry 27	Year 2	Version 2
28. Registry 28	Year 2	Version 2 (data collection yet to start)
29. Registry 29	Year 2	Unresponsive
30. Registry 30	Year 2	Version 2 (partial)

Theme 2: Dataset compliance

Table 6: Average and range of dataset compliance across 10 pilot,8 year 1 and 8 year 2 registries.

Compliance	Mandatory Items	Non-mandatory Items
Clinician reported (n16)	89%	83%
Dual reported (n6)	87%	82%
Patient reported (n4)	89%	71%
Average	86%	80%
Range	48% - 100%	52% - 100%

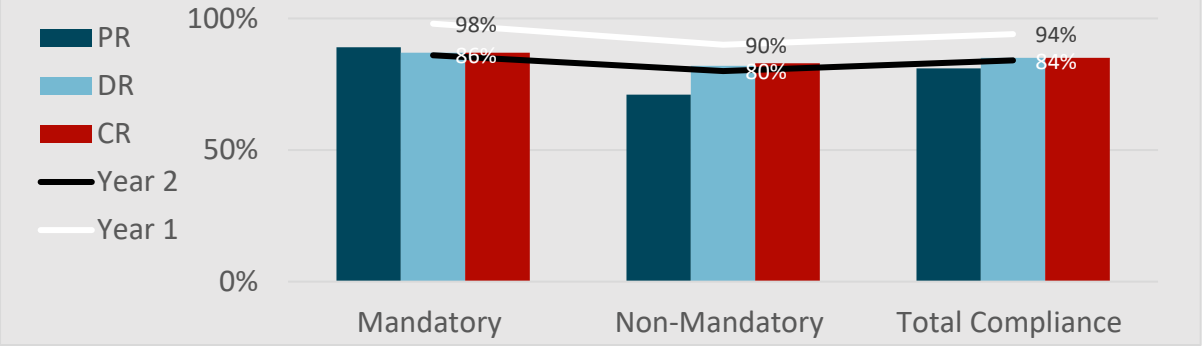
These results are influenced due to the inclusion of registry 22 (dual reported) which is based at a genetic testing centre and therefore only collects a very limited set of data at baseline and has no follow up with patients. When we exclude registry 22, there is an 8% increase for mandatory and 4% increase for non-mandatory data items across the dual reported registries and a slight overall increase of 2% and 1% for all registries, as illustrated in table 7 below.

Table 7: Average and range of dataset compliance across 10 pilot,8 year 1 and 7 year 2 registries.

Compliance	Mandatory Items	Non-mandatory Items
Clinician reported (n16)	89%	83%
Dual reported (n6)	95% (+8%)	86% (+4%)
Patient reported (n4)	89%	71%
Average	88% (+2%)	84% (+1%)
Range	62% - 100%	52% - 100%

Overall, the compliance rate has dropped by 10% (9% if excluding registry 22) from year 1 to year 2. We believe this is due to the increase in the number and diversity of registries participating, and the introduction of the version 2 dataset halfway through the reporting year. To avoid wasted effort, most year 2 registries waited until version 2 was released (October 2020) before starting work on implementation, therefore this cohort is not as advanced in the process as they would otherwise have been. Additionally, registries have been thinner on resource and more restricted in their data collection activities due to restrictions put in place related to the ongoing Covid-19 pandemic.

Fig 3: SMA Core dataset v2 compliance rates across participating registries:



A full breakdown of data items *not* being collected, by registry, can be found in appendix 3. The most common missing items are:

Mandatory

- **CGI-I (Clinical Global Impression of Improvement)** is collected by 50% (of 22) despite being mandatory for registries with a clinician reported element.
- **PGI-S and PGI-I (Patient Global Impression of Severity/Improvement)** is collected by 48%. During the teleconference interviews we noted (1) a lack of awareness of the nature of these items (many assumed they were a separate PRO scale), (2) a common assumption that these items are not mandatory because they appear in the PROMs section, and PROM scales are not mandatory, and (3) several registries reporting that they (or their participating clinicians) do not believe these items are useful enough to balance the additional burden of data collection. The lack of awareness and misconceptions were addressed during the interviews, and during the next dataset revision we propose to re-examine the justification for inclusion and discuss alternative options. If the items are to remain, we will propose to move them to a different section and improve the labelling/description.
- **Peak cough flow** was collected by only 27% of registries at the time of the teleconference interviews. Although this is mandatory for registries with a clinician reported element, this was a new addition in version 2 of the core dataset so we believe compliance rates will improve over the next year.

Non-mandatory

SMN2 variant C859GtoC and its **testing method** are collected by 31% and 35% respectively of participating registries.

Theme 3: Outcome measures

Table 8: Motor outcome measures used by registry (CR & DR)

	Registry 22	Registry 1	Registry 2	Registry 23	Registry 3	Registry 24	Registry 25	Registry 13	Registry 4	Registry 26	Registry 27	Registry 14	Registry 8	Registry 15	Registry 28	Registry 7	Registry 9	Registry 16	Registry 17	Registry 10	Registry 18	Registry 30	Registry 19	Registry 20	Registry 12	Registry 11	
N/A Patient Reported Registry						x										x					x					x	
10MWT		1	1					1				1		1					1			1	1		1		9
6MWT		1	1	1	1			1	1		1	1		1	1			1	1	1		1	1	1	1		17
9HPT		1															1					1					3
ACTIVE																											0
AIMS														1													1
BBT		1																									1
Brooke Scale of Upper Extremity Function		1	1		1			1									1					1	1	1	1		9
BSID-III composite motor score/percentile											1																1
CHOP-INTEND		1	1		1	1	1	1			1	1			1		1	1	1	1		1	1	1	1		17
EK2		1																				1	1	1	1		5
ES9HPT																											0
HFMS		1	1	1	1	1	1		1		1		1				1						1		1		12
HFMS-E		1	1		1	1	1	1				1			1		1	1	1	1		1	1	1	1		16
HINE		1	1		1		1				1	1	1		1				1				1		1		11
MFM-20		1	1		1			1									1	1	1	1		1	1		1		11
r9HPT																											0
Revised Brooke		1			1																				1		3
RHS					1									1													2
RULM		1	1	1	1		1	1				1			1		1	1	1			1	1	1	1		15
TIMPSI																											0
TUG		1	1		1												1					1		1	1		7
Vignos																								1			1
WHO Motor Milestones		1			1										1		1					1		1	1		7
Other - CHOPATEND		1			1												1						1				4
Other - grip and dynometers																	1										1
Other - FIM																	1										1
Other - MFM 32																							1				1

There appears to be a natural consensus emerging across the registries on motor measures; the most commonly used being CHOP-INTEND, HFMS-E, RULM, and 6MWT. These measures offer a wide coverage of potential patient cohorts and cover all function levels: This year, the registries we spoke to reported collecting an average of 7.6 different outcome measures (across the 22 registries with a clinician-reported element), compared to an average of 4.9 different outcome measures across the 16 registries we spoke to for last year's Year 1 report. This represents a 55% increase in the average number of outcome measures collected per registry which may be linked to increased therapy availability and the need to collect data for regulators and payers. We believe that a collected effort to drive consensus in outcome measures would be beneficial to ensure data is comparable.

