Setting the Scene

Craig Campbell
TGDOC Chair

Joanne Bullivant
TREAT-NMD SMA Dataset Project Manager

WELCOME
TREAT-NMD SMA DATASET WORKSHOP

December 2019

TREAT-NMD SMA DATASET WORKSHOP

INTRODUCTIONS
AGENDA
REIMBURSEMENTS: THROUGH TGDOC (HELEN WALKER)

Time		Session	Item	Who*
08:00		Registration & coffee		
08:30	1	Setting the scene	a) Welcome & Introductions b) Project overview and context: Why we are doing this? c) Workshop scope and purpose	CC CC JB
09.00	2	The Universal Platform	Update on the Universal Platform	JB
09:15	3	The expanded dataset	a) The Expanded Dataset b) Clarity on motor measures & PROMs c) Annual revision plan	JB JB JD
10:30		Coffee break		

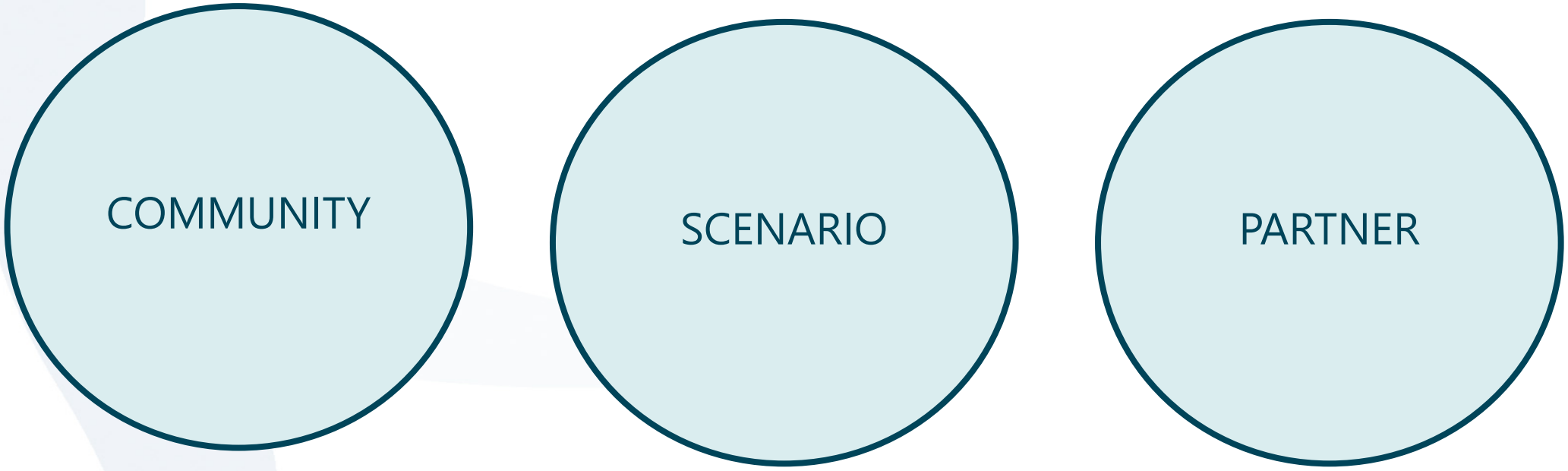
10:30		Coffee break		
Time		Session	Item	Who
10:45	4	Dataset implementation: progress so far	a) Results of internal survey b) Feedback from registries who have already implemented the dataset	MR Group1*
12:00		Lunch		
12:45	5	Support	a) Dataset Bursaries b) Dataset Manual	JD JB
14:00	6	Q&A / Trouble-shooting	Panel Q&A with: - TGDOC Chairs (Craig Campbell, Nathalie Goemans, Anna Ambrosini) - SMA Subgroup Lead: Miriam Rodrigues - Project Manager: Jo Bullivant - Group1*	All
14:45	7	What next?	Project Plan, milestones and deliverables	JB
14:55	8	Final thoughts		CC
15:00		Close of workshop		

TREAT-NMD response to novel therapies for SMA

The expanded SMA dataset project

Craig Campbell MD
Chair TREAT-NMD Registry Committee
December 2019

Context for the expanded dataset project



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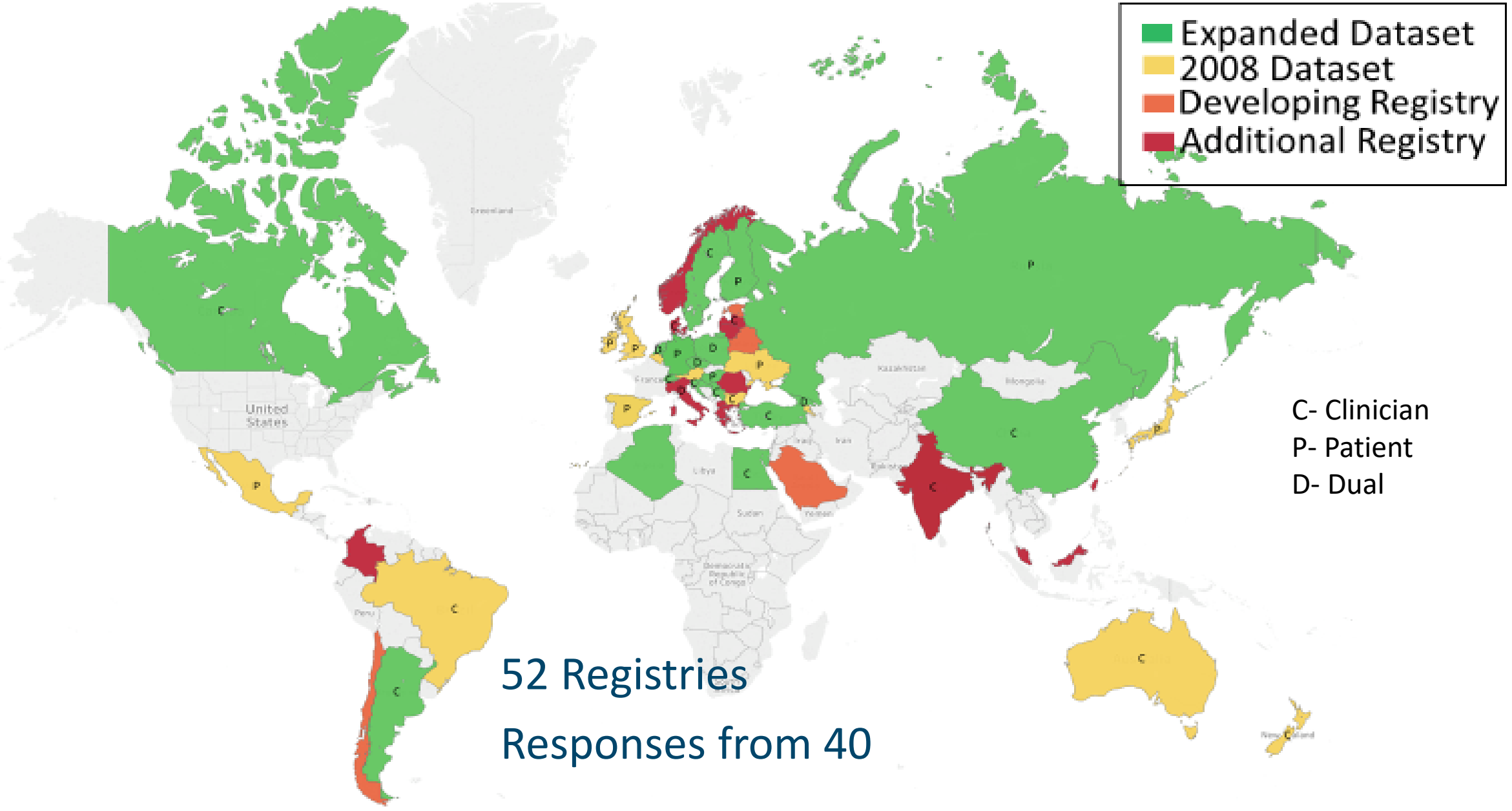
SMA WORKING GROUP LEADS: Victoria Hodgkinson and Miriam Rodrigues

Jo Bullivant

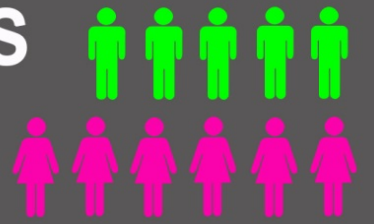
SMA Expanded Dataset
Project Manager

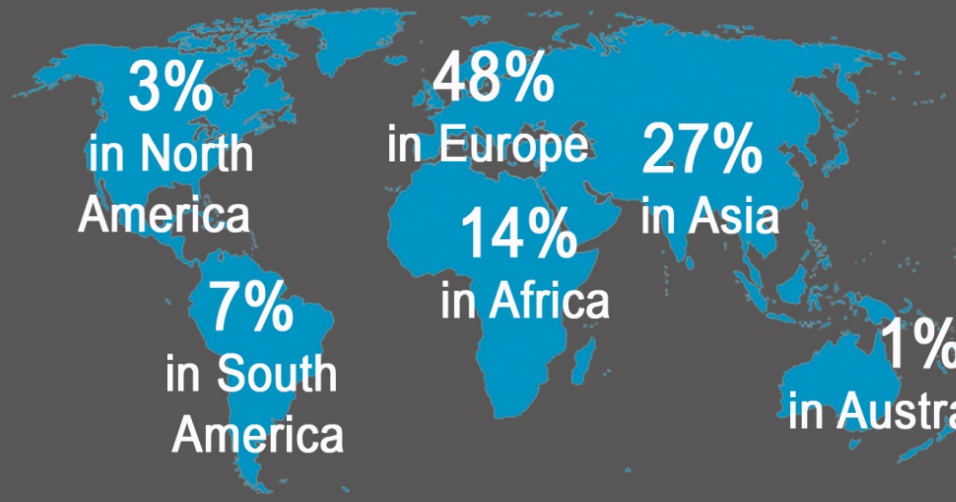
COMMUNITY


Expanded Dataset
2008 Dataset
Developing Registry
Additional Registry
C- Clinician
P- Patient
D- Dual
52 Registries
Responses from 40

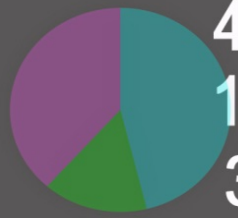
TREAT-NMD GLOBAL SMA REGISTRY SURVEY 2019

Over 9100 patients represented



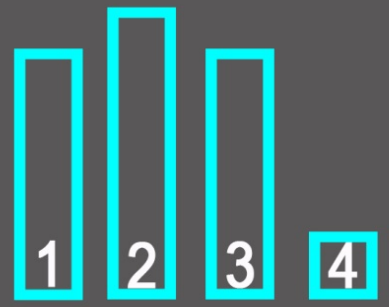


37 registries participated



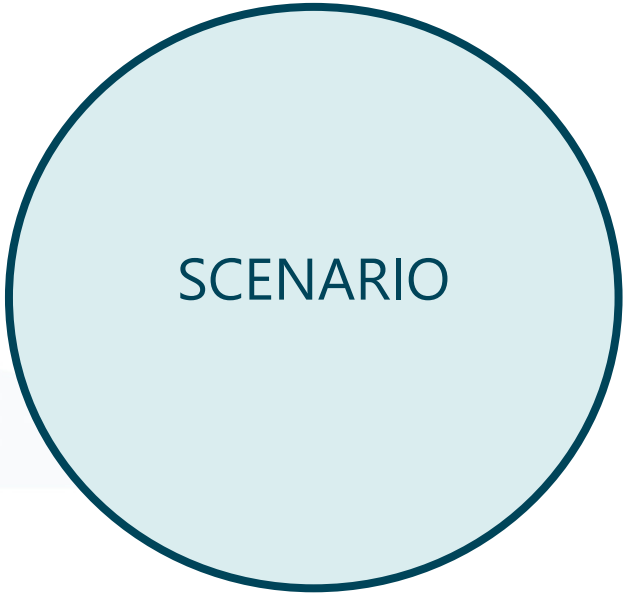
46% clinician-entered
15% patient-entered
39% combination

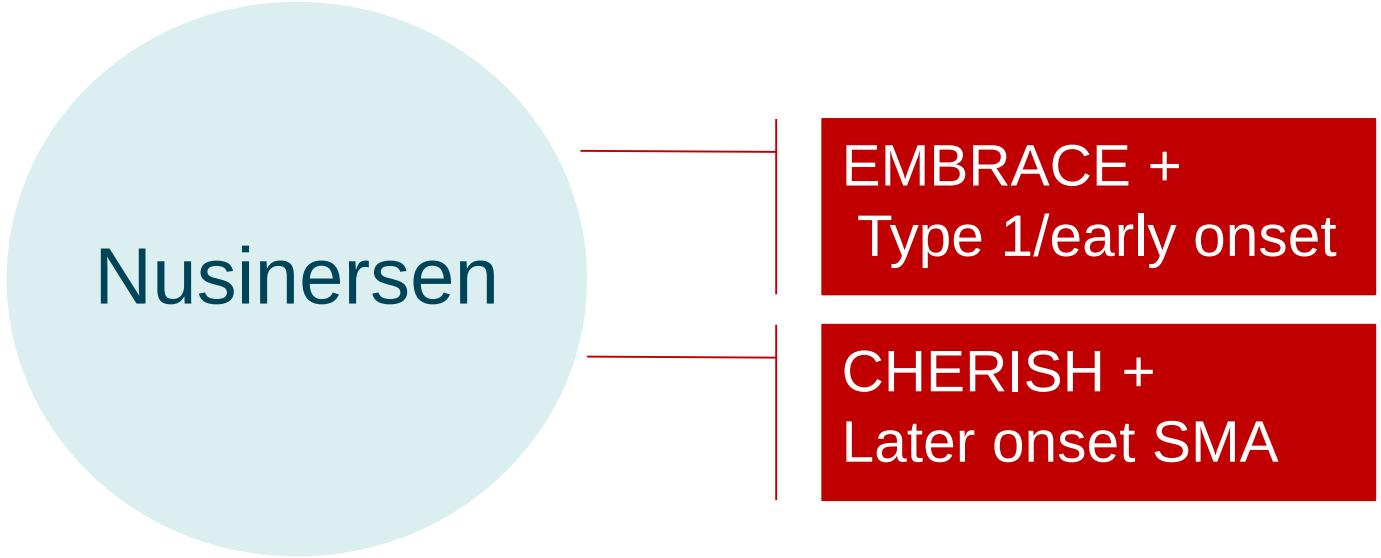
15% patient organisations
19% hospital
54% university
4% government
8% other

