Registries and Trial Readiness

Hanns Lochmüller

Patient Registries

- Standardized genetic and clinical data necessary for trial recruitment

- Many benefits to registered patients
  - Feedback on standards of care and new research developments
  - Feeling a sense of “belonging” to a broader community
  - Not being left behind as clinical trials develop
  - A link to the research community

- Many benefits to industry/ academia
  - Easy access to patient community
  - Clear concept of target market
  - Feasibility and planning of clinical trials
  - Recruitment of patients into clinical trials
  - Research tool

A core dataset for SMA registries

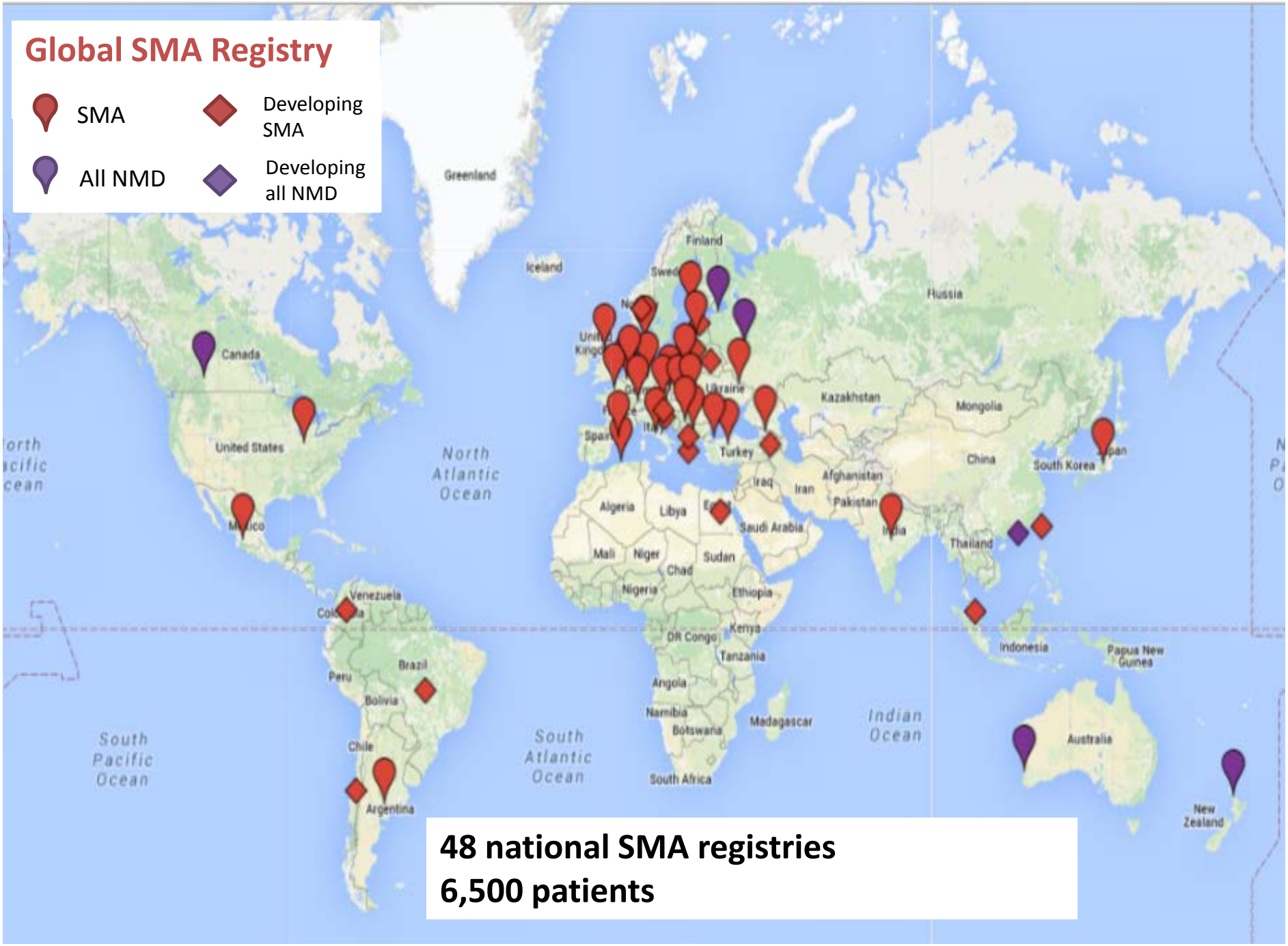
- This is shared common dataset that all TREAT-NMD SMA affiliated registries use
- Allows compatibility between registries across the world – powerful tool for feasibility and recruitment