Table 9: Popular OM suitability (taken from OML)

	Suitable age ranges				Suitable function levels		
Outcome Measure (OM)	≤2 yrs	3-5 yrs	6-17 yrs	≥ 18 yrs	Non-sitter	Sitter	Walker
6MWT	No	Yes[1]	Yes	Yes	No	No	Yes
CHOP-INTEND	Yes	Yes[1]	No	No	Yes	No	No
HFMS-E	No[1]	Yes	Yes	Yes	Yes	Yes	Yes
RULM	No	Yes	Yes	Yes	Yes	Yes	Yes

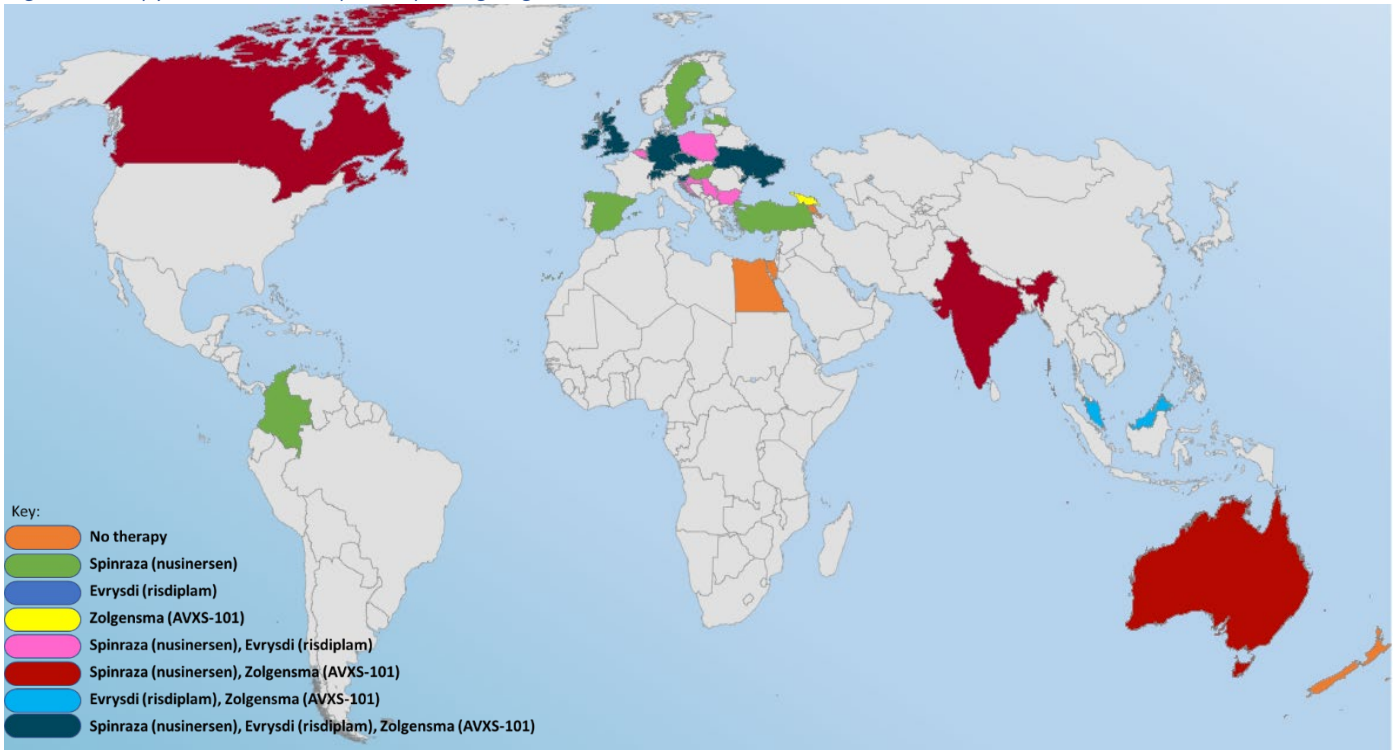
A need for access to training on outcome measures for both physiotherapists and physicians was also a consistent theme in this area.

Theme 4: Therapy availability

The 26 registries represented in this report cover 25 countries. 23 of the 26 registries reported some level of national availability of one or more disease modifying therapies. The countries reporting no access at all were Armenia and Egypt (which has 2 registries), and the level of access across the other countries varies significantly.

Of the 23 countries with access, Nusinersen is available on some level in all except Malaysia and Georgia.

Fig 4: Therapy access across participating registries countries:



4. Registry-level summaries

Standardised summaries of the information were gathered from each registry during individual teleconference calls : year 2 (n8), year 1 (n8), and pilot study (n10) registries.

5. Looking ahead to Year 3

Year 3 of the Expanded SMA Dataset Implementation Project runs from 01-06-2021 to 31-05-2022. We have re-contacted any registries who previously showed interest in the core dataset but have not been ready to commit, and we have reached out via the current TGDOC Chair (Anna Ambrosini) to any existing TGDOC registries who collect data on SMA but have not yet formally engaged with this project.

Through our registry contacts we have delivered outreach via the ALAME (Latin American SMA Alliance) which comprises 16 patient organisations, 9 of which have patient registries and are interested in joining TGDOC and implementing the SMA core dataset. On Friday 18 May we held a 2-hour interpreted induction meeting to introduce them to TREAT-NMD, TGDOC, the SMA Core Dataset and the Global Registries Platform. Helen Walker is now working with the interested patient organisations to complete the TGDOC membership process.

Communications and support

We will continue the more structured communication and support approach in year 3 which was established for year 2; this maintains more frequent contact with the registries, improves availability of support from the project team, creates a greater feeling of community between the registries, and prompts the discussion and resolution of any issues as soon as they arise. When the Year 3 registries are confirmed, we will hold a Year 3 Welcome Meeting and monthly Project Support Drop-ins during which the project team are available to discuss progress, give updates, or answer questions.

Table 11: Year 3 key events:

Date	Title of Event	Details	Target Audience
May 2021	Joint workshop on Dataset Specification with other disease areas	Virtual meeting	TGDOC SMA, LGMD and DMD registry curators
June 2021	Cure SMA Conference	Virtual conference and poster	SMA Clinicians, researchers, and industry.
Sep 2021	Deliverable: SMA Dataset Workshop	Virtual Meeting	Primarily Year 3 Curators, however others will be invited participate
Sep 2021	WMS Conference	Virtual conference and poster	Clinicians, researchers, and industry
Nov 2021	TGDOC Curators' Meeting	Virtual Meeting	TGDOC curators
Monthly	Support Calls	Virtual Drop-in Sessions	Primarily Year 3 Curators, however others may be invited participate
Mar/Apr 2022	Individual registry calls	Online survey and teleconference interviews	All years including pilot
May 2022	Final Project Report	Written report	Biogen

Publications

We are collaborating with the DMD and LGMD core dataset project teams to produce a publication outlining the development of the TREAT-NMD Core Datasets. The methodology will focus on the consensus-building, decision-making, and standardisation processes, and illustrate how TREAT-NMD has evolved the technique to learn from experience and adapt according to the needs of the different disease areas. The datasets themselves will be presented in the results.

Joanna Das presented a poster at the Cure SMA Conference in June 2021 titled '**Global Collaborative Real-world Evidence Collection by the TREAT-NMD Network of Spinal Muscular Atrophy Registries'**. The poster outlined the key success from the project to date and is available in Appendix 5. A second poster will be presented at the WMS Conference in September 2021 which will have a heavier focus on the power of the data held within the TREAT-NMD Global SMA Registry, as a result of the expanded dataset project.

Year 3 Deliverables

Table 12: Year 3 deliverables

Deliverable	Due	Completion date
D10: Financial support available for year 3 registries not receiving direct Biogen funding	M25 (June 2021)	
D11: Year 3 workshop for dataset implementation support/harmonisation	M28 (Sep 2021)	
D12: Final Project Report	M36 (May 2022)	

Testimonials from Registry Curators:

'Our impression regarding expanded dataset is very positive. Information it collects are valuable as well as the whole process of acquiring the information. It points to the potential weakness in data we collect, especially concerning patient history, and draws out issues that require more focus in the future thanks to their potential significance in improving the care for the patients as well as their academic and scientific value. Opportunities for improving were identified in the dataset workshop through discussions which hold great value for research.'

'First, we noticed an improvement in the quality of the data. More patients have been entered and data fields are more complete compared to previous collections for which we had a TREAT-NMD SMA section (using the v0 core dataset) in our general registry. Further, we received several requests for data from pharmaceutical companies within the context of a drug reimbursement application. Without the [SMA Core Dataset] we would not be able to answer these requests.'

'We know that working on an expanded SMA registry is very difficult, but at the same time very, very useful'

6. Additional considerations

Global Registries Platform.

In December 2020, the TREAT-NMD Global Registries Platform ('the Platform') began the beta testing phase of the clinician portal and the development phase of the patient portal. On 14 June 2021, the

clinician portal of the SMA module went live and TREAT-NMD are working with several 'early adopter' registries which have chosen to use the Platform as their main data collection tool. TREAT-NMD are also engaging with registries which will continue to use their existing data collection platforms to provide a safe and efficient means of data submission to facilitate TREAT-NMD Global Registry enquiries.