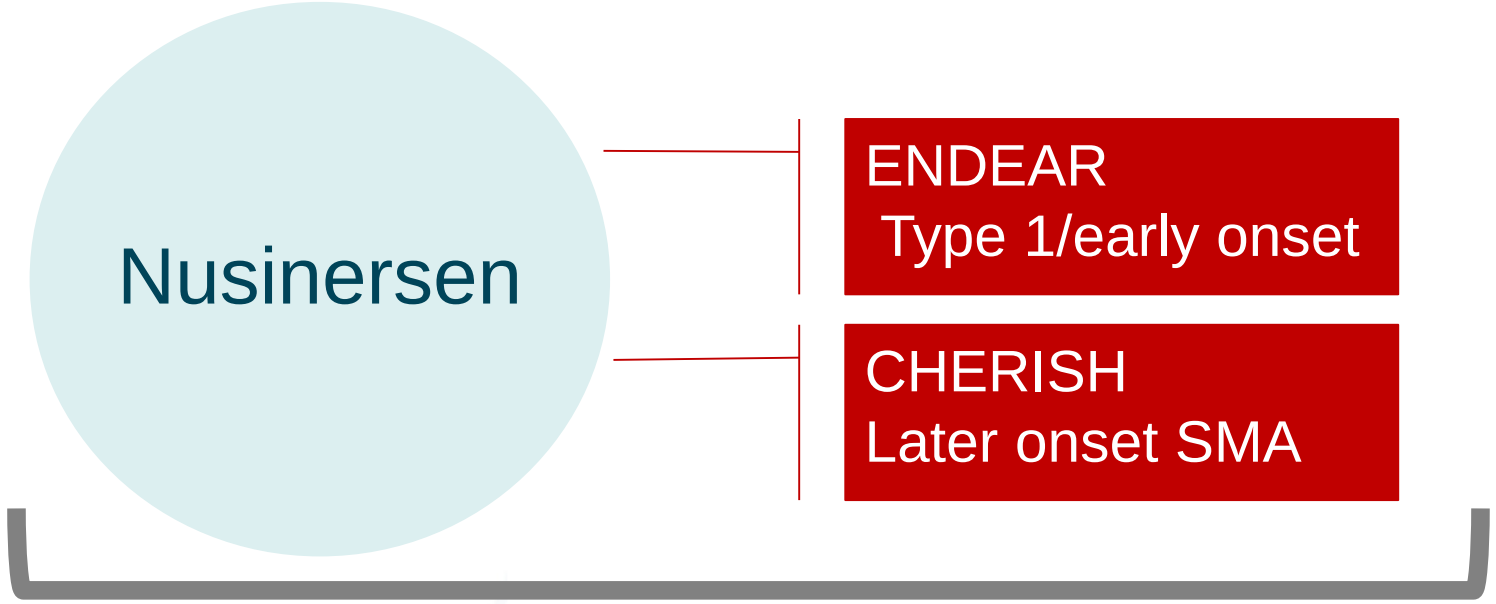


29% SMA I
38% SMA II
30% SMA III
2% adult onset
<1% undefined 5q

Prepared by Victoria Hodgkinson 2019


SCENARIO

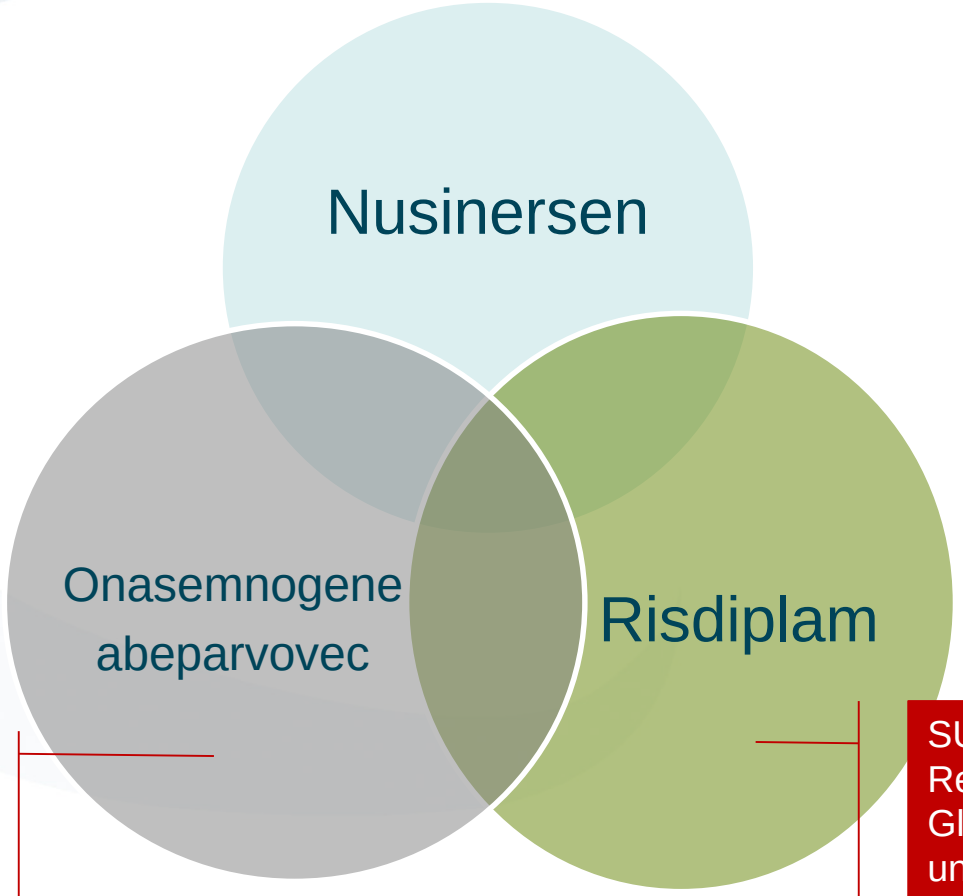

Nusinersen
EMBRACE +
Type 1/early onset
CHERISH +
Later onset SMA



- Newborn screening
- Pre-symptomatic
- Advanced SMA
- Adults

- Variable access
- Differing start / stop criteria
- Uncertainty about monitoring

SMA therapies approved or under regulatory review



- Regulatory response
- Combinatorial treatment
- Clinical opinion
- Reimbursement criteria
- Long term profile

Phase 1 trial +
FDA approved 2019: <2 years
MAP established

SUNFISH TRIAL +
Regulatory submissions started
Global compassionate program underway

Post-marketing surveillance paradigms

REAL WORLD EVIDENCE

Drug specific registry

- Published data limited by industry filter
- EMA and others encouraging a focus on real world evidence approach

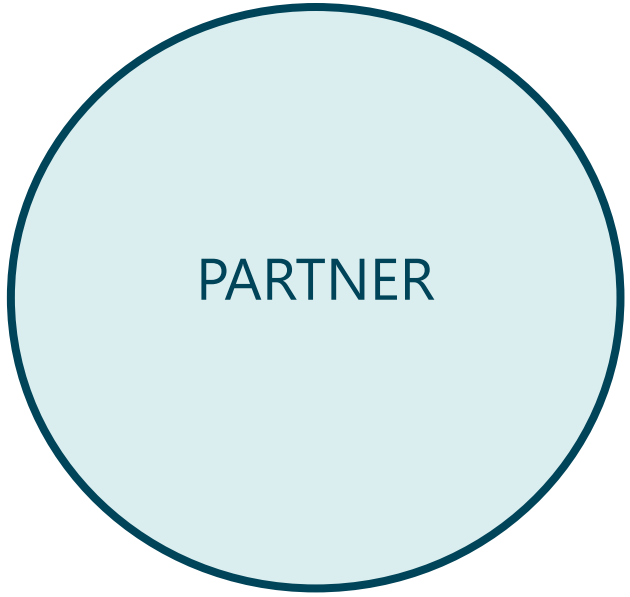
Regular pharmacovigilance and regulatory/payer structure

- Limited information, relies on clinicians/HCP to report
- Information from start/stop criteria collected but may be limited and not usable

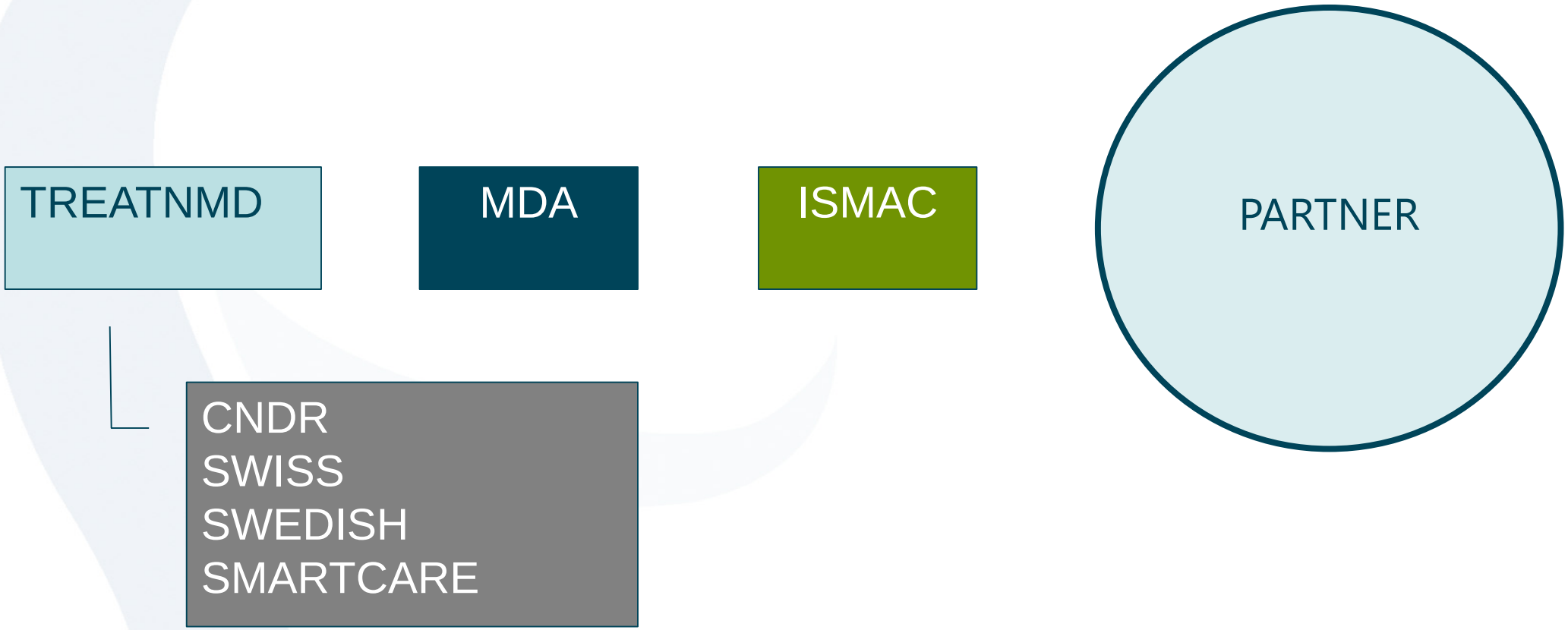
Academic or independent registry

- Data collection for a wider set of stakeholders
- Sustainability and publication of data limited by funding and commitment

BIOGEN MORE THAN A FUNDER



ROSES REGISTRY PROGRAM FOR POST-MARKETING SURVEILLANCE



SMA Post Marketing

- Meeting in Amsterdam May 2017
  - Pre and post consultation with multiple stakeholders
  - Patient organizations, physiotherapy, medical practitioners
- New data set derived that meets needs of commercial drug and new natural history
  - 131 items added
- Phase 1: Pilot registries to assess feasibility
  - 12 pilot registries
- Revisions and ongoing stakeholder engagement
- Significant funding contributions from Biogen with no direct data access

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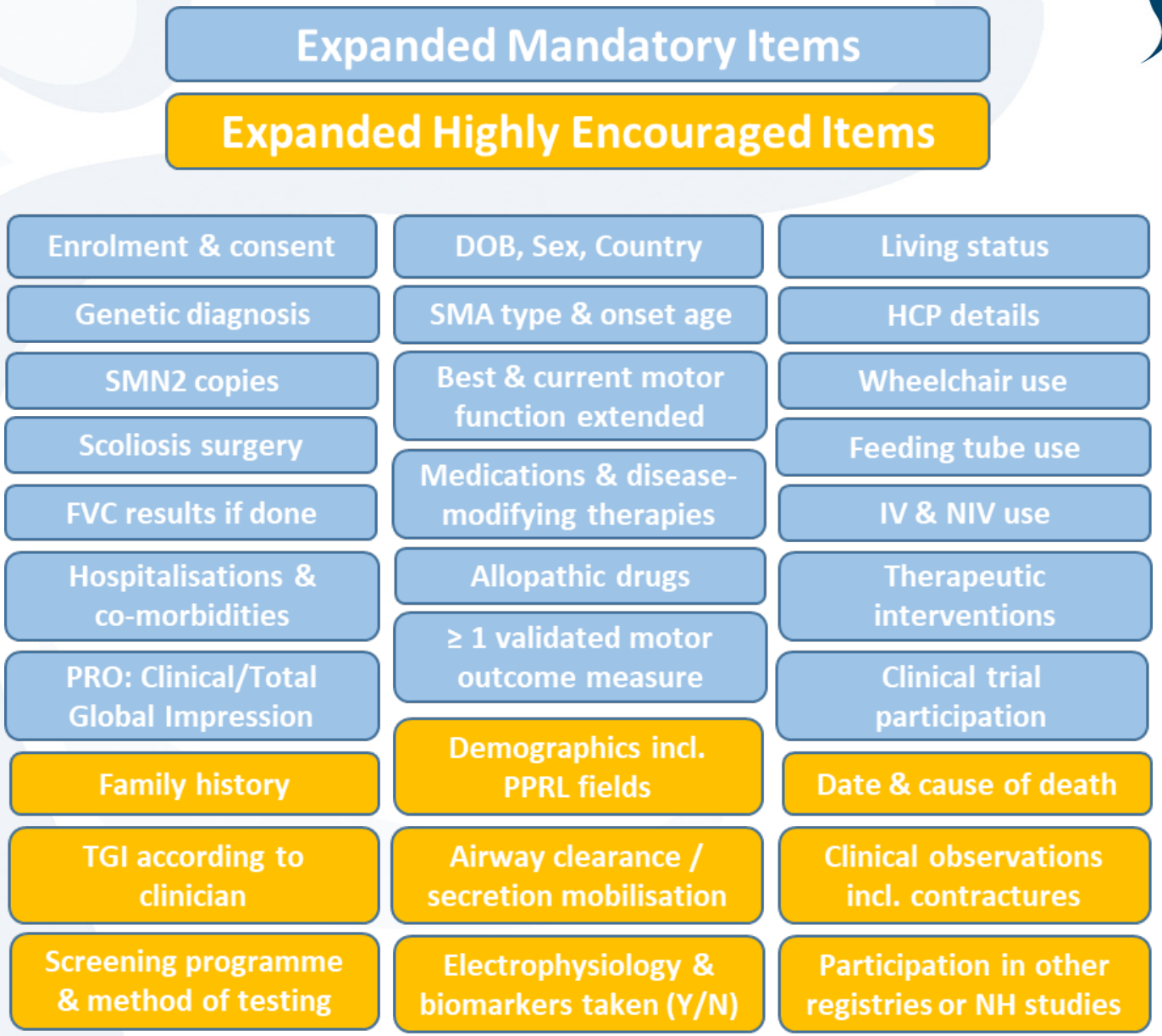