Mandatory data items:

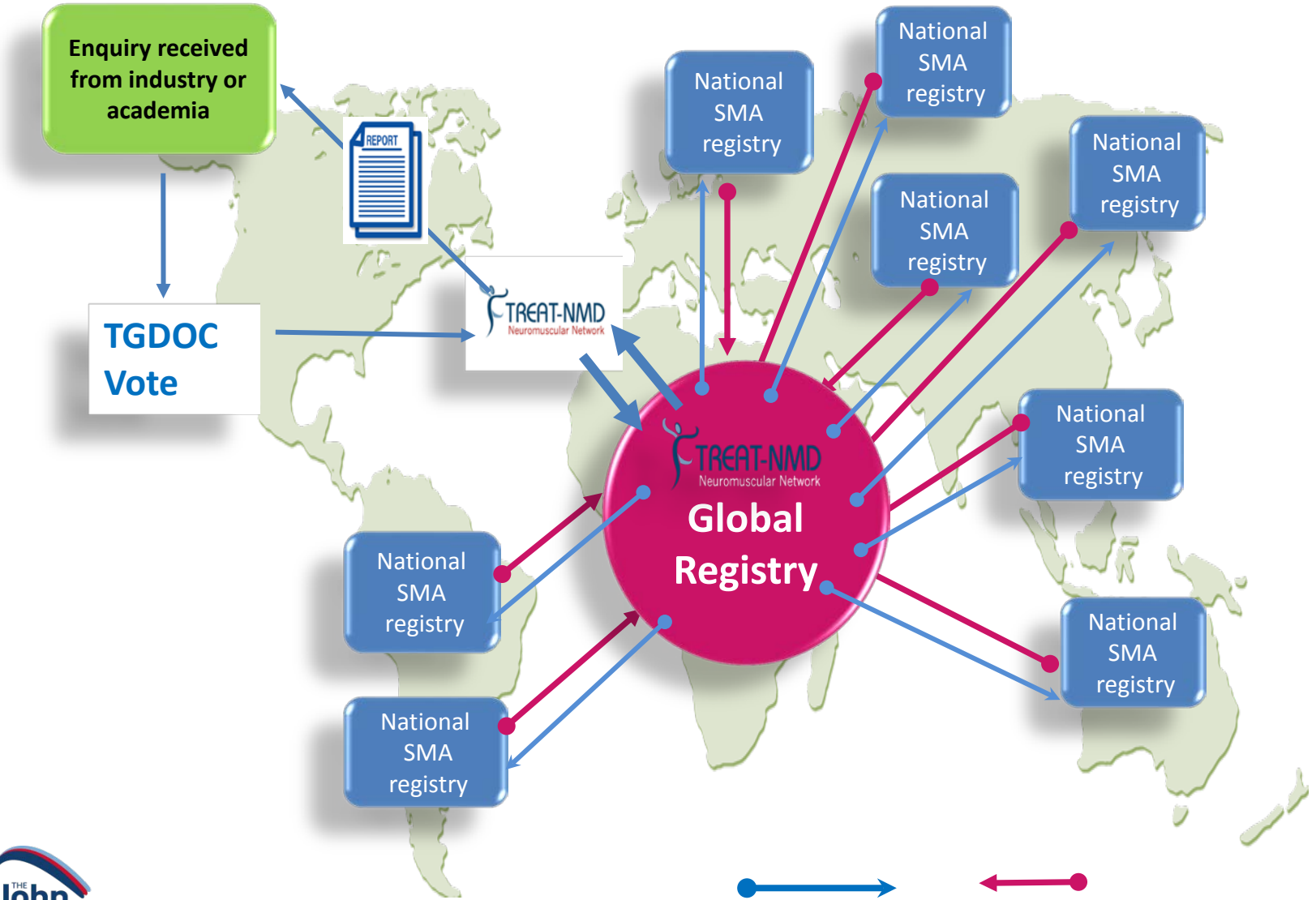
- Personal Data
- Clinical Diagnosis
- Genetic test result
- Ambulation
- Best motor function achieved
- Wheelchair use
- Scoliosis surgery
- Gastric/nasal tube
- Participation in a clinical trial

Highly encouraged data items:

- Ventilation
- Details of pulmonary function
- Positive family history
- SMA classification (type I,II,III)
- Molecular data