Project team coverage

Jo Bullivant moved to a new role within the JWMDRC team in March 2021. Recruitment of a new Project Manager was successful, and the new Project Manager (Julie Bohill) will start in August 2021. To mitigate the risk from this gap in resource, both Jo Bullivant and Joanna Das increased their working hours. Jo has been working 1 extra day per week dedicated to this project, and Joanna has been working overtime as and when needed.

COVID-19

The UK went into lockdown on 23rd March 2020 with the university limiting face to face contact from Tuesday 17th March 2020 by asking all staff to work from home. This is still the case for office-based staff and there is currently no clear indication from the university of when this might change. Wherever organisational and project need dictates, the following adjustments have been made:

- Working hours and patterns have been adjusted and are more flexible
- Reduced or increased hours where necessary to accommodate additional commitments
- Increased utilisation of MS Teams and other shared working tools such SharePoint
- All meetings are now virtual

Additionally, COVID-19 impacted the registries with many having to suspend clinical appointments, during which they would usually have assessed patients and updated their registry information. Many clinicians were pulled away from their normal work which required more flexibility for the individual teleconference calls (sometimes evening or weekends) for the collection of information for this report.

7. Discussion & conclusions

Year 2 of the expanded SMA dataset implementation progressed according to plan, despite continued challenging circumstances, with no significant barriers or concerns identified and an excellent level of dataset compliance (average 84% or 85% with outliers removed). 8 of the year 2 registries have the capacity to collect version 2 the expanded dataset for new and follow-up patients, in addition to 11 from the pilot and year 1 registries. All of the deliverables have been achieved with some flex on timelines kindly granted by Biogen.

The expanded dataset represents a marked increase in the minimum numbers of data items to be collected by a large number of very diverse registries, and therefore inevitably presents more of a challenge to some than others. The bursaries provide an invaluable source of funding and are predominantly used for additional staff time and platform software development. In addition to the bursaries, registries appreciated the in-depth guidance provided on the v2 dataset during the Year 2 SMA Dataset Workshop, as well as the opportunity to learn and seek advice from other registries.

The curator calls highlighted the challenges associated with collecting such a complex dataset due to its size and constraints on time. However, the curators were also extremally positive about the benefits of using the dataset and being involved in the project, which included the ability to secure industry sponsorship, improve data quality and data collection practices, and having the data available to help lobby for therapy access.

Feedback from the registries has not uncovered any significant problems with or barriers to dataset compliance and revealed an overall positive opinion of the expanded dataset and strong support for the aims of the project. A natural consensus on motor measures continues to emerge which has the potential to inform stronger guidance from TREAT-NMD in future about which outcome measures the registries in the network should be encouraged to collect.

The last 12 months have seen a much wider use of DMT's globally for all three SMA therapies with 23 of the 25 countries involved in this project reporting some level of access to not only Spinraza but also Zolgensma and Risdiplam. This is exciting to see and the dataset has been updated to accurately capture the important data needed for the post marketing surveillance of them. Lessons learnt from year 2 and specifically the revision process will be implemented during the next formal dataset revision.

Overall, we have seen a continuation of the excellent progress made in year 1 we are looking forward to continuing the success into year 3.

The project team and the TGDOC Chairs would like to express thanks to Biogen for funding this important initiative and for their support of TREAT-NMD.

Appendix 1: Curator Call Survey

Jisc Online surveys

Year 2 Report Survey

Response ID	Completion date

1	Please provide the following information:
1.1	Registry curator name
1.1.a	
1.2	Please confirm your registry name
1.2.a	

2	Please select which term best describes the coverage of your registry:
2.a	Please specify:
2.b	In which country/countries is your registry based?

3	Are you receiving any direct funding from Biogen to support your Registry's data collection activities?
3.a	Have you applied for your SMA Dataset Bursary?
3.a.i	How has it helped (or how will it help) you to implement the SMA Core Dataset in your registry?
3.a.ii	Please tell us why?

4	'Has your registry completed the new TGDOC Membership process?
4.a	Please specify:

5	Please provide the number of living patients included in this registry, under each version of the dataset. (only provide the most recent data for each patient, e.g. patient 33 has data in v2 and historical data in v1, only include them as a total against v2)
5.1	SMA Type 0
5.1.a	v0 (2009)
5.1.b	v1 (2018)
5.1.c	v2 (2020)
5.1.d	Total
5.2	SMA Type 1
5.2.a	v0 (2009)
5.2.b	v1 (2018)
5.2.c	v2 (2020)
5.2.d	Total
5.3	SMA Type 2
5.3.a	v0 (2009)
5.3.b	v1 (2018)
5.3.c	v2 (2020)
5.3.d	Total
5.4	SMA Type 3a
5.4.a	v0 (2009)
5.4.b	v1 (2018)
5.4.c	v2 (2020)
5.4.d	Total
5.5	SMA Type 3b
5.5.a	v0 (2009)
5.5.b	v1 (2018)
5.5.c	v2 (2020)
5.5.d	Total
5.6	SMA Type 3 (if sub-type not known)
5.6.a	v0 (2009)
5.6.b	v1 (2018)
5.6.c	v2 (2020)
5.6.d	Total
5.7	SMA Type 4
5.7.a	v0 (2009)
5.7.b	v1 (2018)
5.7.c	v2 (2020)
5.7.d	Total

5.8	Unspecified type but genetically confirmed
5.8.a	v0 (2009)
5.8.b	v1 (2018)
5.8.c	v2 (2020)
5.8.d	Total
5.9	Total
5.9.a	v0 (2009)
5.9.b	v1 (2018)
5.9.c	v2 (2020)
5.9.d	Total

6	Please explain your data collection process (Review of clinical notes? Clinicians complete 'live' in clinic? Clinicians send paper forms to Curator? Patients enter data online? Curator telephones patients?)
6.a	How often do you try to update individual patient data?
6.a.i	Please specify:
6.a.ii	Please tell us how often the visits are.
6.a.iii	Please provide more details.

7	How do you manage data from patients lost to follow up, and how long do you keep it in your registry?

8	What system do you currently use to collect/store your data?
8.a	please specify
8.b	Are you waiting for the URP (Universal Registry Platform) to become available for your registry to use?
8.b.i	What is the decision process for your registry in using the URP? e.g. impact assessment needed, ethics committee review...

9	Which version of the SMA Core Dataset do your current data collection forms comply with?
9.a	If you have not yet implemented version 2, when do you expect to do this?

For questions 10-24 you only need to pick out the items which your registry is NOT currently collecting. Please give a brief reason for each one:

10	Privacy-preserving record linkage
10.1	First name at birth (CR) (PR)
10.1.a	
10.1.b	Reason not collecting
10.2	Last name at birth (CR) (PR)
10.2.a	
10.2.b	Reason not collecting
10.3	Full date of birth (CR) (PR)
10.3.a	
10.3.b	Reason not collecting
10.4	Sex at birth (CR) PR)
10.4.a	
10.4.b	Reason not collecting
10.5	Country of birth (CR) (PR)
10.5.a	
10.5.b	Reason not collecting
10.6	Place of birth (CR) (PR)
10.6.a	
10.6.b	Reason not collecting

11	Demographics
11.1	Date of birth (CR) (PR)
11.1.a	
11.1.b	Reason not collecting
11.2	Sex (CR) (PR)
11.2.a	
11.2.b	Reason not collecting
11.3	Country of residence (CR) (PR)
11.3.a	
11.3.b	Reason not collecting
11.4	Is family member affected (CR) (PR)

11.4.a	
11.4.b	Reason not collecting
11.5	Affected family member relation
11.5.a	
11.5.b	Reason not collecting
11.6	Affected family member sex
11.6.a	
11.6.b	Reason not collecting
11.7	Affected family member side
11.7.a	
11.7.b	Reason not collecting

12	Living status
12.1	Alive (CR) (PR)
12.1.a	
12.1.b	Reason not collecting
12.2	Date of death
12.2.a	
12.2.b	Reason not collecting
12.3	Cause of death code
12.3.a	
12.3.b	Reason not collecting
12.4	Cause of death classification
12.4.a	
12.4.b	Reason not collecting