FACTORS:
- importance
-value to post-marketing data
- validity of item
- feasibility

Data harmonization:

- iSMAC
- CureSMA
- MDA

Direct input and advice:

- SMA Europe
- Industry partners: Biogen primary funder
- Many people from many SMA registries helping us to optimize the expanded dataset

Key partners:

- SMArtCARE
- OpenApp
- TREAT-NMD exec

- Phase 2 of project started: 3 year plan
  - Quality control
  - Active processes to address feasibility issues
  - Training and shared learnings
- SMA expanded data set meeting in Leiden Dec 13 2019
- Revision planned for March 2020: aligned with other SMA registries
- Common data platform is still under development
- EMA qualification process started

- Data sharing discussions ongoing with other registries
- Encourage stakeholders to use this RWE

DMD Expanded Dataset Project

Attendees

Working Group: Adnan Manzur, Nathalie Goemans, Anna Mayhew, Craig Campbell, Michela Guglieri, Elizabeth Vroom, Ann Martin, Ilaria Zito, Tina Duong, Ryan Fischer, Anna-Karin Kroksmark, Volker Straub, Eugenio Mercuri, Ulrike Schara, Neil Bennet, Jana Haberlova, Anna Ambrosini, Erik Niks, Alex Johnson

EMA: Xavier Kurz, EMA

FAIR data team: Mark Thompson, LUMC

OpenApp: Cormac O'Brien, OpenApp

Secretariat: Cathy Turner, Heather Hilsden, Becca Leary

Industry representatives: Ashish Dugar, Madeleine Billeter (Sarepta), Paolo Bettica (Italfarmaco), Kerry Rosenfeld (Solid Bioscience), Matthew Anderton (Wave), attendee tbc (Santhera), Abdallah Delage (PTC)

Facilitator: Mark Crabtree, FlintSpark, UK

- DMD stakeholders meeting June 2019
  - revising the dataset to address new natural history and post marketing surveillance
  - Funded by Sarepta
- Pre/post meeting stakeholder engagement
- Workplan developed for pilot phase
- EMA qualification process started

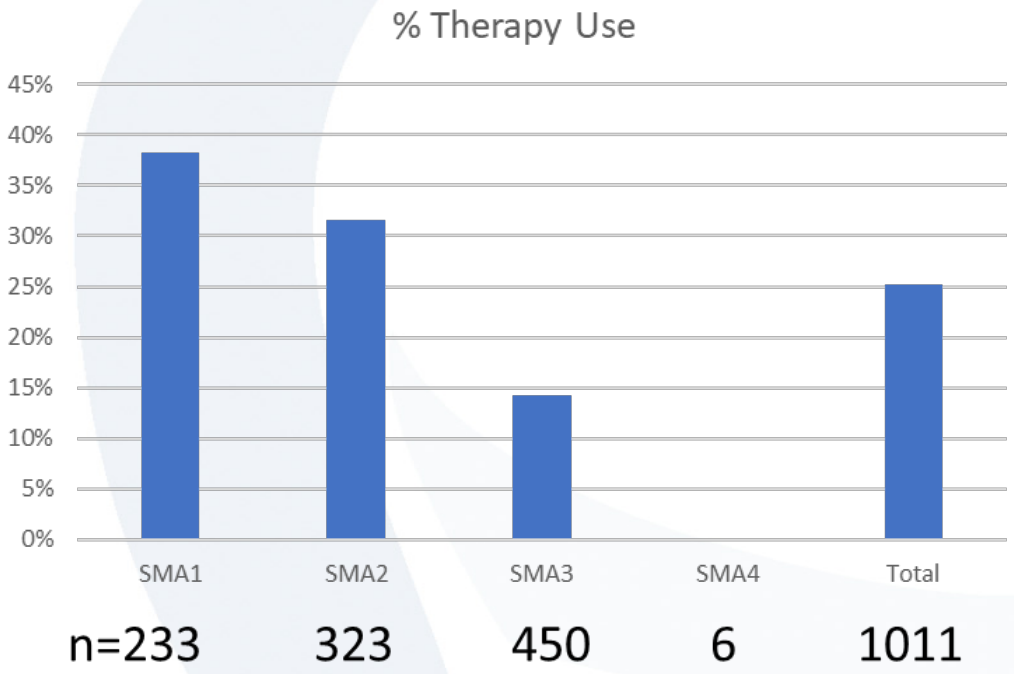
THANK YOU

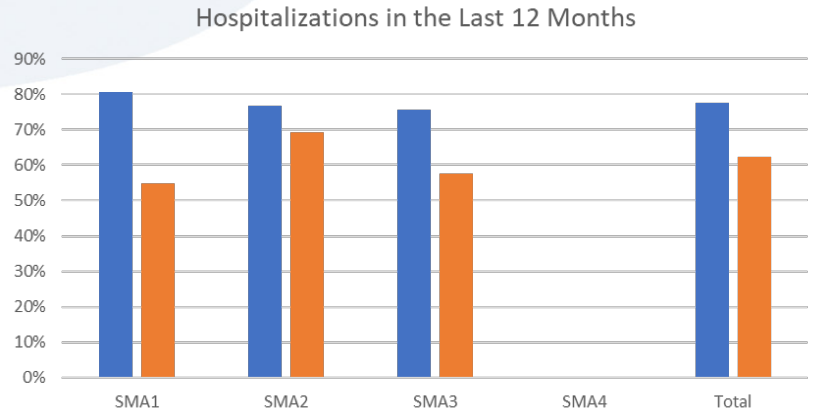
Patients and Families

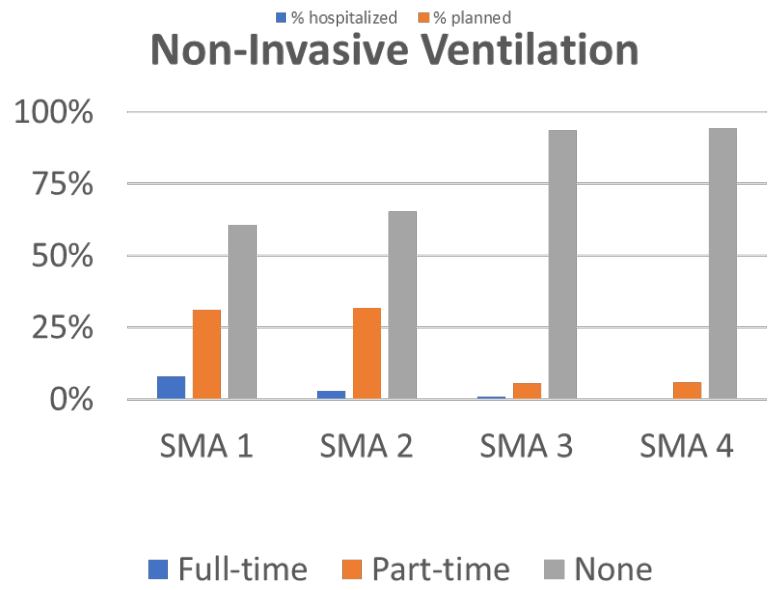
- TREAT-NMD Executive
- TREAT-NMD Secretariat
- Curators and registry leaders across the globe
- Funders and industry partners

THANK YOU

Results from the first phase of data collection







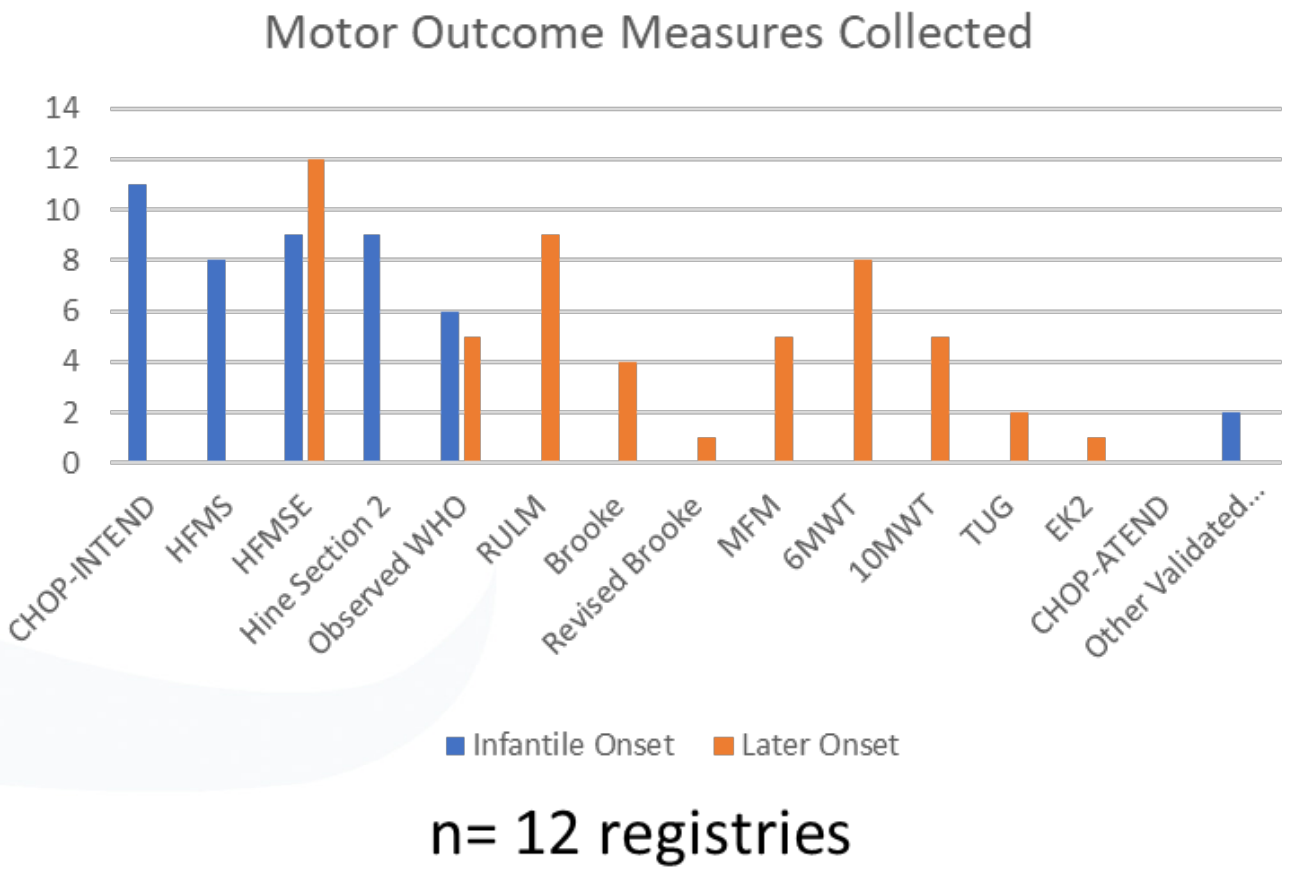
Results from the first phase of data collection

Comorbidities	SMA1	SMA2	SMA3	SMA4	Total
Infectious and Parasitic	1	0	4	0	5
Neoplasms	1	0	5	0	6
Blood and Blood-forming	1	7	3	0	11
Endocrine, Nutritional, Metabolic	32	23	48	0	103
Mental, Behavioral, Neurodevelopmental	2	5	14	0	21
Nervous System	4	6	8	1	19
Eye and Adnexa	4	5	5	0	14
Ear and Mastoid Process	0	0	0	0	0
Circulatory	9	17	41	1	68
Respiratory	74	89	78	1	242
Digestive	27	25	18	0	70
Skin and Subcutaneous	2	7	5	0	14
Musculoskeletal	44	78	78	4	204
Genitourinary	11	16	22	1	50
Preganancy, Childbirth, Puerperium	3	0	0	0	3
Perinatal Period	4	0	0	0	4
Chromosomal Abnormalities	0	4	5	0	9
Other	1	3	3	0	7

Results from the first phase of data collection

Issues

- Motor measures
  - Standardization
  - Untreated population
- SAE's
- hospitalizations



n= 12 registries

SMA Dataset Workshop: Scope and purpose

Scope:

- Target audience: TGDOC Registries taking part in the Expanded SMA Dataset Implementation Plan.
- Also open to: Other registries in the TREAT-NMD network who are working (or intending to work) with the expanded SMA Dataset, or are interested in learning more about the project.

Purpose:

- Provide information and guidance to curators on implementation of the new dataset.
- Provide information about support available.
- Update on this project and related projects.
- Discuss progress and issues.
- Share solutions and best practice between registries

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SMA Dataset Workshop: Feedback on Dataset

- Collecting feedback on the expanded SMA Dataset is not the primary purpose of this workshop.
- The process for feedback and revisions will be presented in Session 3.
- Feedback and suggestions will inevitably arise during discussions today, and this is welcomed and encouraged.
- However we are unable to spend a lot of time discussing suggestions so we will keep a record of everything raised and it will be considered for v2.

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The Universal Platform

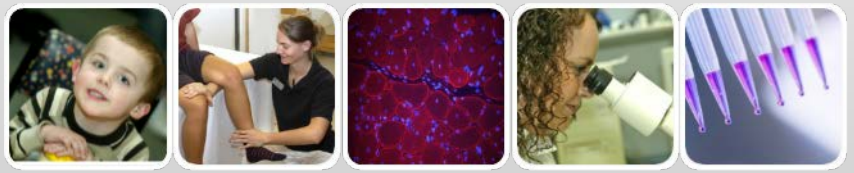
Joanne Bullivant

TREAT-NMD SMA Dataset Project Manager

TREAT-NMD Universal Registry Platform (URP)

Update

Ben Watling (CEO, TREAT-NMD Services Ltd)
Presented by Jo Bullivant (SMA Dataset Project Manager)



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What is the Universal Registry Platform?

Working title: URP

A dual-purpose web-based IT solution:

1. **Support the Global Registry enquiry process** by providing a tool for TREAT-NMD to securely and efficiently accept quality-checked data from different registries, and aggregate/analyse to produce global enquiry reports.