Global SMA Registry
SMA
Developing SMA
All NMD
Developing all NMD
48 national SMA registries
6,500 patients
Greenland
Iceland
Finland
Russia
Canada
United States
Mexico
North Atlantic Ocean
Kazakhstan
Mongolia
China
South Korea
Japan
Turkey
Iraq
Iran
Afghanistan
Pakistan
India
Thailand
Indonesia
Papua New Guinea
Australia
New Zealand
Saudi Arabia
Algeria
Libya
Mali
Niger
Chad
Sudan
Nigeria
Ethiopia
Kenya
DR Congo
Tanzania
Angola
Namibia
Botswana
South Africa
Madagascar
Indian Ocean
South Atlantic Ocean
South Pacific Ocean
Venezuela
Peru
Brazil
Bolivia
Chile
Argentina

Global SMA registry enquiries



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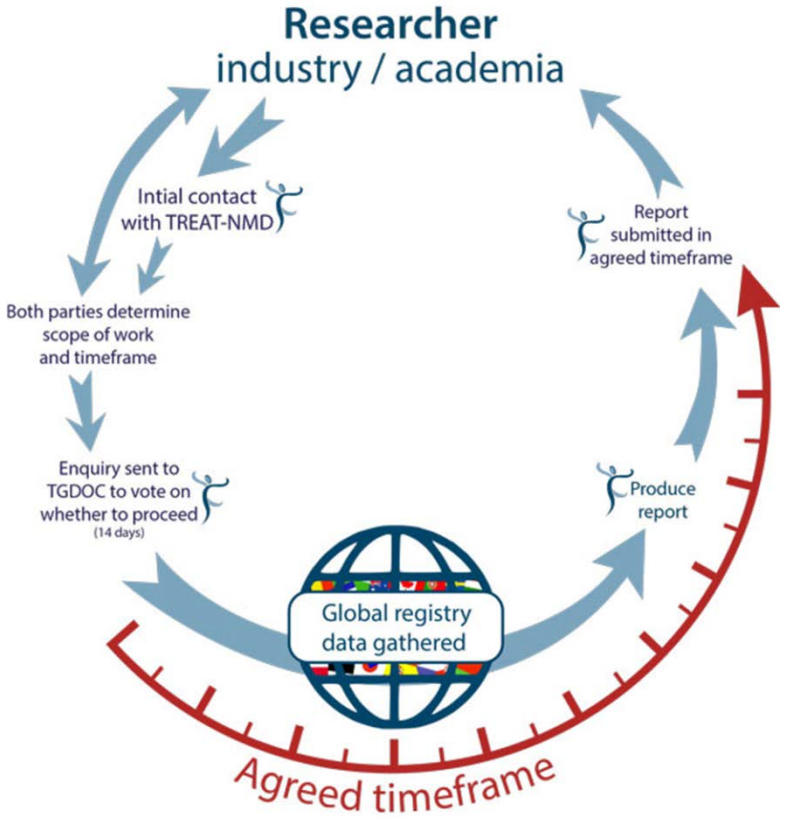
Patient registries

Key benefits of the global SMA registry:

- One single entry point for access to patient data
- Accurate, verified genetic diagnosis together with key clinical data items
- Detailed information on individual patients and thus are not simply a statistical tool but a recruitment tool
- Patient data is updated at least once a year
- Powerful feasibility tool: can filter patients by precise mutation, age, ambulation status and location
- Powerful recruitment tool: patients have consented to being contacted about trials for which they may be eligible
- Post marketing surveillance



CTSR

Care and Trial Site Registry

Welcome to the Care and Trial Site Registry
for neuromuscular and neurodegenerative diseases

https://ctsr.uniklinik-freiburg.de

To see a complete list of the sites in the CTSR click here.

Sites in CTSR:

- 51 countries
- 340 centres

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NHS Foundation Trust

TREAT-NMD
Neuromuscular Network

Information collected in CTSR

Patient cohort	Patients stratified by disease and age range (currently 10 NMDs including subtypes e.g. SMA I, II, III).
	Diagnostic tools as most appropriate for each condition.
Care settings	Availability of specialists and services in-centre.
	Arrangements for transition care.
	Availability of particular pulmonary, cardiac, muscle and bone function tests in-centre.
	Availability of particular physiotherapy facilities and equipment in-centre.
	Availability of emergency care in-centre.
	Experience of centre in conducting skeletal muscle biopsies.
Research and education	Extent of use of centre data in research, research funding arrangements, and papers authored by staff at centre
	Extent to which staff at centre have been involved in providing training at national and international levels
Clinical trial infrastructure	Available personnel (e.g. Study Nurses, Physiotherapists, Pharmacists)
	Previous experience (e.g. details of past participation in Phase I, II, III, IV clinical trials)
	Availability and details of equipment (e.g. refrigerators, IT support)

Patient registries and CTSR

Patient registries:

- exact information on an individual patient
- allows direct contact with individual patients