13	Genetic diagnosis
13.1	Genetic confirmation (CR) (PR)
13.1.a	
13.1.b	Reason not collecting
13.2	Screening
13.2.a	
13.2.b	Reason not collecting

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13.3	Genetic Report (CR) (PR)
13.3.a	
13.3.b	Reason not collecting
13.4	SMN1 variant (CR) (PR)
13.4.a	
13.4.b	Reason not collecting
13.5	SMN1 variant HGVS (CR) (PR)
13.5.a	
13.5.b	Reason not collecting
13.6	SMN1 testing method
13.6.a	
13.6.b	Reason not collecting
13.7	SMN2 copy number (CR) (PR)
13.7.a	
13.7.b	Reason not collecting
13.8	SMN2 copy number testing method
13.8.a	
13.8.b	Reason not collecting
13.9	SMN2 variant c859GtoC
13.9.a	
13.9.b	Reason not collecting
13.10	SMN2 variant c859GtoC testing method
13.10.a	
13.10.b	Reason not collecting

14	Clinical Observations
14.1	Symptom onset (CR) (PR)
14.1.a	
14.1.b	Reason not collecting
14.2	Symptom onset date (CR) (PR)
14.2.a	
14.2.b	Reason not collecting
14.3	SMA type (CR) (PR)

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14.3.a	
14.3.b	Reason not collecting
14.4	Clinician Global Impression of Severity (CR) - baseline
14.4.a	
14.4.b	Reason not collecting
14.5	Clinician Global Impression of Improvement (CR) - follow-up
14.5.a	
14.5.b	Reason not collecting
14.6	Height
14.6.a	
14.6.b	Reason not collecting
14.7	Height measurement method
14.7.a	
14.7.b	Reason not collecting
14.8	Weight
14.8.a	
14.8.b	Reason not collecting
14.9	Head circumference
14.9.a	
14.9.b	Reason not collecting
14.10	Shoulder contractures
14.10.a	
14.10.b	Reason not collecting
14.11	Elbow contractures
14.11.a	
14.11.b	Reason not collecting
14.12	Wrist contractures
14.12.a	
14.12.b	Reason not collecting
14.13	Finger contractures
14.13.a	
14.13.b	Reason not collecting

14.14	Hip contractures
14.14.a	
14.14.b	Reason not collecting
14.15	Knee contractures
14.15.a	
14.15.b	Reason not collecting
14.16	Ankle contractures
14.16.a	
14.16.b	Reason not collecting
14.17	Jaw contractures
14.17.a	
14.17.b	Reason not collecting

15	Scoliosis
15.1	Scoliosis diagnosis (CR) (PR)
15.1.a	
15.1.b	Reason not collecting
15.2	Cobb angle
15.2.a	
15.2.b	Reason not collecting
15.3	Scoliosis surgery performed (CR) (PR)
15.3.a	
15.3.b	Reason not collecting
15.4	Scoliosis surgery date
15.4.a	
15.4.b	Reason not collecting

16	Motor function
16.1	Motor ability (CR) (PR)
16.1.a	
16.1.b	Reason not collecting
16.2	Motor ability status (CR) (PR)
16.2.a	

16.2.b	Reason not collecting
16.3	Motor ability observed in clinic (CR) (PR)
16.3.a	
16.3.b	Reason not collecting
16.4	Motor ability episode (CR) (PR)
16.4.a	
16.4.b	Reason not collecting

17	Wheelchair usage
17.1	Wheelchair usage (CR) (PR)
17.1.a	
17.1.b	Reason not collecting
17.2	Wheelchair usage episode (CR) (PR)
17.2.a	
17.2.b	Reason not collecting
17.3	Wheelchair usage frequency (CR) (PR)
17.3.a	
17.3.b	Reason not collecting

18	Nutrition
18.1	Feeding tube usage (CR) (PR)
18.1.a	
18.1.b	Reason not collecting
18.2	Feeding tube usage episode (CR) (PR)
18.2.a	
18.2.b	Reason not collecting
18.3	Feeding tube usage type (CR) (PR)
18.3.a	
18.3.b	Reason not collecting

19	Pulmonary Function
19.1	Invasive ventilation usage (CR) (PR)
19.1.a	
19.1.b	Reason not collecting
19.2	Invasive ventilation episode (CR) (PR)
19.2.a	
19.2.b	Reason not collecting
19.3	Invasive ventilation duration (CR) (PR)
19.3.a	
19.3.b	Reason not collecting
19.4	Non-invasive ventilation usage (CR) (PR)
19.4.a	
19.4.b	Reason not collecting
19.5	Non-invasive ventilation episode (CR) (PR)
19.5.a	
19.5.b	Reason not collecting
19.6	Non-invasive ventilation duration (CR) (PR)
19.6.a	
19.6.b	Reason not collecting
19.7	Airway clearance assistance
19.7.a	
19.7.b	Reason not collecting
19.8	Pulmonary function test performed (CR) (PR)
19.8.a	
19.8.b	Reason not collecting
19.9	Forced vital capacity volume (CR)
19.9.a	
19.9.b	Reason not collecting
19.10	Forced vital capacity percentage (CR)
19.10.a	
19.10.b	Reason not collecting
19.11	Peak cough flow (CR)
19.11.a	
19.11.b	Reason not collecting

20	Disease-modifying therapies (DMT)

20.1	DMT received (CR) (PR)
20.1.a	
20.1.b	Reason not collecting
20,2	DMT episode (CR) (PR)
20,2,a	
20,2,b	Reason not collecting
20,3	DMT (CR) (PR)
20.3.a	
20.3.b	Reason not collecting
20.4	DMT status (CR) (PR)
20.4.a	
20.4.b	Reason not collecting
20.5	DMT single administration date (CR) (PR)
20.5.a	
20,5,b	Reason not collecting
20,6	DMT stopping reason (CR)
20,6,a	
20,6,b	Reason not collecting
20,7	DMT dosage value (CR)
20.7.a	
20.7.b	Reason not collecting
20.8	DMT dosage unit (CR)
20.8.a	
20,8,b	Reason not collecting
20,9	DMT administration route (CR)
20,9,a	
20,9,b	Reason not collecting
20.10	DMT administration intervals
20.10.a	
20.10.b	Reason not collecting
20.11	DMT administration schedule deviation (CR)
20.11.a	

20.11.b	Reason not collecting
20.12	DMT administration schedule deviation reason (CR)
20.12.a	
20,12,b	Reason not collecting
20,13	DMT corticosteroid administration duration (CR)
20,13,a	
20,13,b	Reason not collecting
20,14	DMT corticosteroid drug (CR)
20.14.a	
20.14.b	Reason not collecting
20.15	Anti-AAV9 Antibody test result
20.15.a	
20,15,b	Reason not collecting
20,16	Anti-AAVp antibody test days before administration
20,16,a	
20,16,b	Reason not collecting

21	Medication and rehabilitation
21.1	Allopathic drug usage (CR) (PR)
21.1.a	
21,1,b	Reason not collecting
21,2	Allopathic drugs (CR) (PR)
21,2,a	
21,2,b	Reason not collecting
21.3	Other allopathic drugs (CR) (PR)
21.3.a	
21.3.b	Reason not collecting
21.4	Allopathic drug episode
21.4.a	
21.4.b	Reason not collecting
21.5	Allopathic drug
21,5,a	
21,5,b	Reason not collecting

21.6	Other allopathic drug
21.6.a	
21.6.b	Reason not collecting
21,7	Rehabilitative interventions usage (CR) (PR)
21,7,a	
21,7,b	Reason not collecting
21,8	Rehabilitative interventions (CR) (PR)
21.8.a	
21.8.b	Reason not collecting