2. **Offer a registry platform where needed**, with relevant core datasets pre-built, to allow affiliated registries to independently* collect/store/analyse their data, and conduct registry management activities. (Thereby also supporting the quality and sustainability of NM registries and registry data across the network)

**TREAT-NMD will not have access to data stored within each registry, nor become involved in the local running of registries (other than providing best-practise guidance where appropriate)*

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Purpose of the Platform

1. Support TGDOC registries in the collection of TREAT-NMD core datasets.

2. Provide a secure and efficient way for registries to submit data for Global Registry enquiries

3. Provide registries with a fit-for-purpose, free of charge registry platform to use **if they wish**

4. Easy to work with and user-friendly

5. Disease modules: accommodate new disease areas and/or treatment options easily

6. Provide quality-assured data for analysis

7. Foster independence and collaboration

8. Support effective real-world data collection and postmarketing surveillance activities to facilitate patient access to appropriate treatment options

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The URP Vision

OPTION 2
- Develop or keep own platform solution and server
- Must include T-NMD core dataset
- Upload requested data to the URP in specified format (manual or automated)

Consent
Redaction
Release

OPTION 1
- Separate & independent 'study' within platform
- Data collected locally from HCPs or patients/carers or both
- Local DM (Curator), independent governance & data ownership
- Secure URP server solution (no T-NMD access to data)
- Core TREAT-NMD dataset pre-built
- No cost to the registry unless:
  - Customisations (e.g. additional data items)
  - Historic data mapping/automated import

Consent
Redaction
Release

Data aggregation
- Historically done locally before submission
- In future, PMS activities may require:
  - More stringent in-built quality controls
  - More agile central analysis
- Careful thought and consultation needed
- Will never be 'one size fits all' and our core global enquiries will continue so both options must be possible in the URP

Co
to
in pla

Redacti
be released or acc

Rel e: Data will be transferred in a timely manner subject to the TREAT-NMD Charter. Release may be automated or manual, immediate or scheduled, and subject to completeness checks by the Central DM.

Data governance boundary

T-NMD Global Data Warehouse
De-identified data with consent confirmation
(under T-NMD / TGDOC governance)

ral T-NMD Roles:
Data Manager (DM)
System Administrator (SA)
Project Manager, Statistician, Admin/Helpdesk

- TGDOC vote/approval
- Data aggregation
- **Consent/redaction/release compliance**

New

Data reports for 3rd party enquiries

Industry/ Academic Research

Feasibility Enquiry

Facilitation of clinical trial recruitment

Postmarketing Surveillance/ Pharmacovigilance data

SAE reports

Natural History

Comparison of treatments

PROM data

Efficacy data

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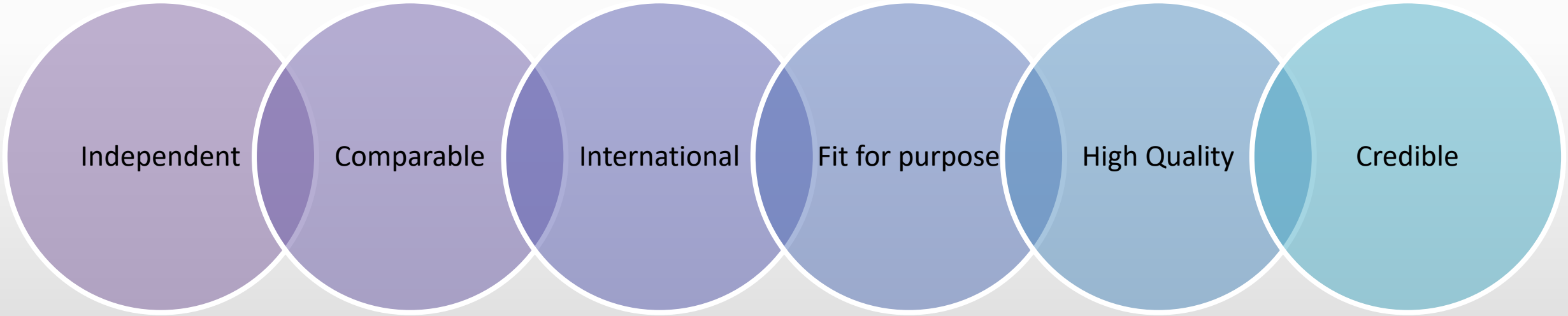
THE URP OFFER TO INDUSTRY

A way of obtaining real world data that is:



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URP Development Status

- **SMA module** approx. 70% complete. Development paused early 2019 due to withdrawal of funding.
- Alternative funding is being sought to complete the work and we are confident this will be in place soon.
- **DMD module** has been commissioned and is in scoping phase with software developers.
- Development of **both SMA & DMD** modules is planned for 2020 with estimated completion by Q4 2020.
- A small group of registries will get the opportunity to ‘pilot’ the modules from Q3 2020.

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The Expanded Dataset

Joanne Bullivant
Project Manager

Joanna Das
Project Co-ordinator

TREAT-NMD SMA Dataset Project Team

Expanded SMA Dataset

Original Mandatory Items

Original Highly Encouraged Items

- Demographics
- Best & current motor function
- SMA type
- SMN2 Copies
- Genetic test result
- Wheelchair use
- Clinical trials
- Pulmonary function
- Family history
- Clinical diagnosis
- Scoliosis surgery
- Feeding function
- Participation in other registries

Expanded Mandatory Items

Expanded Highly Encouraged Items

- Enrolment & consent
- Genetic diagnosis
- SMN2 copies
- Scoliosis surgery
- FVC results if done
- Hospitalisations & co-morbidities
- PRO: Clinical/Total Global Impression
- Family history
- TGI according to clinician
- Screening programme & method of testing
- DOB, Sex, Country
- SMA type & onset age
- Best & current motor function extended
- Medications & disease-modifying therapies
- Allopathic drugs
- ≥ 1 validated motor outcome measure
- Demographics incl. PPRL fields
- Airway clearance / secretion mobilisation
- Electrophysiology & biomarkers taken (Y/N)
- Living status
- HCP details
- Wheelchair use
- Feeding tube use
- IV & NIV use
- Therapeutic interventions
- Clinical trial participation
- Date & cause of death
- Clinical observations incl. contractures
- Participation in other registries or NH studies

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Expanded SMA Dataset

SMA Dataset v1 documents:

1. **SMA Dataset Overview** (high level overview of data items only)

	6. Scoliosis	
6.00	Scoliosis diagnosis?	
6.01		If 'Yes': Cobb angle
6.02	If Yes; has had Scoliosis surgery?	
6.03		If Yes; Surgery technique
6.04		If Yes; Date of first surgery

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Expanded SMA Dataset

SMA Dataset v1 documents:

1. **SMA Dataset Overview** (high level overview of data items only)
2. **SMA Dataset** (data items, response options, baseline/follow-up)

Section 6: SCOLIOSIS

Item no.	Data item description	Coding	Baseline	Follow-up
6.00	Has the patient been diagnosed with scoliosis?	Yes; No; Unknown	X	X
6.01	If 'Yes' to 6.00: Cobb angle according to radiology results	[Numerical value] degrees	X	X
6.02	If 'Yes' to 6.00: has the patient had surgery for the scoliosis?	Yes; No	X	X
6.03	If 'Yes' to 6.02: Surgery technique	Arthrodesis; Growing Rods; Other (specify); Unknown	X	X

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Expanded SMA Dataset

SMA Dataset v1 documents:

1. **SMA Dataset Overview** (high level overview of data items only)
2. **SMA Dataset** (data items, response options, baseline/follow-up)
3. **SMA Dataset Patient-reported Wording** (suggested wording for patient-reported registries)
   - Will be sent next week to all patient-reported registries and patient organisations to invite feedback and will then be aligned with other documents in annual revision process.

Section 6: SCOLIOSIS

Item no.	Mandatory data items	Highly encouraged data items	Coding	Baseline	Follow-up
	Scoliosis Scoliosis is a common complication in people with SMA. It is characterised by a curvature of the spine (usually to one side) and is caused by a weakening of the muscles that support the spine, as the disease progresses.				
6.00	Have you been diagnosed with scoliosis?		Yes; No; Not known	X	X
6.01		If you have been diagnosed with scoliosis, please tell us the Cobb angle recorded on the latest radiology results, if you know it.	[Numerical value] degrees	X	X
6.02	If you have been diagnosed with scoliosis, have you had any surgery for the scoliosis?		Yes; No	X	X
6.03		If you have had surgery for scoliosis, please tell us what kind of surgery you had, if you know.	Arthrodesis; Growing Rods; Other (please specify); Not known	X	X
6.04		If you have had surgery for scoliosis, please tell us the date of your surgery (month & year).	MM-YYYY	X	X

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Expanded SMA Dataset

SMA D

1. SM
2. SM
3. SM
   - ill then be aligned with other
4. SM

6.
Hi

6.
M

Re

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

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Expanded SMA Dataset

SMA Dataset v1 documents:

1. **SMA Dataset Overview** (high level overview of data items only)
2. **SMA Dataset** (data items, response options, baseline/follow-up)
3. **SMA Dataset Patient-reported Wording** (suggested wording for patient-reported registries)
   - Will be sent next week to all patient-reported registries and patient organisations to invite feedback and will then be aligned with other documents in annual revision process.
4. **SMA Dataset Manual** (definitions, guidance on collection and submission, standardised text)

Supporting documents

1. **Annual SMA Dataset Revision Process**
2. **Outcome Measure Toolkit** (May 2020. Information and guidance for registries on the selection and collection of appropriate motor measures and patient-reported outcomes. Signposting to relevant training resources.)

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Expanded SMA Dataset

Crucial to note:

1. Ease and timescales of implementation vary considerably across different registries, for many reasons. TGDOC strives for inclusivity and if registries are not able to implement the full expanded dataset immediately, we encourage open communication and discussion on feasible implementation plans and any support requirements.

2. 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.

3. Data submission process for global enquiries remains unchanged (ad-hoc requests, aggregate data, emailed in Excel). As we discussed yesterday, this may change but this is being carefully investigated and discussed – perspectives from registries are very welcome and helpful.

4. Mandatory vs Highly encouraged. Where an item is marked as mandatory in the TREAT-NMD Dataset, this means it is mandatory for the registry to include this item in its CRF. It does not necessarily mean that it should be a mandatory field in the CRF; for example if it is subject to conditional logic.

    - E.g. 6.00 and 6.02 are both mandatory items so they should both be included in a registry CRF. However 6.02 would not need to be a mandatory field in the CRF as it may be N/A
    - 6.00 Has the patient been diagnosed with scoliosis?
    - 6.02 If 'Yes' to 6.00: Has the patient had surgery for the scoliosis?

5. 'Minimum' Core Dataset. TGDOC registries are free to collect additional data items according to their local needs and/or priorities.

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Expanded SMA Dataset

Crucial to note:

6. As best practise, all data entries and updates should be date-stamped (and time-stamped if possible).

7. If the Unknown / Don't know response option for any given item is not appropriate for your registry, it may be omitted or re-worded (e.g. "To be confirmed" may encourage users to return and complete missing data).

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

7. Annual Dataset Revision Process has been developed to ensure that the core SMA dataset remains appropriate, feasible, collaborative, harmonised with other initiatives, and responsive to the needs of the SMA community WHILST managing the burden of dataset changes on stakeholders.

8. Data Sharing process from the Global Registry remains unchanged (i.e. subject to vote/approval by TGDOC, aggregate data reports provided to 3rd parties).

9. Publications: TGDOC registries dedicate a great deal of hard work, resource and expertise to collection of core datasets. TGDOC want to ensure this is appropriately acknowledged so the Publications Committee are developing a TREAT-NMD Global Registries Publications Policy. Committee Chair: Dr Rasha El Sherif (dr.rashaelsherif@gmail.com)

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Expanded SMA Dataset

Dataset Version 2 (2020) formatting improvements – other suggestions welcome

Version 1

Item no.	Data item description	Coding	Baseline	Follow-up
2.00	Date of birth	DD-MM-YYYY	X	
2.01	First name	[Free text]	X	X
2.02	First name given at birth (if different)^	[Free text]	X	
2.03	Last name	[Free text]	X	X
2.04	Last name given at birth (if different)^	[Free text]	X	
2.05	Sex	Male; Female; Unspecified	X	X
2.06	Sex assigned at birth (if different)^	Male; Female; Unspecified	X	

Version 2

Item no.	Mandatory Data Items	Highly Encouraged Data Items	Coding	Baseline	Follow-up
2.00	Date of birth		DD-MM-YYYY	X	
2.01		First name	[Free text]	X	X
2.02		First name given at birth (if different)^	[Free text]	X	
2.03		Last name	[Free text]	X	X
2.04		Last name given at birth (if different)^	[Free text]	X	
2.05	Sex		Male; Female; Unspecified	X	X
2.06		Sex assigned at birth (if different)^	Male; Female; Unspecified	X	

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Clarity on Outcome Measures in the Dataset

- **Lack of global consensus on most appropriate motor and patient-reported outcome measures to collect; particularly for postmarketing surveillance**
- **Collaborative and inclusive network – felt not appropriate for TREAT-NMD to impose preferences or 'take sides'**
- **However - wish to encourage/support collection of validated outcome measures to track the progression of all patients**
- **Solution for the core dataset v1:**
  - **Clinician-reported registries to collect a mandatory minimum of one validated motor measure per patient.**
  - **PROMs are not mandatory but highly encouraged**
  - **Selection of most appropriate outcome measures is up to the individual registry / clinician**
  - **List of suggested options included in the dataset (split by early/later onset, with recommendations based on SoC and prior use in clinical trials)**
  - **Data requested: Score and date for each OM taken**
  - **Capacity for registries to report any other validated motor measures / PRO used**
- **In development for May 2020: TREAT-NMD Outcome Measure Toolkit**
  - **Summary information about each OM**
  - **Guidance on appropriate populations / conditions for use**
  - **Signposting to training resources**
  - **Links to publications and further information**
- **Annual Dataset Revision Process to respond to (and drive) emerging global consensus**

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TREAT-NMD SMA Dataset Annual Revision Process

Joanna Das
TREAT-NMD SMA Dataset Project Co-ordinator

What is the Annual Revision Process?

The Annual 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.

The Revision Process document outlines:

- Objectives of the Revision Process
- Stakeholders involved and principles of their involvement
- Process and timelines
- Metrics and evaluation

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Annual Revision Process Objectives:

- Allow the dataset (and dataset manual) to be responsive to the needs of the SMA community, but also…
- 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 registries using the dataset on a day to day basis
- Demonstrate feedback is being considered and acted upon where appropriate
- Facilitate continuous improvement

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Our Stakeholder Groups:

- SMA patients and their families
- SMA Patient Advocacy groups and organisations
- Pharmaceutical industry
- Regulators and Payers
- Registry Curators and owners
- Healthcare professionals
- The wider TREAT-NMD and TGDOC community
- Other academic groups or registry initiatives

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Examples of feedback gathered so far….