Care and Trial Site Registry (CTSR):

- database of neuromuscular centres
- contains only the number of patients in an age group

Utility of patient registries and CTSR

- Trial readiness (feasibility and recruitment)
- Standards of care
- Prevalence study
- Natural history
- Outcome measures
- Biomarker discovery and validation
- Burden of illness (health economics)

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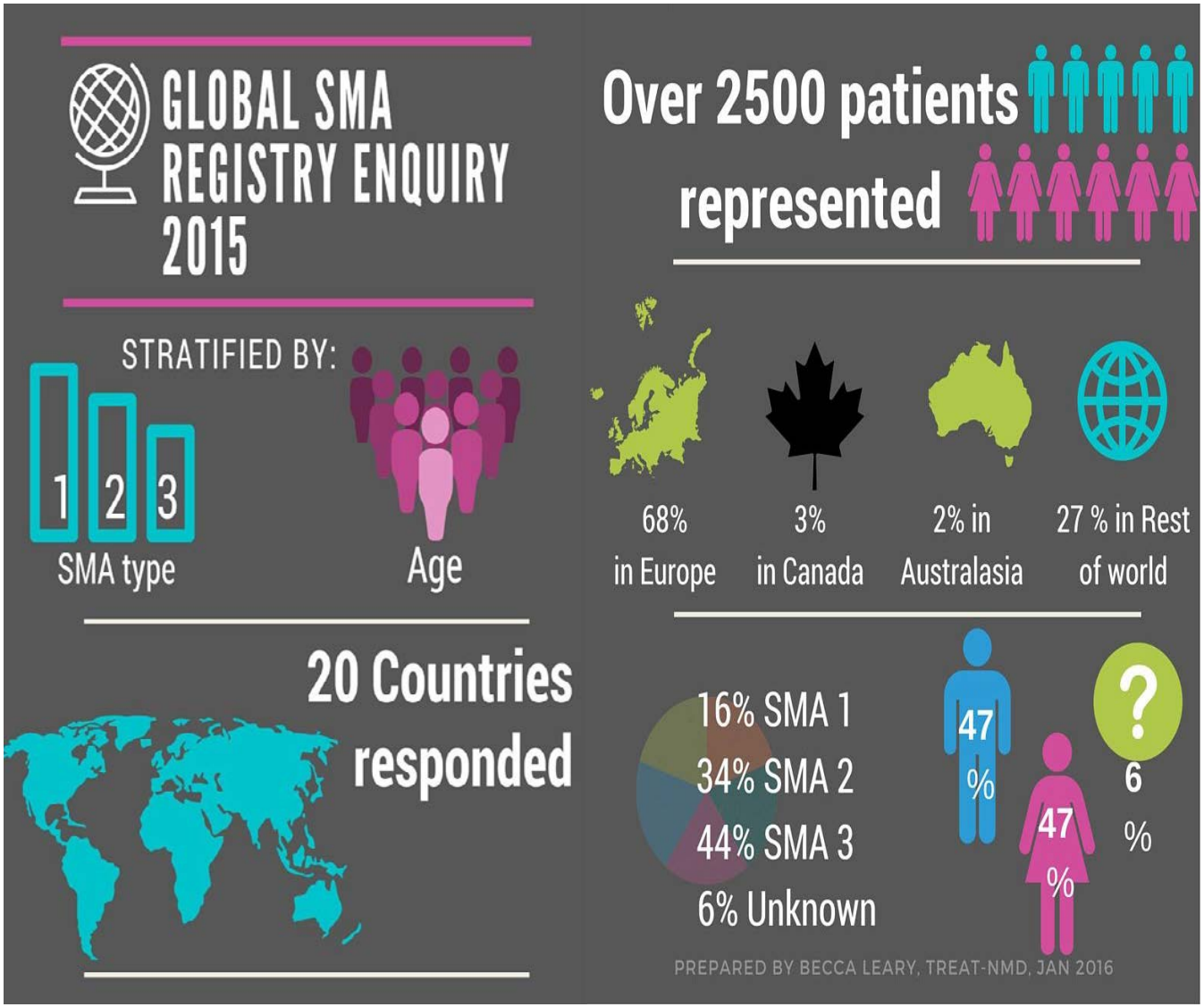
Example of a recent feasibility enquiry



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"Mapping the differences in care for 5000 Spinal Muscular Atrophy patients, a survey of 24 national registries in North America, Australasia and Europe", Bladen C.L. *et al*, *Journal of Neurology* 2013

Number of SMA patients included in the study:
- 5,098 SMA patients

Number of registries that contributed to the study:
- **24** registries

Size of the SMA registries analysed:
- the smallest had **3** patients (Macedonia)
- the largest one had **2834** patients (USA)
- UK registry had **368** patients at the time

Number of studies using SMA registries
SMA registries used for **15** studies worldwide

Types of studies that registries were used for:
- clinical research (including recruitment)
- natural history surveys
- epidemiological research
- genotype/phenotype analysis
- mutation data collection
- social and healthcare services planning

Clinical trials
40% of registries used for identifying patients who fulfil the inclusion criteria (feasibility)
60% of registries were used for recruitment
The UK SMA registry was used for both

Differences in standards of care between various countries.