22	Hospitalisations and comorbidities
22,1	Hospitalisation occurred (CR) (PR)
22,1,a	
22,1,b	Reason not collecting
22,2	Hospitalisation type (CR) (PR)
22.2.a	
22.2.b	Reason not collecting
22.3	Hospitalisation nights (CR) (PR)
22.3.a	
22.3.b	Reason not collecting
22,4	Hospitalisation acute reason code (CR)
22,4,a	
22,4,b	Reason not collecting
22,5	Hospitalisation acute reason classification (CR)
22.5.a	
22.5.b	Reason not collecting
22.6	Hospitalisation planned reason (CR)
22.6.a	
22.6.b	Reason not collecting
22.7	Hospitalisation SAE (CR)
22.7.a	
22,7,b	Reason not collecting
22,8	Hospitalisation SAE DMT (CR)
22.8.a	
22.8.b	Reason not collecting
22.9	Comorbidities diagnosed (CR) (PR)
22,9,a	
22,9,b	Reason not collecting
22,10	Comorbidity episode (CR) (PR)
22,10,a	
22,10,b	Reason not collecting
22,11	Comorbidity code (CR) (PR)
22,11,a	
22,11,b	Reason not collecting
22,12	Comorbidity classification (CR) (PR)
22,12,a	
22,12,b	Reason not collecting
22,13	Comorbidity SAE (CR) (PR)
22,13,a	
22,13,b	Reason not collecting
22,14	Comorbidity SAE DMT (CR) (PR)
22,14,a	
22,14,b	Reason not collecting

23	Clinical research
23,1	Clinical trial participation (CR) (PR)
23,1,a	
23,1,b	Reason not collecting
23,2	Clinical trial name (CR) (PR)
23,2,a	
23,2,b	Reason not collecting
23,3	Clinical trial drug (CR) (PR)
23,3,a	
23,3,b	Reason not collecting
23,4	Other registry participation
23,4,a	

23.4.b	Reason not collecting
23.5	Other registry
23.5.a	
23,5,b	Reason not collecting

24	Electrophysiology and biomarkers
24.1	CMAP performed
24.1.a	
24.1.b	Reason not collecting
24.2	DEXA performed
24,2,a	
24,2,b	Reason not collecting
24,3	Muscle imaging performed
24,3,a	
24.3.b	Reason not collecting

25	Which motor outcome measure(s) are you collecting?
25.a	Please specify:
25,b	Please provide the reason.

26	If no motor measure is taken at a visit, do you collect the reason?
26.a	Please provide the reason:

27	Please tell us if your registry is not currently collecting the following PROMS data items and the reason why:
27,1	Patient Global Impression of Severity (CR) (PR) - baseline
27,1,a	
27,1,b	Reason not collecting
27,2	Patient Global Impression of Improvement (CR) (PR) - follow-up
27.2.a	
27.2.b	Reason not collecting

28	Which (if any) patient-reported outcome measures (PROMs) are
28.a	Please specify:
28.b	Please tell us the reason

29	What is the status of disease-modifying therapy availability in your country?
29.1	Spinraza (nusinersen)
29.1.a	Available:
29.1.b	Access:
29.1.c	Eligibility:
29.2	Evrysdi (risdiplam)
29.2.a	Available:
29,2,b	Access:
29,2,c	Eligibility:
29,3	Zolgensma (AVXS-101)
29,3,a	Available:
29.3.b	Access:
29.3.c	Eligibility:

30	What has been your biggest challenge with the expanded SMA Core Dataset?

31	How are you tackling this?

32	In what ways has your registry benefitted from participation in the SMA Dataset Pilot/Implementation project?

Appendix 2: Data items *not* being collected by registry

	Registry 1	Registry 2	Registry 3	Registry 4	Registry 5	Registry 6	Registry 7	Registry 8	Registry 9	Registry 10	Registry 11	Registry 12	Registry 13	Registry 14	Registry 15	Registry 16	Registry 17	Registry 18	Registry 19	Registry 20	Registry 21	Registry 22	Registry 23	Registry 24	Registry 25	Registry 26
Year	2	0	0	2	0	2	2	1	0	2	2	1	0	1	2	0	0	1	1	0	1	2	1	1	0	0
First name at birth (CR) (PR)			1							1			1	1			1									
Last name at birth (CR) (PR)			1							1			1	1			1									
Full date of birth (CR) (PR)			1										1													
Sex at birth (CR) PR)			1										1	1												
Country of birth (CR) (PR)			1										1	1			1									
Place of birth (CR) (PR)			1										1	1			1		1				1			
Affected family member relation					1																1			1		
Affected family member sex																					1			1	1	
Affected family member side			1												1								1	1	1	
Alive (CR) (PR)						1																				
Date of death	1																									
Cause of death	1		1									1				1	1				1	1				
Cause of death classification	1		1		1							1				1	1				1	1		1		
Screening	1			1					1				1	1			1							1		1
Genetic Report (CR) (PR)			1											1								1				
SMN1 variant (CR) (PR)																								1		

SMN1 variant HGVS (CR) (PR)				1		1						1						1				1		1		
SMN1 testing method				1		1		1													1			1		
SMN2 copy number (CR) (PR)	1																							1		
SMN2 copy number testing method	1			1	1	1															1	1		1		
SMN2 variant c859GtoC	1		1	1	1	1	1	1	1	1		1		1	1			1	1	1		1		1	1	
SMN2 variant c859GtoC testing method	1		1	1	1	1	1	1	1	1		1		1	1			1			1	1		1	1	
Symptom onset (CR) (PR)																	1									
Symptom onset date (CR) (PR)																	1							1		
Clinician Global Impression of Severity (CR)	1				1					1			1	1			1		1	1		1			1	
Clinician Global Impression of Improvement (CR)	1			1	1					1			1	1			1		1	1		1			1	
Height						2											1				1					
Height measurement method						1									1		1				1					
Weight						2											1									
Head circumference				1	2	2									2	1	1									2
Shoulder contractures					2	2		2									2									
Elbow contractures					2	2		2									2									
Wrist contractures					2	2		2									2									
Finger contractures					2	2		2									2									
Hip contractures					2	2		2									2									
Knee contractures					2	2		2									2									
Ankle contractures					2	2		2									2									
Jaw contractures			1		2	2		2									2						2			
Scoliosis diagnosis (CR) (PR)	2																									

Cobb angle	2									1						1										2
Scoliosis surgery performed (CR) (PR)	1																									
Scoliosis surgery date	1																									
Motor ability (CR) (PR)										1												1				
Motor ability status (CR) (PR)										1												1				
Motor ability observed in clinic (CR) (PR)			1							1						1	1	1			1	1				1
Motor ability episode (CR) (PR)										1								2	2			2				
Wheelchair usage (CR) (PR)	1																	1								
Wheel chair usage episode (CR) (PR)	2		2																2							
Wheelchair usage frequency (CR) (PR)	1													1												
Feeding tube usage (CR) (PR)	1																									
Feeding tube usage episode (CR) (PR)	1																		2							
Feeding tube usage type (CR) (PR)	1																									
Invasive ventilation usage (CR) (PR)	1																									
Invasive ventilation episode (CR) (PR)	2																									
Invasive ventilation duration (CR) (PR)	1		1			1																				
Non-invasive ventilation usage (CR) (PR)	1																									
Non-invasive ventilation episode (CR) (PR)	2																									
Non-invasive ventilation duration (CR) (PR)	1		1			1																				
Airway clearance assistance	1			1													1				1					

Pulmonary function test performed (CR) (PR)	1																									
Forced vital capacity volume (CR)	2			2														2								
Forced vital capacity percentage (CR)	2																									
Peak cough flow (CR)	2		2	2			2			2		2		1				2	1							
DMT received (CR) (PR)	1								1	1							1									
DMT episode (CR) (PR)	2								2	2							2	2								
DMT (CR) (PR)	1								1	1							1									
DMT status (CR) (PR)	1								1	1							1									
DMT single administration date (CR) (PR)	1								1	1							1									
DMT stopping reason (CR)	1								1	1							1									
DMT dosage value (CR)	1								1	1						1	1				1		1			1
DMT dosage unit (CR)	1								1	1						1	1				1		1			1
DMT administration route (CR)	1								1	1							1				1					
DMT administration intervals	1		1						1	1						1	1									1
DMT administration intervals	1								1	1						1	1									1
DMT administration schedule deviation (CR)	1								1	1						1	1									1
DMT administration schedule deviation reason (CR)	1				1				1	1						1	1									1
DMT corticosteroid administration duration (CR)	1		1		1				1	1		1					1	1				1	1		1	1
DMT corticosteroid drug (CR)	1		1		1				1	1							1	1				1	1		1	1
Anti-AAV9 Antibody test result	1		1	1	1				1	1		1		1			1	1	1		1	1	1	1	1	