- At the genetic test Result section, field “SMN2 test”. You might consider changing the name to : “SMN2 Copies test”
- Consistency and rationale for inclusion of ‘Not known’ option
- 12.01 Include ‘Unknown’ option for type of hospitalisation
- 10.01 and 10.04 frequency of IV / NIV – part-time could be further broken down into +/- 16 hours per 24 hours
- As some answers ask for age (YY-MM) and some ask for date (MM-YYYY), should we draw attention to either **AGE** or **DATE** by putting it in caps/bold or similar?
- 11.00 Define what is included in ‘disease modifying therapy’. suggests: Spinraza (nusinersen), Risdiplam, Zolgensma

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Examples of feedback gathered so far….

Consistency and rationale for inclusion of ‘Not known’ option

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12.01 Include ‘Unknown’ option for type of hospitalisation

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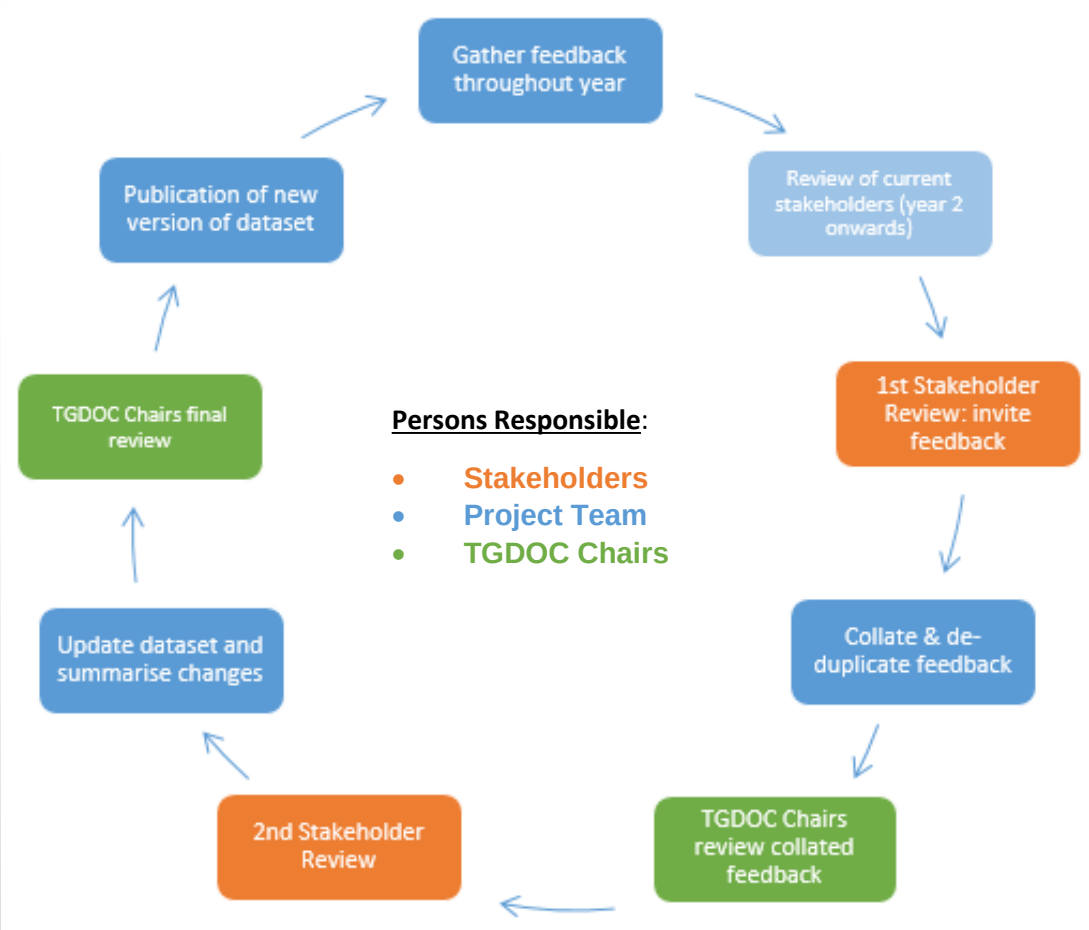
The Process:



Activity	Weeks 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Hold Short Webinar															
2. Circulate current dataset															
3. Collate/Analysie/ Review all feedback															
5. Provide TGDOC Chairs with feedback analysis															
6. Hold TGDOC meeting to agree responses to feedback															
7. Prepare final draft version for circulation															
8. Circulate final draft to stakeholders for feeback															
9. Collate/Analysie/ Review all feedback															
10. Prepare revised documents for approval															
11. Final review by TGDOC Chairs															
12. Publish revised version of documents															
13. Circulate to stakeholders															
14. Update Website															

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Questions?

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Coffee Break

Dataset implementation: Progress so far

Miriam Rodrigues

SMA Subgroup Lead and Curator or Neuromuscular Disease Registry New Zealand

Results of internal survey

- Miriam Rodrigues
- SMA Subgroup Lead and Curator or Neuromuscular Disease Registry New Zealand

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Feedback from registries who have already implemented the dataset

- Sureshkumar Sankeran (India)
- Jana Baberlova (Czech Republic & Slovakia)
- Said M'Dahoma (Canada)
- Marcel Heidemann/ Simone Thiele (Germany – Munich)

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Czech and Slovak SMA registry

Jana Haberlová

Pediatric neurologist, NM Centre Prague

Magda Bařinová

Institute of Biostatistics and Analyses Ltd

Czech and Slovak SMA registry

- Already exist for 8 years

- Run by clinicians with expert supervision (curator)
- Patients themselves can access the registry structure and use the “quality of life” form
- Under IT platform of spin-off company of the Masaryk University

- For Czech and Slovak SMA patients

- From the beginning only basic clinical data were included (3 min form)

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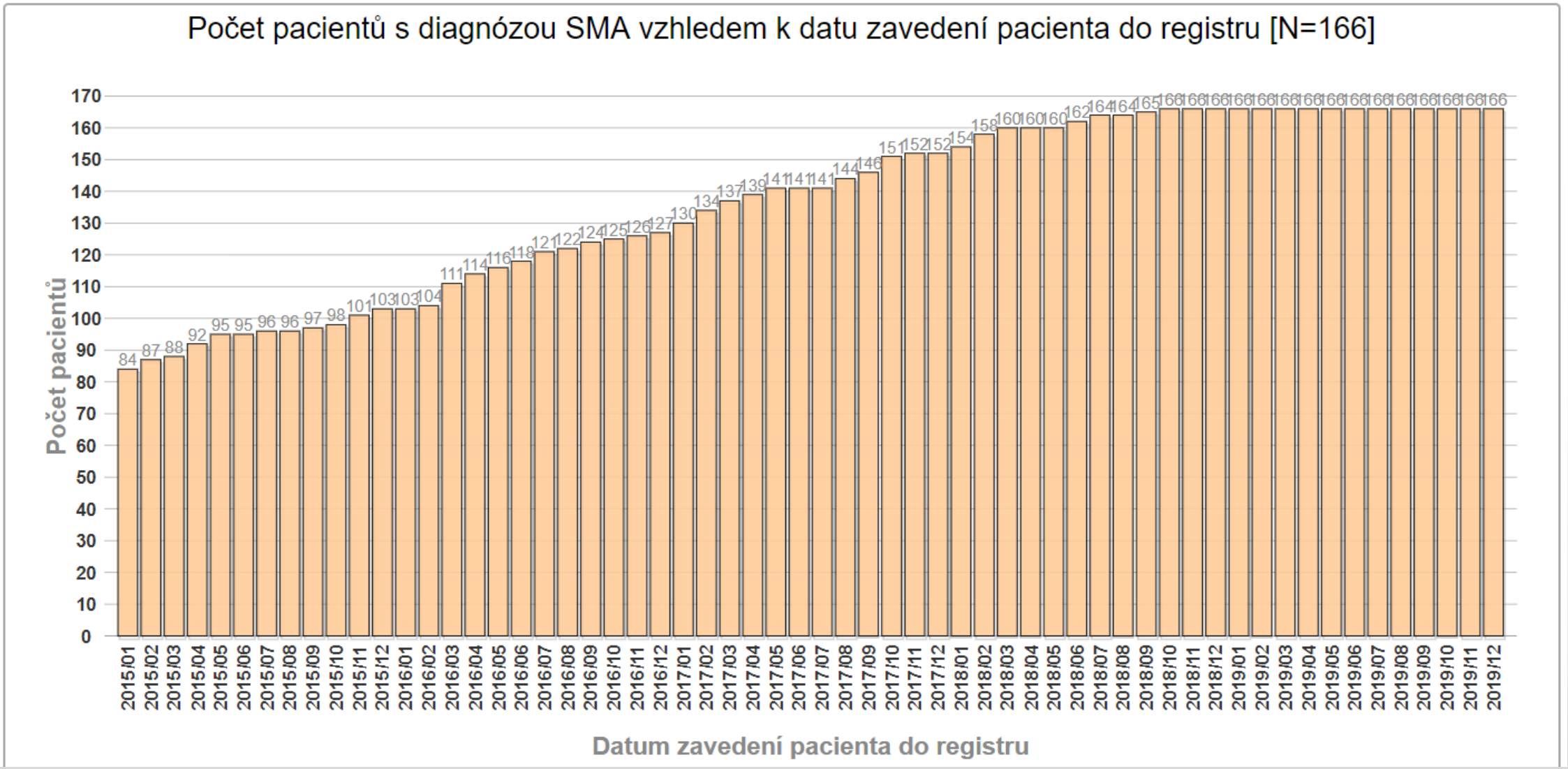
Všechny diagnózy | DMD/BMD | DM | FSHD | SMA | vše | CZ | SK



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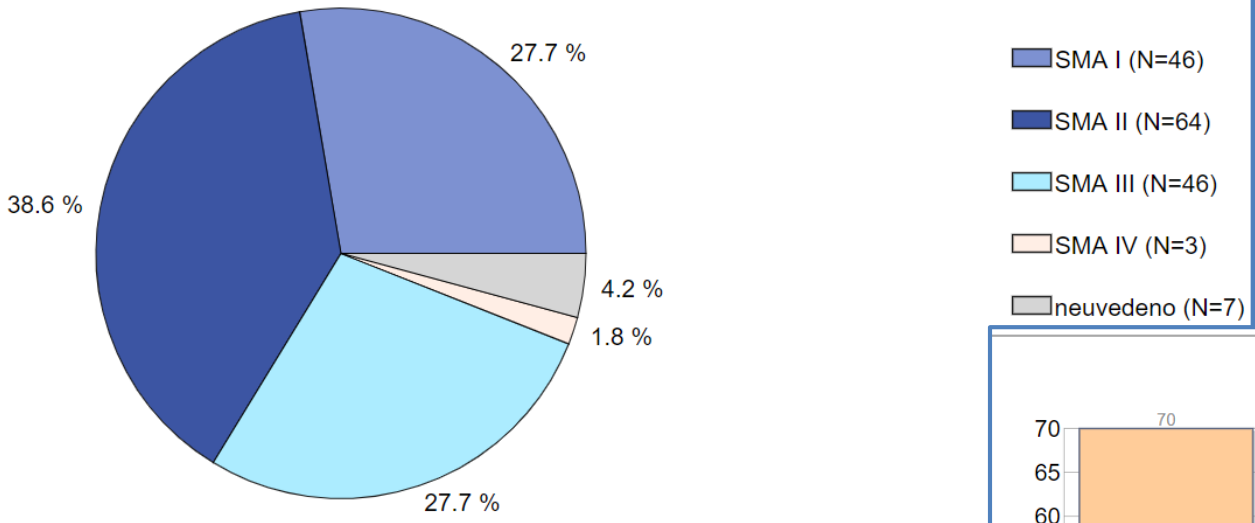
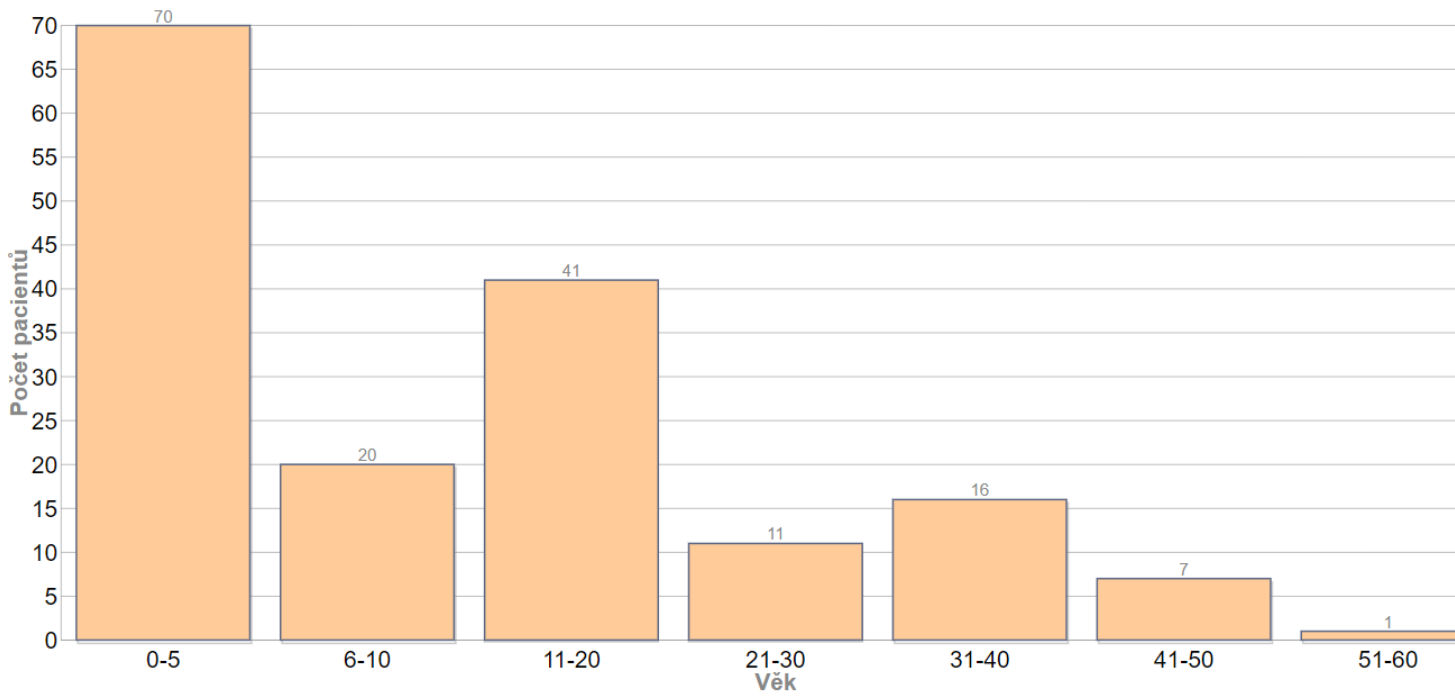
CZ 10 mil, SK 5 mil inhabitants