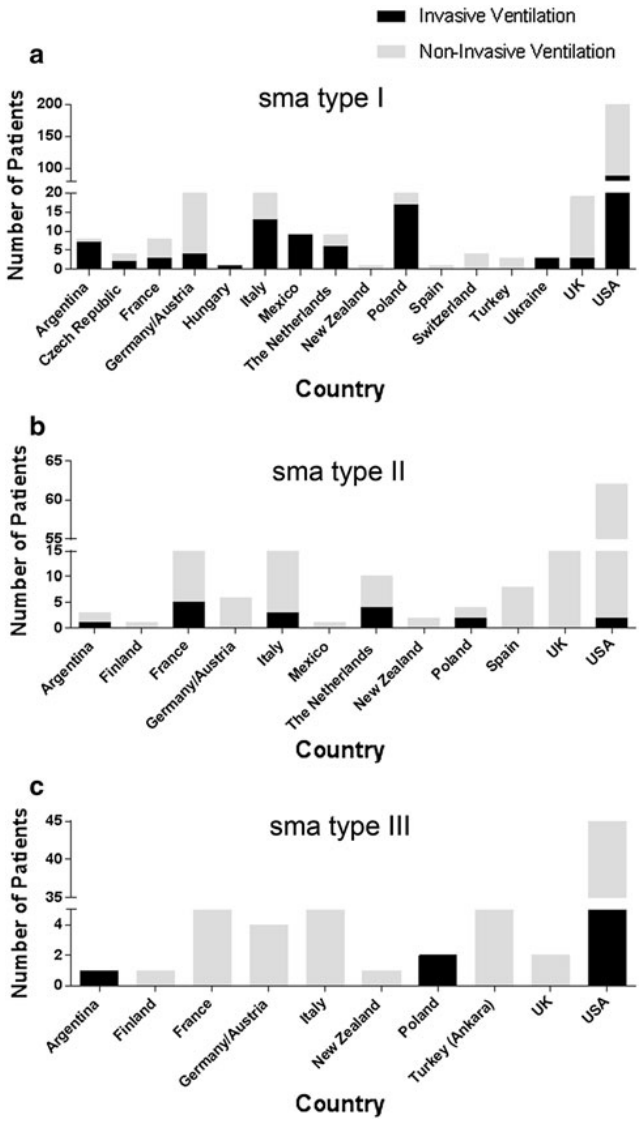
Snapshot of findings

Bladen C.L. *et al*, *Journal of Neurology* 2013

Ventilation:

Country specific variations in the use of invasive ventilation in type I SMA :

- some countries not having any registered patients using invasive ventilation in their SMA type I patients (e.g. Bulgaria, Macedonia, Romania, Serbia)
- others using invasive ventilation in their SMA type I patient populations



SMA prevalence and incidence

- Current knowledge:
  - Prevalence ~1-2 per 100 000
  - Incidence 1 in 10 000
- Limitations: based on few studies
  - Predating genetic testing
  - In small areas
- Need for SMA prevalence/ incidence study worldwide

SMA prevalence study
(in collaboration with Biogen)

- **TREAT-NMD Global SMA Registry enquiry**
  - 26 registries (29 countries) participated
  - Total 4,526 patients identified (as of 1 Sept 2015)
- **TREAT-NMD Care and Trial Sites Registry enquiry**
  - Data from 42 countries
  - Total 6,559 patients identified (as of15 Dec 2015)
- **Online survey among genetic laboratories**
  - Identified 294 genetic testing laboratories (in 53 countries) worldwide via databases (e.g. Orpha.net), other websites, patient registries etc.
  - Total 158 laboratories (40 countries) responded - a (fairly) good response rate in 17 countries in Europe
  - Period 2011-2015: 4653 patients (931 patients per year in Europe)

New approach to prevalence and incidence

- This approach is a way to estimate the prevalence and incidence of the SMA population that is **findable** and **reachable** because it is:
  - part of the health care system
  - part of the research and trial readiness infrastructure

- SMA population ready for:
  - trial planning and recruitment
  - other research activities
  - regulatory processes