Anti-AAVp antibody test days before administration	1		1	1	1				1	1		1		1			1	1	1		1	1	1	1	1	1
Allopathic drug usage (CR) (PR)	1		1														1									
Allopathic drugs (CR) (PR)	1																1									
Other allopathic drugs (CR) (PR)	1																1									
Allopathic drug episode	2		2	1												2	2									1
Allopathic drug	1															1	1									1
Other allopathic drug	1															1	1									1
Rehabilitative interventions usage (CR) (PR)	1		1									1		1			1				1					
Rehabilitative interventions (CR) (PR)	1		1											1			1				1					
Hospitalisation type (CR) (PR)			1																							
Hospitalisation nights (CR) (PR)			1																							
Hospitalisation acute reason code (CR)	1		1																				1			1
Hospitalisation acute reason classification (CR)																										1
Hospitalisation SAE (CR)					1							1				1		1								1
Hospitalisation SAE DMT (CR)	1				1											1		1								1
Comorbidity diagnosed (CR) (PR)						2											1				1					
Comorbidity episode (CR) (PR)						2											2				2		2			
Comorbidity code (CR) (PR)				1		1											1				1		1			
Comorbidity classification (CR) (PR)				1		1											1				1					1

Comorbidity SAE (CR) (PR)					1	1										1	1				1				1
Comorbidity SAE DMT (CR) (PR)					1	1										1	1				1				1
Clinical trial participation (CR) (PR)			1																						
Clinical trial name (CR) (PR)			1															1							
Clinical trial drug (CR) (PR)			1																			1			
Other registry participation																					2				
Other registry																					2				
Motor measure										2															2
Motor measure score										1							1								1
Validated motor measure non-evaluation reason (CR)			1							1							1								
Patient Global Impression of Severity (CR) (PR)	1		1	1	1	1	1		1	1			1	1			1		1	1			1		
Patient Global Impression of Improvement (CR) (PR)	1		1	1	1	1	1		1	1			1	1			1		1	1					
Patient-reported outcome measure										2					2				2				2		2
Patient-reported outcome measure score										1					1				1				1		1
CMAP performed				1				1					1		1		1					1			
DEXA performed	1			1				1					1		1		1	1							
Muscle imaging performed	1			1				1					1		1		1	1				1			

Appendix 3: Revision Process

TREAT-NMD Spinal Muscular Atrophy (SMA) Core Dataset Dataset Revision Process

Foreword

This document describes the Revision Process for the core dataset for SMA Registries in the TREAT-NMD network. Feedback on this process or document is welcome and can be submitted by sending an email (or an annotated version of the document) to the Project Coordinator Joanna Das: joanna.das@newcastle.ac.uk.
Current versions of all documents are available on the project web page.

Introduction

The TREAT-NMD Global SMA Registry is one of several notable data collection initiatives in operation for Spinal Muscular Atrophy across the world. The model is based on participating registries collecting a common core dataset into which enquiries can be made. The core dataset for SMA registries was expanded in 2017, and following a pilot study the new core dataset was confirmed in September 2018. Considerable work went into ensuring the data collected by the TREAT-NMD registries, through the first iteration of the expanded core dataset, will be comparable with data collected by other initiatives. However, many of these initiatives are still in development or will also be making periodic revisions to their datasets. In addition to this, new therapies are approaching the market and global consensus on the most appropriate and feasible data to collect will continue to evolve over the coming years.

This Dataset Revision Process (hereafter the Revision Process) has been developed to reflect TREAT-NMD's commitment to ensuring its core SMA Dataset remains appropriate, feasible, collaborative, harmonised with other initiatives, and responsive to the needs of the whole SMA community.

This Revision Process will remain a working document for the duration of the project and will itself be subject to version control. This document describes:

1. The **objectives** of the Revision Process - what we want to accomplish.
2. The **version control** approach for the dataset and related documents.
3. The **stakeholder groups** to whom our activities are relevant.
4. **Process** and **timelines** - how we will accomplish our objectives.
5. **The version control** approach for this document.
6. **Contact details** for the SMA Dataset Project Team.

Objectives of the Revision Process:

- Allow the dataset to be responsive to the needs of the SMA community
- Manage and streamline the burden of dataset changes on Curators, Clinicians and Patients
- Promote harmonisation across relevant initiatives globally
- Drive and respond to global consensus on outcome measures
- Respond to feedback from all stakeholders
- Ensure and demonstrate feedback is being considered and acted upon where appropriate
- Facilitate continuous improvement

Version control for the Dataset

To support the Revision Process, a semantic versioning approach[1] will be applied to the following dataset documents:

1. The Dataset
2. The Dataset Manual
3. The Dataset Overview

This approach is explained below and will allow small improvements and 'fixes' to the dataset to be made as needed, without waiting for the next one/two-yearly formal revision. It also enables each change to be categorised according to the impact it will have on ongoing data validity.
All previous versions of the dataset will be available on the project web page for reference. Each time a new version is released, a tracked changes copy of the document will be stored electronically and may be requested from the Project Team for reference if needed.

Semantic Versioning[1]

A version number MAJOR.MINOR.PATCH will be assigned to each iteration of the dataset:

- A **PATCH** increment will be applied when a small change is made in a backwards compatible* way; for example, wording is clarified or a typo is corrected. When a PATCH increment is made it does not affect the MAJOR or MINOR increments, e.g. from v1.5.**2** to v1.5.**3**.

- A **MINOR** increment will be applied when a more significant, but still backwards compatible* change is made; for example, adding a new response option to a data item. When a MINOR increment is made, the PATCH increment reverts to zero, e.g. from v1.**5.2** to v1.**6.0**.

- A **MAJOR** increment will be applied when a change is made which is **not** backwards compatible*; for example, adding a new data item or splitting a response option into two sub-options. When a MAJOR increment is made, both the MINOR and PATCH increments revert to zero, e.g. from v**1.5.2** to v**2.0.0**.

PATCH or MINOR revisions might be made on an ad-hoc basis if deemed necessary. MAJOR revisions will be withheld until the next Formal Revision Process (see section 4). All revisions will be kept to a minimum wherever possible.

***Backwards compatibility[1]**

A change to a data item **is** backwards compatible if a data record conforming to the previous version would still be valid in the new version. For example:

Table 1: Example of a backwards compatible change (for illustration purposes only)

Version 1	**Version 2**
Does the patient use a wheelchair? 1. Yes 2. No	Does the patient use a wheelchair? 1. Yes 2. No 3. Don't know
✓ Version 2 of this data item is **backwards compatible** because a data value collected for v1 (e.g. 'Yes') would still be a valid response in v2.	

A change to a data item **is not** backwards compatible if a data record conforming to the previous version would no longer be valid in the new version. For example:

Table 2: Example of a backwards incompatible change (for illustration purposes only)

Version 1	**Version 2**
Does the patient use a wheelchair? 1. Yes 2. No	Does the patient use a wheelchair? 1. Yes – more than 16 hours per day 2. Yes – less than 16 hours per day 3. No
✖ Version 2 of this data item is **backwards incompatible** because a data value collected for v1 (e.g. 'Yes') would be an invalid response in v2.	

Version Control Table

A Version Control Table on the first page of each new version will track and categorise all changes made within that iteration of the dataset. Information will be displayed as follows:

Table3: Version control table example

Data Item Number	Details of Change	Type of Change	Backwards compatible?
		MAJOR/MINOR/PATCH	Yes / No

Dataset Feedback Log

In between each revision, a Dataset Feedback Log will record all feedback and suggestions received from all stakeholders, and the outcome of each when available (including an explanation if relevant). This will be made publically available as a live document via the project webpage.

[1] https://semver.org/

3. Stakeholder Groups

This Revision Process is based on the principle of collaboration and inclusivity and therefore effective, transparent and sustained communication and engagement with both the SMA and wider neuromuscular and rare disease communities is required.