Počet pacientů vzhledem k diagnóze SMA [N=166]



Věk pacientů s diagnózou SMA při vstupu do registru [N=166]

Věk pacientů s diagnózou SMA při vstupu do registru [N=166]



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Pohlaví pacientů s diagnózou SMA [N=166]

Expanded registry – since April 2019

- **Data set follows the TREAT NMD recommendation**
- **Registry is sponsored by Biogen – 5 years project ⟶ it allows payment for each valid form**

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Difficulties

- **Biogen grant took one year to be administered**
- **Mostly pediatric patients are enrolled in the registry**
- **Only about 70% data forms are valid**

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Positives

- **Data enrolled have high quality (due to the payment and automatic check for validation).**

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Conclusion

- **Collection of natural history data and data of treated SMA patients are highly need it.**

- **In our case data collection is supported by Biogen grant**

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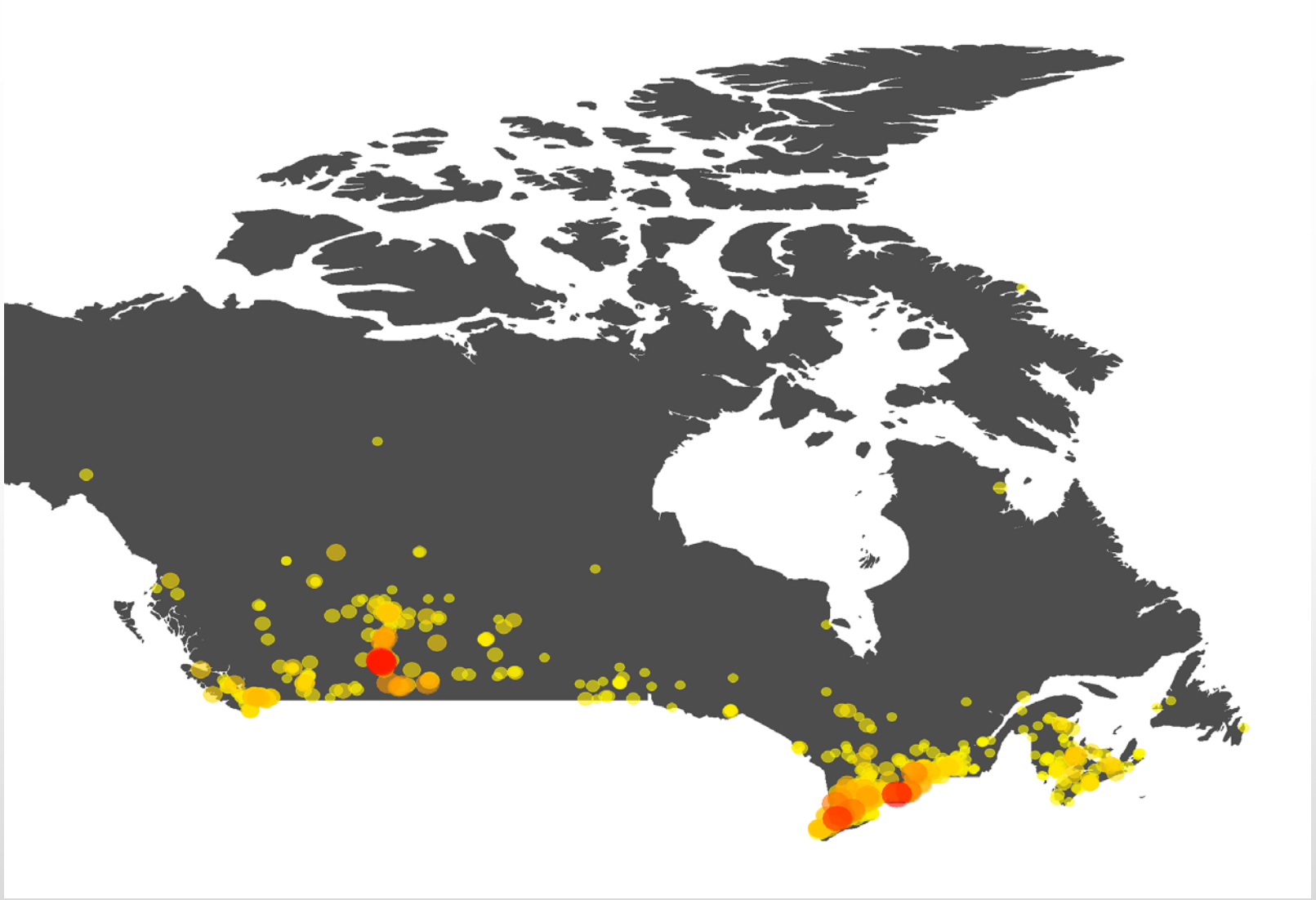
Implementing the SMA expanded dataset in Canada

Said M'Dahoma, PhD

Project Manager, Canadian Neuromuscular Disease Registry (CNDR)

Over *4400* neuromuscular patients from 10 provinces and territories



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cndr.org

Canadian Neuromuscular Disease Registry: A Multi-Centre Collaborative Study

31 clinics (9 new)

55 investigators (9 new)

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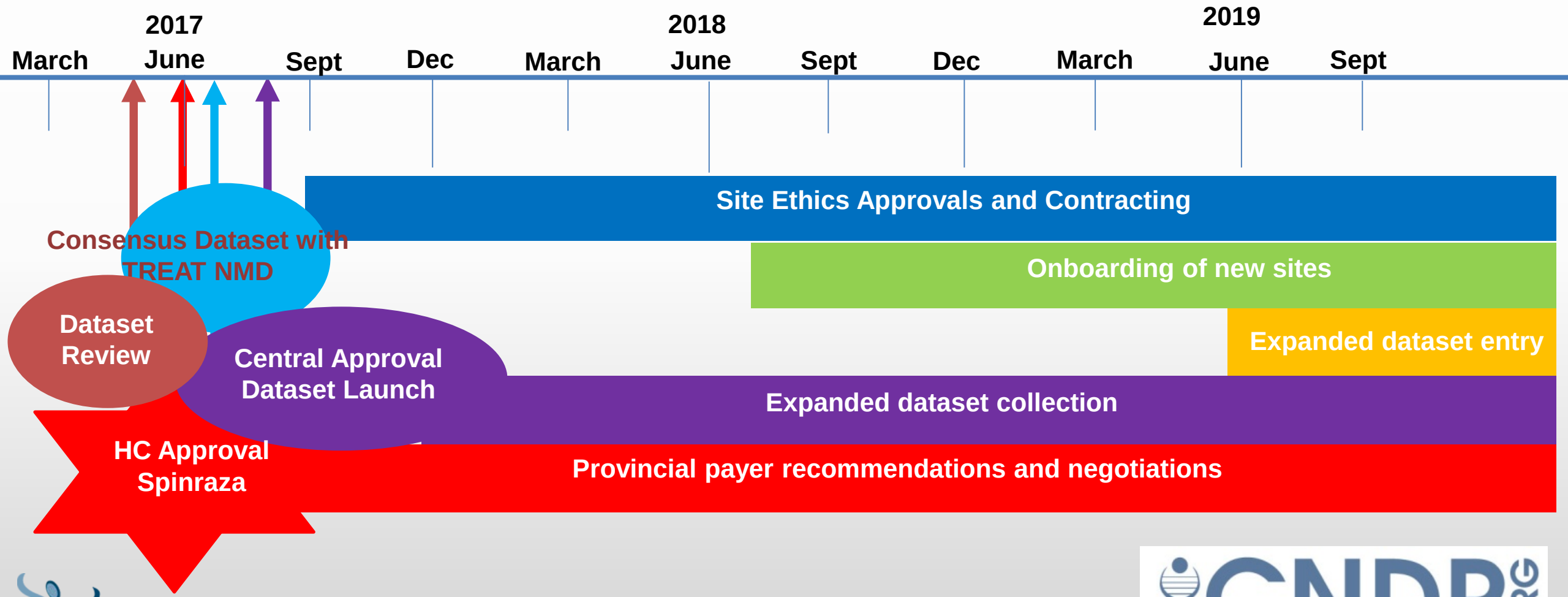
SMA EXPANDED DATASET DERIVATION



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CNDR ORG Canadian Neuromuscular Disease Registry

SMA Pilot Project: RWE Feasibility

- Challenges:
  - Expanded dataset entry has lagged pending ethics and contracting approvals
  - Adult: outcome measures not standard of care for those not on therapy
  - Recruitment Strategies:
    - Provide ongoing recruitment updates to sites
    - Engage PI's, coordinators, and broader team to resolve issues with recruitment and data entry
- Successes
  - Consensus collection of measures
  - Data is being collected across sites, will be entered to platform pending ethics and contracting
  - 220 SMA patients: 71 patients with expanded dataset (including motor measures)

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CNDR Publications in progress

A national spinal muscular atrophy registry for real world evidence.

Hodgkinson V[*1], Oskoui M[*2,3], Lounsberry J[1], M'Dahoma S[1], Butler EA[1], Campbell C,[4] MacKenzie A[5], McMillan H[5], Simard L[6], Vajsar J[7], Brais B[3], Chapman K[8], Chrestian N[9], Crone M[10], Dobrowolski P[11], Dojeiji S[12], Dowling JJ[6], Genge A[3,13], Izenberg A[14], Leung E[15], Lochmüller H[5,16], Mah JK[1,17], Marerro A[18], Massie R[3,13], McAdam L[19], McCormick A[5], Melanson M[20], Mezei MM[8], Nguyen CTE[21], O'Connell C[22,23], O'Ferrall E, Pfeffer G[1], Phan C[11], Plamondon S[1], Poulin C[2,3], Rodrigue X[24], Schellenberg K[25], Selby K[26], Sheriko J[27], Shoesmith C[28], Smith G[29], Taillon M[22,23], Taylor S[20], Warman J[5,16], Worley S[22,23], Korngut L[1]

Submitted for review: CJNS, 2019

The Canadian Neuromuscular Disease Registry 2010-2019: a decade of facilitating clinical research through a nationwide, pan-neuromuscular disease registry.

Hodgkinson V[1], Lounsberry J[1], M'Dahoma S[1], Benstead T[2], Campbell C[3], Johnston W[4], McCormick A[5], Nguyen CT[6], O'Ferrall E[7], Oskoui M[8], Brais B[7], Briemberg H[9], Bourque P[10], Botez S[11], Cashman N[12], Chapman K[13], Chrestian N[14], Crone M[15], Dobrowolski P[4], Dojeiji S[16], Dowling J[17], Dobrowolski P[4], Dupré N[18], Genge A[7], Gibson G[12], Grant I[2], Hasal S[15], Izenberg A[19], Kalra S[4], Katzberg H[20], Krieger C[12], Leung E[21], Linassi G[22], Lochmüller H[23,16], Mackenzie A[23], Mah JK[1], Marrero A[24], Massie R[7], Matte G[25], McAdam L[26], McMillan H[23], Melanson M[27], Mezei MM[28], O'Connell C[29,30], Pfeffer G[1], Phan C[4], Plamondon S, Rodrigue X[31], Schellenberg K[22], Selby K[32], Sheriko J[33], Shoesmith C[34], Smith G[35], Taillon M[29,30], Taylor S[27], Venance S[34], Warman J[16], Worley S[29,30], Zinman L[19], Korngut L[1].

In preparation

Neuromuscular Network

Ongoing and Future SMA Projects

Direct-to-patient

- Patient engagement: for patient perspectives on research/data collection
  - Priorities for research: What data should we be collecting?
  - How would you use online questionnaires/ patient portal?
- Direct-to-patient data collection: ability to build in questionnaires and data sets to send electronically to patients (English and French)

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Thanks

CNDR SMA working group:

Maryam Oskoui (lead)

Craig Campbell (CNDR pediatric lead)

Alex MacKenzie

Hugh McMillan

Jiri Vajsar

Guy D'Anjou

CNDR National Office:

Funding for the CNDR SMA registry provided by:

Biogen

CureSMA Canada

Victoria Hodgkinson

Josh Lounsberry

Said M'Dahoma

Lawrence Korngut

SPINAL MUSCULAR ATROPHY

REGISTRY EVOLUTION-INDIAN SITE PERSPECTIVE

Dr V.Viswanathan DCH, MRCP, PhD
Sr. Consultant Pediatric Neurologist
&
Dr S.Sureshkumar PhD
Sr. Physiotherapist

INCIDENCE OF DISABILITY

- Physically challenged population accounts for 2.22% of the population
- Tamil Nadu accounts for 1.6 million persons with disability
- Visual (19%) Speech (19%), Multiple disability (8%) Movement (20%).

(*Statistical Profile 2016, Ministry of Statistics &Project Implementation*)

Spinal Muscular Dystrophy

- Progressive anterior horn cell disorder
- Starting in fetal life and continues to progress in Infancy & Adulthood
- Incidence being 1:6000 to 1:10000
- Type 1 – commonest
- Highest incidence next to Duchenne Muscular Dystrophy

Spinal Muscular Atrophy

Incidence 1:6000 to 1:10000

- Indian population is around 133 crores people
- Extrapolating from the data we should have approximately **79800-133000 patients with SMA.**
- Second to DMD which accounts for 2 lakhs patients.

Evaluation of SMA patients

Can we have a consensus for which tests to do for whom / which age ?

