Swiss-Reg-NMD

UNIVERSITÄT BERN

Swiss Registry for Neuromuscular Disorders

Annual report for 2020

Swiss-Reg-NMD

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1. Executive Summary

The 'Swiss registry for neuromuscular disorders' (Swiss-Reg-NMD) collects medical information from people with neuromuscular disorders. It is led by specialized physicians from all over Switzerland and located at the Institute of Social and Preventive Medicine (ISPM) in Bern. The registry includes children and adults living in Switzerland who are diagnosed with Duchenne-Becker Muscular Dystrophy (DMD/BMD), Spinal Muscular Atrophy (SMA) and recently also merosin-deficient muscular dystrophy also called *LAMA2*-related muscular dystrophy (MDC1A respectively LAMA2). The registry operates according to the ethics approval #2018-00289.

The Swiss-Reg-NMD pursues the following objectives:

- to register and to collect relevant health data of any patient affected by a neuromuscular disorder living in Switzerland
- to facilitate the participation of patients in National and International therapeutic trials
- to facilitate the establishment of study centers in Switzerland
- to harmonize diagnosis and care on a national level (standards of care)
- to establish a national platform for Post-Marketing Follow-up

On 31.12.2020, a total of 285 patients with neuromuscular disorders were registered in the Swiss-Reg-NMD, (not reported as deceased): 172 patients are affected by a dystrophin associated muscular dystrophy (DMD/BMD/IMD), 104 patients by SMA and 9 patients by LAMA2.

As in previous years, the registry answered requests from multiple stakeholders, in 2020 we answered: 1) from investigators in university hospitals on the feasibility of clinical studies and 2) from the Federal Social Insurance Office on the effectiveness of drugs. In 2020, 11 DMD patients participated in the TAMDMD study and <5 DMD patients in the SIDEROS study. <5 DMD patients were enrolled in an observational study conducted at the University Children's Hospital Zürich investigating cardiac involvement in DMD/BMD. In 2020, <5 SMA patients participated in the Jewelfish and <5 SMA patients in the Sunfish trial. <5 SMA patients participated in an observational study at the University Hospital Zürich investigating cardiac and muscle involvement in SMA.
Additionally in 2020, <5 DMD patients treated in Switzerland participated in a clinical study abroad.

In addition to facilitating the inclusion of patients into trials, the registry aims to assess the effectiveness and side effects of new drugs after their marketing approval. We also want to learn more on the health, care and needs of people with a neuromuscular disorder in Switzerland. This requires the collection of clearly defined medical data. In 2020, we have finalized the new database for DMD/BMD and all already existing data have been entered. We have defined the medical dataset for LAMA2 that is collected in the registry. To reach patients who do not know the local languages, we have translated the patient information and consent form into English.
Finally, we have formalized the organizational structure of the Swiss-Reg-NMD and defined the rules for data sharing and dissemination of Swiss-Reg-NMD information.

In 2020 the Swiss-Reg-NMD received funding from 'Schweizerische Muskelgesellschaft', 'Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires', 'Associazione malattie genetiche rare della svizzera italiana','SMA Schweiz', 'Duchenne Schweiz' and the 'Schweizerische Stiftung für die Erforschung der Muskelkrankheiten', from Biogen Switzerland, PTC Therapeutics, Sarepta International and Pfizer Switzerland. We thank these organisations and companies for their support.

Zusammenfassung

Das 'Schweizer Register für neuromuskuläre Erkrankungen' (Swiss-Reg-NMD) sammelt medizinische Informationen von Menschen mit neuromuskulären Erkrankungen. Es wird von Fachärzten aus der ganzen Schweiz geführt und ist am Institut für Sozial- und Präventivmedizin (ISPM) in Bern angesiedelt. Das Register erfasst Kinder und Erwachsene, die in der Schweiz leben und bei denen Duchenne-Becker-Muskeldystrophie (DMD/BMD), Spinale Muskelatrophie (SMA) und seit kurzem auch Merosin-negative Muskeldystrophie, auch LAMA2-assozierte Muskeldystrophie (MDC1A bzw. LAMA2) genannt, diagnostiziert wurde. Das Register arbeitet gemäss der Ethik-Genehmigung #2018-00289.

Das Swiss-Reg-NMD verfolgt die folgenden Ziele:

- die Registrierung und Erfassung relevanter Gesundheitsdaten aller in der Schweiz lebenden Patienten mit neuromuskulären Erkrankungen
- die erleichterte Teilnahme von Patienten an nationalen und internationalen therapeutischen Studien
- die erleichterte Einrichtung von Studienzentren in der Schweiz
- die Harmonisierung von Diagnose und Versorgung auf nationaler Ebene (Versorgungsstandards)
- die Einrichtung einer nationalen Plattform für das Post-Marketing Follow-up

Am 31.12.2020 waren im Swiss-Reg-NMD insgesamt 285 Patienten mit neuromuskulären Erkrankungen registriert (und nicht als verstorben gemeldet): 172 Patienten sind von einer Dystrophin-assoziierten Muskeldystrophie (DMD/BMD/IMD), 104 Patienten von SMA und 9 Patienten von LAMA2 betroffen.