The SMA Dataset project team will identify and engage with the following stakeholder groups for the purposes of the Revision Process:

- SMA patients and their families
- SMA Patient Advocacy groups and organisations
- Pharmaceutical industry
- Regulators and Payers
- SMA Registry Curators and owners
- Healthcare professionals (clinicians, physiotherapists, geneticists)
- The wider TREAT-NMD and TGDOC community
- Other academic groups or registry initiatives
- Expert consultants as needed: for example FAIR data experts, registry software providers, bioinformaticians

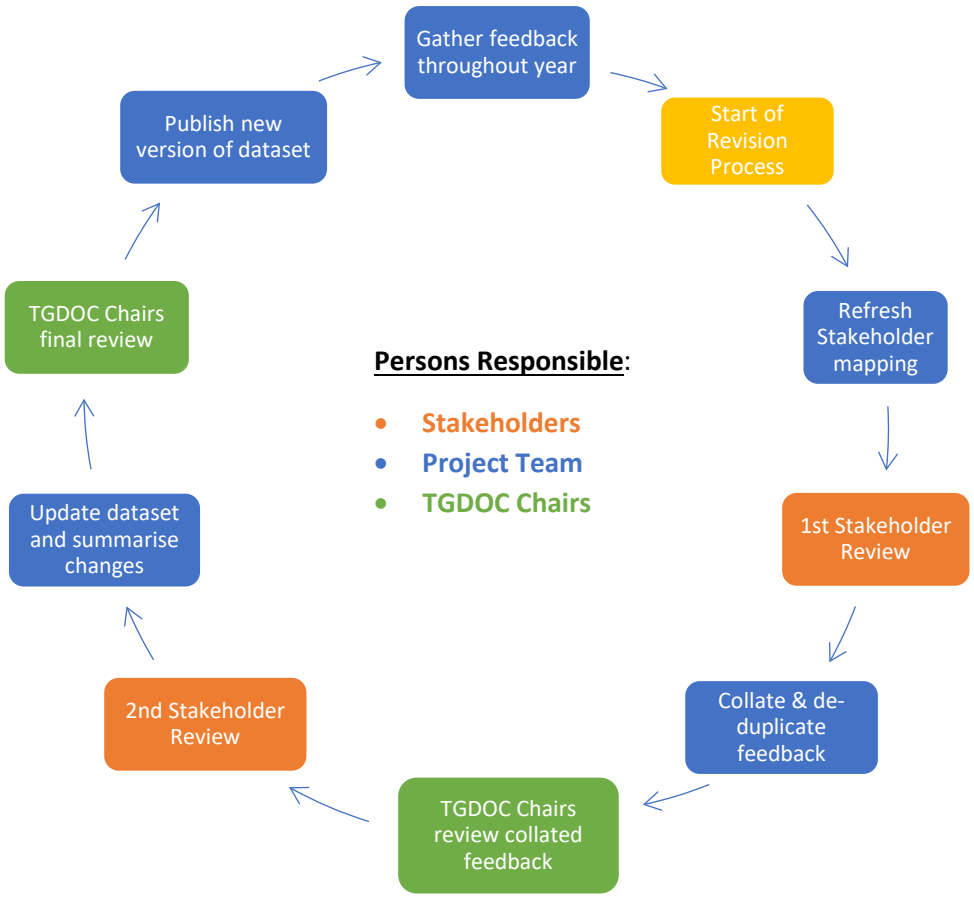
4. Formal Revision Process and Timelines

This Revision Process allows stakeholders to provide feedback and suggestions continuously, as well as being proactively consulted at the start of each **Formal** Revision Process described below.
The SMA Dataset project team will make every effort to align the timings of each Formal Revision Process with those of other known initiatives, to maintain dataset harmonisation. Each Formal Revision Process will be initiated by the sharing of a short pre-recorded webinar to:

- Explain the context of the SMA Dataset.
- Recap the dataset itself.
- Provide guidance on the Revision Process.

The Formal Revision Process will then be undertaken in an open and transparent way; seeking feedback from relevant stakeholders at the stages outlined below.

Figure 1: Formal Revision Process cycle



Timelines

All revisions will be kept to a minimum wherever possible.
PATCH or MINOR (backwards compatible*) revisions may be made at any time if deemed necessary; although every effort will be made to minimise burden on registries and participants.
MAJOR revisions will be withheld until the next Formal Revision Process as described above. This is planned to take place annually for the first 2 years (Mar-Jun 2020 and Mar-Jun 2021), and every 2 years thereafter (may be subject to change, stakeholders would be notified).
Each Formal Revision Process will take 15 weeks, as described below:

Table 4: Formal Revision Process Timeline

	Weeks														
Activity	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Short webinar to launch revision process															
2. Circulate current dataset															
3. Collate/analyse/review feedback															
4. TGDOC Chairs review feedback analysis															
5. Meet with TGDOC Chairs to agree responses to feedback															
6. Prepare draft version for circulation															
7. Circulate draft to stakeholders for feedback															
8. Collate/analyse/review any further feedback															
9. Prepare revised documents															
10. Final review/approval by TGDOC Chairs															
11. Publish new version of documents															
12. Circulate to stakeholders and update website															

For all revisions (MAJOR/MINOR/PATCH), registries will be asked to:

- Implement applicable revisions as soon as possible, but within a maximum of 6 months from the revision date.
- Notify the project team as soon as the revision has been implemented.

5. Version control for this document

This document itself will be subject to version control under the following naming convention:

- **TREAT-NMD SMA Dataset Revision Process_v1.0**
  - TREAT-NMD SMA Dataset Revision Process_draft_v1.1
  - TREAT-NMD SMA Dataset Revision Process_draft_v1.2
- **TREAT-NMD SMA Dataset Revision Process_v2.0**

Minor Revisions; for drafts. Each new draft version of the document will be reflected in an increase of the decimal number, e.g. v1.0 to draft_v1.1, draft_v1.2 and so on.
Major Revisions; will take effect when a new version of the dataset has been approved by the TGDOC Chairs and will be reflected in an increase in the whole number by 1, e.g. draft_v1.3 to final_v2.0.
Feedback received on this document or the Revision Process itself will be considered and implemented for subsequent revisions if appropriate, and the outcome communicated to the individual who provided the feedback.

6. Project Contacts

Any questions or feedback about this process or the SMA Dataset itself can be directed to:

- Joanna Das (Project Coordinator) at joanna.das@newcastle.ac.uk.
- Jo Bullivant (Project Manager) at joanne.bullivant@newcastle.ac.uk.

Appendix 5: CURESMA Poster - Global Collaborative Real-world Evidence Collection by the TREAT-NMD Network of Spinal Muscular Atrophy Registries

Global Collaborative Real-world Evidence Collection by the TREAT-NMD Network of Spinal Muscular Atrophy Registries

Authors:

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Institutions

1. John Walton Muscular Dystrophy Research Centre, Newcastle University, UK
2. Department of Clinical Neurosciences and Hotchkiss Brain Institute, University of Calgary, Calgary, Canada
3. Department of Neurology, Auckland District Health Board, New Zealand
4. Fondazione Telethon, Milan, Italy
5. Western University, London, Canada
6. Georgian Association of Pediatric Neurologists and Neurosurgeons, Tbilisi, Georgia
7. Referral Centre for Pediatric Neuromuscular Disorders, Clinical Medical Center, Zagreb, Croatia
8. Clinic of Neurology and Psychiatry for Children and Youth, Medical Faculty, University of Belgrade, Serbia
9. Scienseno, Brussels, Belgium
10. Department of Pediatrics, University of Gothenburg, Sweden
11. Myo-Care National Neuromuscular Foundation, Cairo, Egypt
12. Murdoch Children's Research Institute, Melbourne, Australia
13. Fundación Atrofia Muscular Espinal, Madrid, Spain
14. Hacettepe University, Ankara, Turkey
15. Czech Society of Neurology, Prague, Czech Republic
16. Pediatrics, Faculty of Medicine, Ain Shams University, Cairo, Egypt
17. Friedrich-Baur-Institute in Munich, Germany
18. UMHAT Alexandrovska, Sofia, Bulgaria
19. Semmelweis Medical University, IInd Pediatric Clinic, Budapest, Hungary
20. Chapter of Child Neurology and Developmental Paediatrics, Malaysian Society of Neurosciences, University of Malaya Medical Centre, Kuala Lumpur, Malaysia
21. Institute of Social and Preventative Medicine, University of Bern, Switzerland
22. Charitable Foundation Children with SMA, Kharkiv, Ukraine
23. Center of Medical Genetics and Primary Healthcare, Yerevan, Armenia
24. Department of Neurology, Medical University of Warsaw, Poland
25. Children's Clinical University Hospital, Riga, Latvia
26. Children's Hospital Ljubljana, University Medical Center, Ljubljana, Slovenia
27. M. Iashvili Children's Central Hospital, Tbilisi, Georgia
28. LMU Munich, Germany
29. Muscular Dystrophy Association India, Chennai, Tamil Nadu, India