- Hammersmith Functional Motor Scale (HFMC)
- Hammersmith Neonatal Neurological Examination (HNNE)
- Hammersmith Infant Neurological Examination (HINE)
- Gross Motor Function Measure
- Egen Klassifikation Scale (Wheel chair Functioning)
- Bayley Scales of Infant Development

Requirement

- Height & Weight Machine
- Inch tape
- Knee hammer
- Mattress
- Bolsters
- Laptop
- Staircase
- Scanner
- Printer
- Internet Connection
- 150 sqft room
- Table & Chairs
- Stationeries







Our Approach – MDA India - SMA registry

- We maintain a **secure Google Based Platform with the help of our IT expert – Mr.Venkatesh**
- It is a **clinician entered** data entry
- **Consent** is obtained before data is collected from the family
- All patients with **genetically confirmed SMA** are entered from our OPD clinics
- All patients are **children** either newly entered or on follow up at our clinics
- **1st time entry** is considered **first visit** for the registry at present.
- We intend to **follow up once every** 6 months

Process Flow

- Demographics
- Clinician Assessment
- Physical therapy Assessment

Planning for Registry

	First Visit (Initial)	Second Visit (6 months)	Third Visit (One year)	Fourth Visit (Year Two)
Demographics	X			
Anthropometrics & Family Pedigree	X			
Clinical Examination	X	X	X	X
Xrays	X			
DEXA	X			
Nutritional Assessment	X			
Swallowing Assessment	X			
Physical Evaluation • Motor	X	X	X	X

Contracting / Agreements

- **MDA India** – for the data entry operator
- **MDA India -** for website development, Laptop, physiotherapy evaluation equipments.
- **Scans World** – for X rays of spine / bone densitometry – **limitations** is lack of standardization for this age group – we are slowly evolving our own basic standards with the help of Dr.Gopinath
- **Sugan Hospitals** for pulmonary function tests

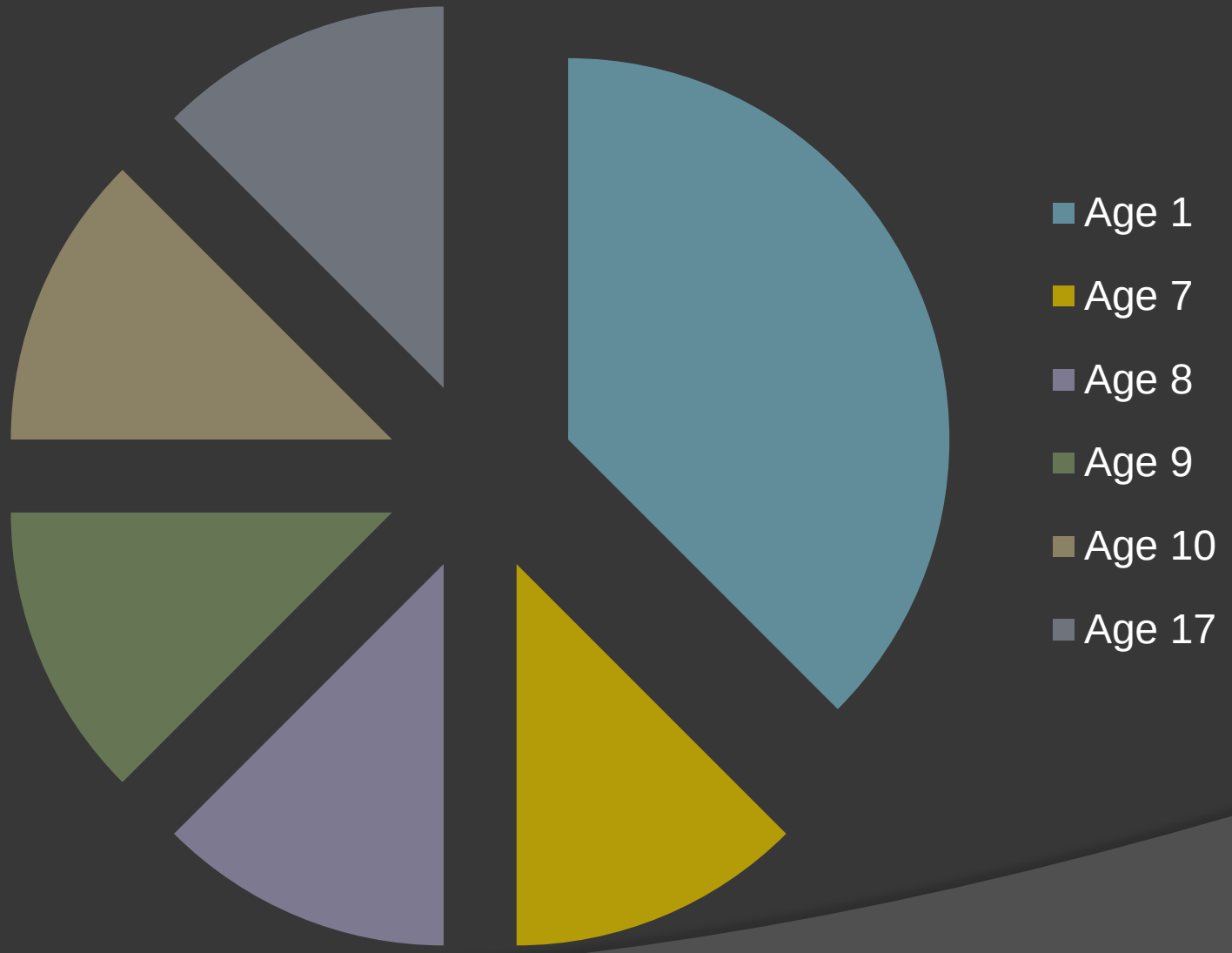
Tools Used

- Hammersmith Neonatal Neurological Examination (HNNE)
- Hammersmith Infant Neurological Examination (HINE)
- Hammersmith Functional Motor Scale (HFMS)
- Child above six years Pulmonary Function tests

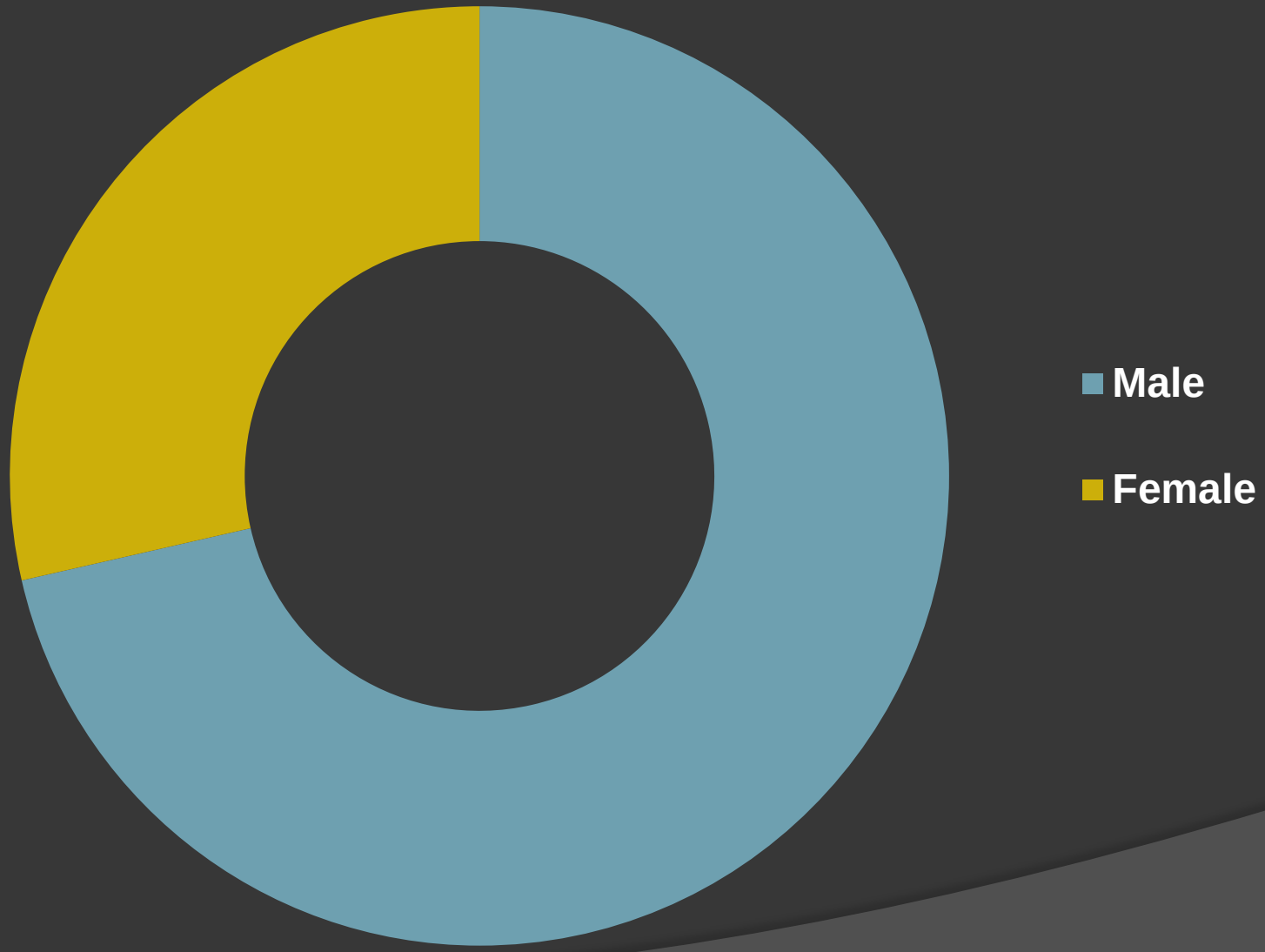
Other Investigation

- X-rays
- DEXA Scan

Distribution in Age



Sex Distribution



Issues

- Common presentation is **Type 1 SMA** – very **difficult to get clear cut measurements which are uniform** at different centers and at different times even in the same child.
- Even though there are many assessment scales, it is **still not clear** how to assess the children at which ages – **needs further clarification and training**
- HNNE, HINE & HFMS for different age groups
- In ambulatory adult apart from the motor measure we did Pulmonary function testing

MDA India new efforts

- We have now succeeded in persuading the **Indian Council for Medical Research (ICMR)** and **National registry for NMD** has just commenced – with **DMD, SMA and LGMD**
- **4 Nodal centers** and **49 resource centers** all over India have showed interests in participating in the national registry.
- **ICMR project** is being **funded by the Govt of India** under the rare Disorders Registry

Future

- We should have more **clear statistics** about DMD, SMA and LGMD by the end of 2020
- Our intention is to **follow up** all these patients at all the centers
- As the centers **involve different parts of India** we hope to have more wide coverage of the different parts of India
- Help with **more research** happening in India and help with **more interventional studies** in India

SMA Patient Registry for Germany and Austria

Simone Thiele, Marcel Heidemann

Friedrich-Baur-Institut, Ludwig-Maximilians-Universität München

TREAT-NMD Neuromuscular Network

Registry Overview

- Launch in 2008 with the TREAT-NMD minimal and highly encouraged dataset
- Currently approx. 900 SMA patients
- Web-based, patient-reported system
- Custom web application based on Java EE

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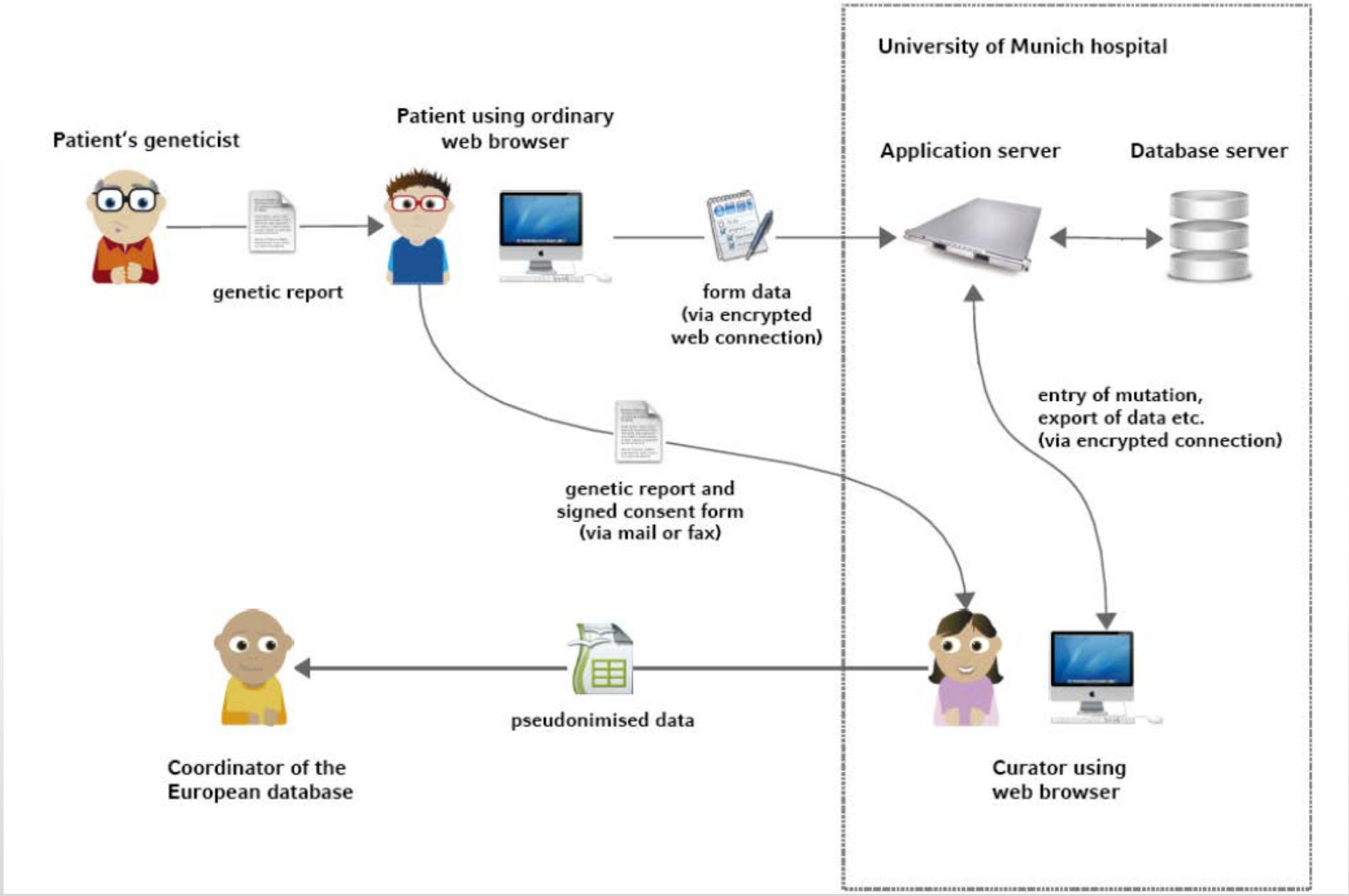

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Sie sind mit der E-Mail-Adresse post@marcelheidemann.de angemeldet.
ABMELDEN

FSHD | PAM/MFM | IBM | CMT | DMD/SMA-PATIENTENREGISTER | DM | FKRP | NETZWERK

- ÜBER DAS REGISTER
- BEHANDLUNGSSTANDARDS
- KLINISCHE STUDIEN
- NEWSLETTER
- KONTAKT AUFNEHMEN
- ÜBERSICHT
- IHRE PATIENTENDATEN
  - Fragebogen (Teil 1)
  - Fragebogen (Teil 2)
  - Genetik

Fragebogen (Teil 1)

Diese Seite enthält den ersten Teil der Fragen zu Ihrem Gesundheitszustand. **Bitte beantworten Sie alle Fragen auf dieser Seite,** da alle Angaben notwendig sind, um Ihre Daten in das europäische Register einzutragen. Wenn Sie jedoch eine Information momentan nicht parat haben, belassen Sie die Antwort zunächst auf „Keine Angabe" und fahren Sie mit den anderen Fragen fort; die fehlende Antwort können Sie dann später nachtragen.