Project Background:

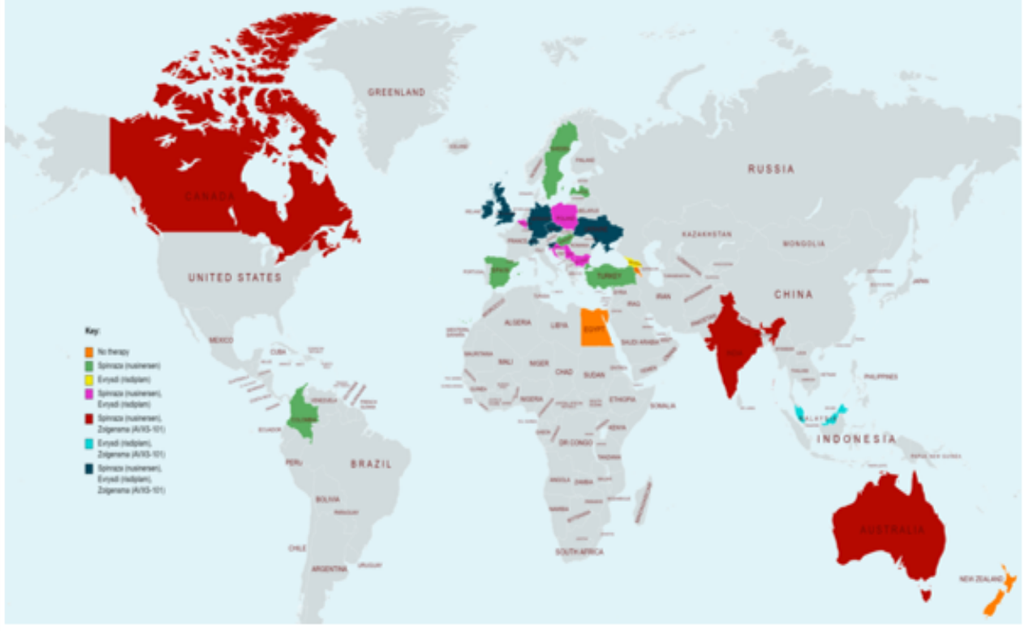
The TREAT-NMD Alliance, established in 2007, is a neuromuscular network providing infrastructure to advance the diagnosis, care and treatment of individuals ensuring the most promising new therapies reach patients as quickly as possible. It has a global network of 49* disease-specific neuromuscular patient registries (registries), including 28* Spinal Muscular Atrophy (SMA) which collect a common core dataset and are governed by the TREAT-NMD Global Database Oversight Committee (TGDOC). Researchers and industry can request anonymised and aggregate data via the committee as a single point of access to this diverse and extensive dataset.

In 2008 an agreed SMA Core Dataset (version 0) was introduced to help with clinical trial readiness and recruitment. As clinical trials moved towards approved therapies for SMA the SMA Core Dataset was updated and expanded the SMA Core Dataset to better inform on the natural history of SMA, provide context to understand the safety and effectiveness of new treatments, and support post marketing surveillance (PMS).

In September 2018, following a successful pilot study, TREAT-NMD expanded its SMA Core Dataset (version 1). The results from the pilot study informed the final contents of the dataset as well as a plan for the 3-year phased implementation project to support the remaining SMA registries to adopt the expanded dataset. The 3 year implementation project is currently at the end of year 2 and this poster provides a snapshot into is progress so far.

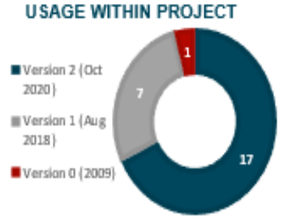
** There are an additional 30 registries still completing their TGDOC memberships so these numbers will increase*

THERAPY ACCESS ACROSS PARTICIPATING REGISTRIES COUNTRIES

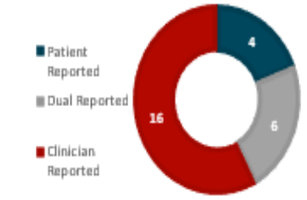


NUMBER OF PARTICIPATING REGISTRIES BY YEAR:

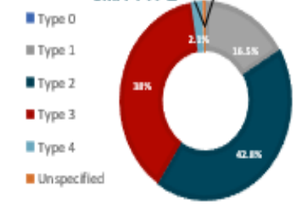
SMA DATASET VERSION USAGE WITHIN PROJECT



SOURCES OF REGISTRY DATA



PATIENT NUMBERS (%) BY SMA TYPE



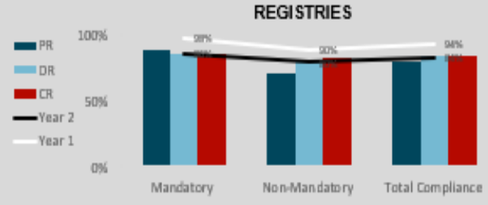
Collaborative Dataset Development:

Workshops and a pilot study were held between May 2017 and June 2018 involving clinicians, physiotherapists, registry curators, patient representatives, industry representatives, and other stakeholders from across the world. This led to the release of an expanded SMA Core Dataset (version 1) in September 2018.

Informed by the pilot project a 3 year phased implementation project began in May 2019 to support the remaining TGDOC SMA Registries in implementing the expanded SMA Core Dataset (version 1). The dataset was further revised in 2020 to respond to the needs of the SMA community and promote global harmonisation across relevant initiatives. This was done through 2 rounds of extensive and inclusive consultation with a wide range of stakeholders including patient advocacy groups, industry, regulators and payers, registry curators and owners, healthcare professionals and other academic groups and registry initiatives. Over 700 individual items of feedback were received for consideration and version 2 of the SMA Core Dataset was released in October 2020.

To date the project has worked with 30 TREAT-NMD SMA registries representing 4over 4800 patients to support the implementation of the SMA Core Dataset and thereby significantly improve the availability of standardised data on SMA from around the world.

SMA CORE DATASET V2 COMPLIANCE RATES ACROSS PARTICIPATING REGISTRIES



Reduction in compliance rate from year 1 to year 2 is due to the increase in the number of registries participating and the majority of registries are still implementing version 2 of the dataset which was updated in October 2020.

> 4800 Patients

from 26 Registries

TREAT-NMD SMA Core Dataset item groupings:

	Privacy-preserving record linkage	Demographics
Clinical Observations	Genetic Diagnosis	Living Status
Motor Function	Wheelchair usage	Scoliosis
Pulmonary function	Disease-modifying therapies (DMT)	Nutrition
Hospitalisations and comorbidities	Clinical research	Medication and rehabilitation
Motor measures	Patient-reported outcome measures	Electrophysiology and biomarkers

Data item comparison v1 to v2:

	Version 1 (Sep 2018)	Version 2 (Oct 2020)
Mandatory Clinician Reported	113	117
Mandatory Patient Reported	92	91
Non-Mandatory	50	37
Total Items	167	154

Conclusion:

With SMA therapies now available, the TREAT-NMD SMA Core Dataset aims to facilitate the availability of real-world data from patient registries to support PMS. It has been developed collaboratively with this aim in mind, and a formal revision plan will ensure that it continues to evolve over time, as our understanding of these needs progresses

Participating registries report that their data quality and utility has improved, as had registry credibility, and that they have seen an increase in demand for their registry data, from both pharmaceutical companies and from regulators and payers. They also report an ability to provide better evidence to lobby nationally for therapy access and reimbursement.

Acknowledgements: This project is funded by Biogen.