Sie können jeweils nur eine der möglichen Antwort auswählen. Falls keine der angegebenen Möglichkeiten genau zutrifft, wählen Sie einfach die Antwort aus, die am ehesten passt.

Wenn Sie fertig sind, klicken Sie unten auf den Knopf „Speichern".

Was ist Ihre Diagnose laut Ihres behandelnden Arztes?

- ○ Spinale Muskelatrophie (SMA)
- ○ Spinobulbäre Muskelatrophie Typ Kennedy
- ○ Andere Erkrankung

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Key challenges for the dataset expansion

- Patient burden
- Implementation of items
- Migration and usage of existing data

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Patient burden

- The questionnaire must be short, clear and easy to use
- Long questionnaires may frustrate patients and lead to incomplete data
- Unclear wording may lead to false data
- Limited resources for curation and support

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Implementation of items

- Longitudinality poses the most difficulties
- The data should be: complete, detailed and accurate
- On the other hand, the patient should not have to re-enter data on follow-up

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Example: Ventilation in dataset

Data item description	Coding
Has the patient ever used invasive ventilation?	Never; Previously (start and end date MM-YYYY); Currently (start date MM-YYYY); Unknown
If 'Yes' to 10.00: Frequency of invasive ventilation	Full-time; part-time; unknown
If 'Yes' to 10.00: Invasive ventilation start date (month and year)	MM-YYYY

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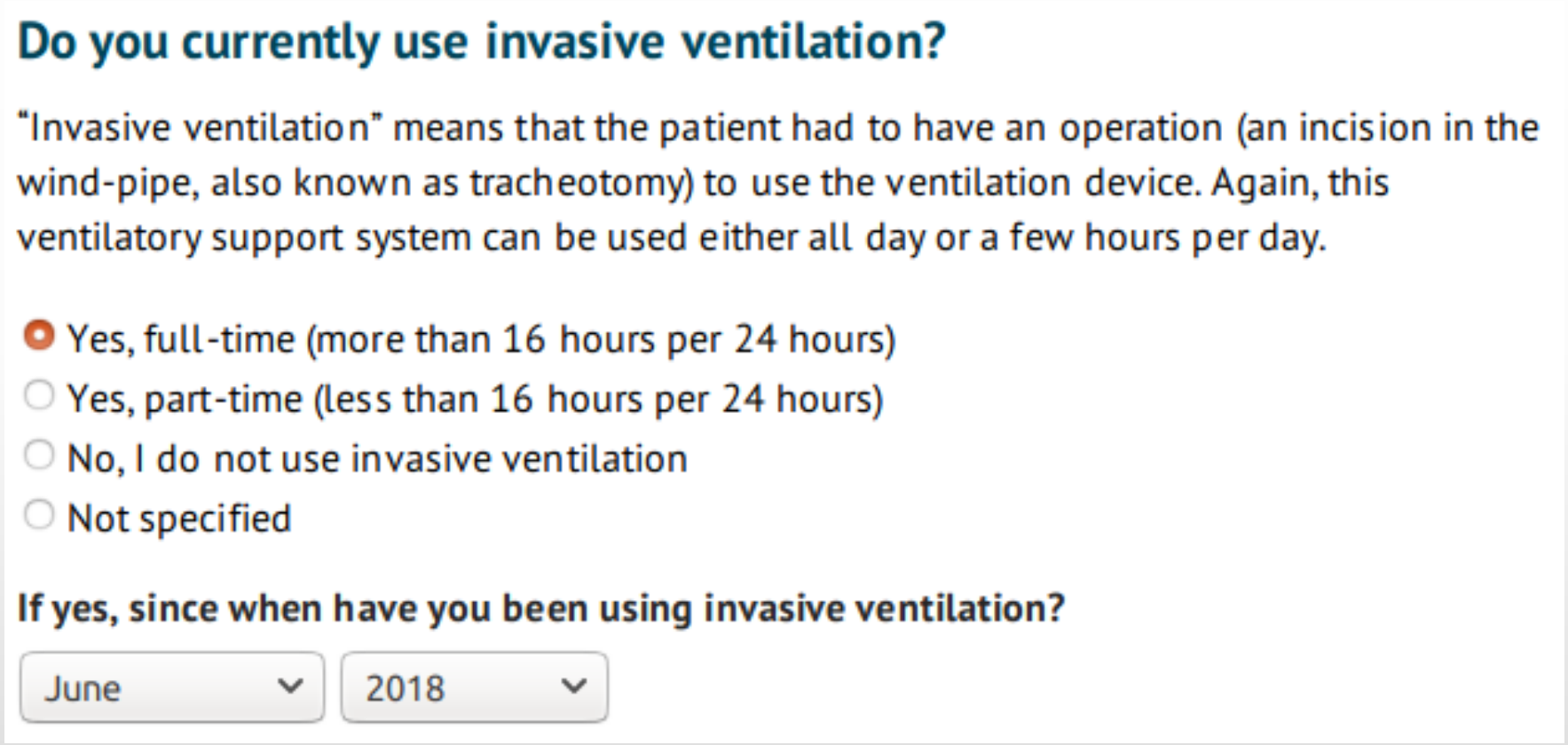
Example: Ventilation in registry (1)



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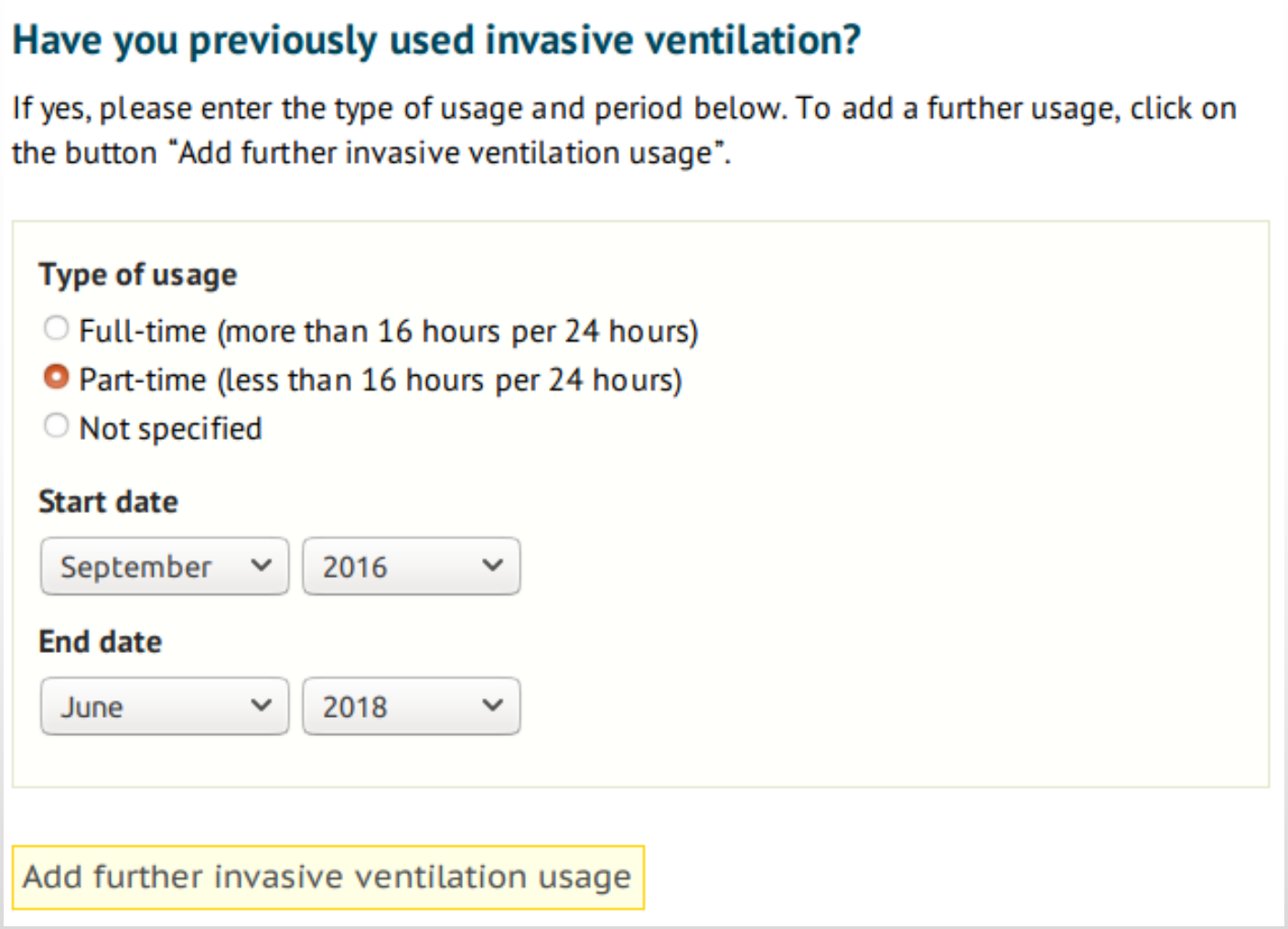
Example: Ventilation in registry (2)



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Migration and usage of existing data

- Many existing items are modified in some way
- In some cases, only further items or options are added
- In other cases, previous options are replaced
- The data already collected should stay usable, but without managing two separate datasets

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Example: Feeding tube

Gastric/nasal tube (Yes / No / Unknown)	Nutritional supplementation via nasogastric or nasojejunal tube or gastrostomy

Data item description	Coding
Has the patient ever used a gastric or nasal feeding tube? (Select all that apply)	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

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Lunch

Support Available

Joanne Bullivant
Project Manager

Joanna Das
Project Co-ordinator

TREAT-NMD SMA Dataset Project Team

SMA Dataset Bursaries

Joanna Das
TREAT-NMD SMA Dataset Project Co-ordinator

Support for Registry Curators

- **Why?**

To support Curators to implement the new core SMA Dataset which can be time consuming and costly.

- **What support is available?**

An €8000 bursary is available to registries taking part in the SMA Dataset Implementation Plan.

- **Who is not eligible?**

Registries receiving financial support directly from Biogen.

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How will it be paid?

- Paid in two parts:
  - **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:
    - evidence of all mandatory items being collected
    - feedback on the dataset and implementation process.

- Both parts can be claimed together if all part B conditions can already be met.

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To request your bursary:

BURSARY PART A	
	Complete **Part A** of the Bursary Request Form and send to the Dataset Project Manager
	The Dataset Project Manager and TGDOC Chairs/Secretariat will review the request and approve/ask for more details if needed
	Once approved, submit an invoice to Newcastle University for the Part A amount.
	Newcastle University (on behalf of TREAT-NMD) pays Part A of the bursary to the registry
BURSARY PART B	
	When Part B conditions are fulfilled complete **Part B** of the Bursary Request Form and send to the Dataset Project Manager
	Repeat Steps 2-4 above

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Questions?

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Dataset Manual

Joanne Bullivant

TREAT-NMD SMA Dataset Project Manager

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Expanded SMA Dataset Manual

What is included?

- **Introduction / context / background / contacts**
- **Important notes on:**
  - **Identifiable data**
  - **Data submissions**
  - **Dataset compliance**
  - **Dataset key**
  - **Response options**
- **Feedback, harmonisation, revisions**
- **Data sharing and publications**
- **Standard (suggested) text for patient information, consent, ethical approval applications, protocols etc**
- **Dataset dictionary, for each data item:**
  - **Mandatory/optional**
  - **Patient / Clinician reported**
  - **Definitions if needed**
  - **Instructions if needed**
  - **Response options**

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SMA Dataset Manual Interactive Session

Group	Sections for review: *20 minute review in groups -> 5 minute feedback to workshop*
1	Section 1 Enrolment Section 2 Demographics Section 3 Living Status
2	Section 4 Genetic Diagnosis Section 5 Clinical Observations
3	Section 6 Scoliosis Section 7 Motor Function Section 8 Wheelchair use
4	Section 9 Nutrition Section 10 Pulmonary Function
5	Section 11 Therapies and Medications
6	Section 12 Hospitalisations and Comorbidities
7	Section 13 (Clinical Research) and Section 14 Motor Measures
8	Section 15 Patient-reported Outcomes Section 16 Electrophysiology and Biomarkers Page 11 Standard text templates

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Q&A and Troubleshooting

TGDOC Chairs

SMA subgroup lead

Project Manager

Group 1

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What Next?

Project Deliverables

Year 1

1. Dataset manual
2. Financial bursaries for Y1 registries
3. Establish Annual Dataset Revision Process
4. Year 1 workshop for Curators
5. Outcome Measure Toolkit
6. Year 1 Project Report

Year 2

7. Financial bursaries for Y2 registries
8. Year 2 workshop for Curators
9. Year 2 Project Report

Year 3

10. Financial bursaries for Y3 registries
11. Year 3 workshop for Curators
12. Final Project Report

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Deliverables timeline

2019	2020	2021	2022
October - Year 1 Bursaries available **December** - Dataset Manual - Revision Process - Year 1 Dataset Workshop	**May** - Outcome Measure Toolkit - Year 1 Project Report **June** - Year 2 Bursaries available **September** - Year 2 Dataset Workshop	**May** - Year 2 Project Report **June** - Year 3 Bursaries available **September** - Year 3 Dataset Workshop	**May** - Final Project Report

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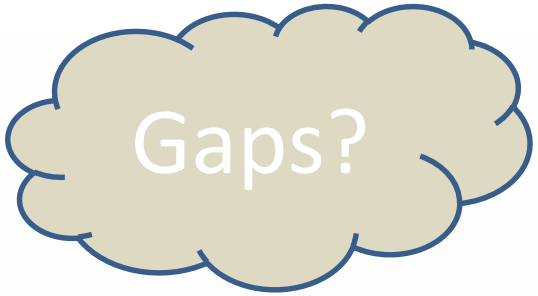
Project timeline



2019	2020	2021	2022
October - Year 1 Bursaries available **December** - Dataset Manual - Revision Process - Year 1 Dataset Workshop	**March** - Start of 2020 Annual Revision Process (v2) **May** - Outcome Measure Toolkit - Year 1 Project Report **June** - Year 2 Bursaries available - Dataset v2 confirmed **September** - Year 2 Dataset Workshop	**March** - Start of 2021 Annual Revision Process (v3) **May** - Year 2 Project Report **June** - Year 3 Bursaries available - Dataset v3 confirmed **September** - Year 3 Dataset Workshop	**March** - Start of 2021 Annual Revision Process (v4) **May** - Final Project Report End of funding **June** - Dataset v4 confirmed

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THANK YOU ALL SO MUCH

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