Wie in den Vorjahren beantwortete das Register im Jahr 2020 Anfragen von mehreren Interessensgruppen: 1) von Universitätskliniken zur Durchführbarkeit klinischer Studien und 2) vom Bundessamt für Sozialversicherungen zur Wirksamkeit von Medikamenten. Im Jahr 2020 nahmen 11 DMD-Patienten an der TAMDMD-Studie und <5 DMD-Patienten an der SIDEROS-Studie teil. <5 DMD-Patienten nahmen an einer Beobachtungsstudie am Kinderspital Zürich teil, die die kardiale Beteiligung bei DMD/BMD untersuchte. Im Jahr 2020 nahmen <5 SMA-Patienten an der Jewelfish- und <5 SMA-Patienten an der Sunfish-Studie teil. <5 SMA-Patienten nahmen an einer Beobachtungsstudie am Universitätsspital Zürich teil, die die kardiale und muskuläre Beteiligung bei SMA untersuchte. Zusätzlich nahmen im Jahr 2020 <5 in der Schweiz behandelte DMD-Patienten an einer klinischen Studie im Ausland teil.

Neben der Erleichterung des Einschlusses von Patienten in die Studien soll das Register auch Daten zur Wirksamkeit und Nebenwirkungen neuer Medikamente nach deren Marktzulassung erfassen. Außerdem wollen wir mehr über den Gesundheitszustand, die Versorgung und die Bedürfnisse von Menschen mit einer neuromuskulären Erkrankung in der Schweiz erfahren. Dies erfordert die Erhebung von klar definierten medizinischen Daten. Im Jahr 2020 haben wir die neue Datenbank für DMD/BMD fertiggestellt und alle bereits vorhandenen Daten eingegeben. Wir haben den medizinischen Datensatz für LAMA2 definiert, der im Register erfasst wird. Um auch Patienten zu erreichen, die die lokalen Sprachen nicht verstehen können, haben wir die Patienteninformation und die Einverständniserklärung ins Englische übersetzt. Schließlich haben wir die Organisationsstruktur des Swiss-Reg-NMD formalisiert und die Regeln für die gemeinsame Nutzung von Daten und die Verbreitung von Swiss-Reg-NMD-Informationen festgelegt.

Im Jahr 2020 erhielt das Swiss-Reg-NMD finanzielle Unterstützung von der 'Schweizerischen Muskelgesellschaft', der 'Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires', der 'Associazione malattie genetiche rare della svizzera italiana', von 'SMA Schweiz', von 'Duchenne Schweiz' und der 'Schweizerischen Stiftung für die Erforschung der Muskelkrankheiten', von Biogen Switzerland, PTC Therapeutics, Sarepta International und Pfizer Switzerland. Wir danken diesen Organisationen und Firmen für ihre Unterstützung.

Sommaire

Le «registre suisse des maladies neuromusculaires» (Swiss-Reg-NMD) recueille des informations médicales de personnes atteintes d'une maladie neuromusculaire. Il est dirigé par des médecins spécialistes de toute la Suisse et se trouve à l'Institut de médecine sociale et préventive (ISPM) à Berne. Le registre inclut des enfants et des adultes vivant en Suisse avec un diagnostic de dystrophie musculaire de Duchenne-Becker (DMD/BMD), d'amyotrophie spinale (SMA) et, plus récemment, de dystrophie musculaire mérosine-négative ou dystrophie musculaire liée à LAMA2 (anciennement MDC1A, ici LAMA2). Le registre fonctionne conformément à l'approbation éthique #2018-00289.

Le Swiss-Reg-NMD poursuit les objectifs suivants :

- enregistrer et collecter les données médicales essentielles de tout patient atteint d'une maladie neuromusculaire vivant en Suisse
- faciliter la participation des patients dans des études cliniques thérapeutiques nationales et internationales
- faciliter la création de sites d'étude clinique en Suisse
- harmoniser le diagnostic et les soins au niveau national (standards de soins)
- mise en place d'une plate-forme nationale pour le suivi post-commercialisation

Au 31.12.2020, un total de 285 patients atteints de maladies neuromusculaires étaient enregistrés dans le Swiss-Reg-NMD, (non déclarés comme décédés) : 172 patients sont atteints d'une dystrophie musculaire (DMD/BMD/IMD), 104 patients d'une SMA et 9 patients de LAMA2.

Comme les années précédentes, le registre a répondu en 2020 aux demandes de multiples acteurs : 1) des chercheurs des hôpitaux universitaires sur la faisabilité des études cliniques et 2) de l'Office fédéral des assurances sociales sur l'efficacité des médicaments. En 2020, 11 patients atteints de DMD ont participé à l'étude TAMDMD et <5 patients atteints de DMD à l'étude SIDEROS. <5 patients atteints de DMD ont été enrôlés dans une étude d'observation à l'hôpital universitaire pour enfants de Zürich sur l'implication cardiaque dans la DMD/BMD. En 2020, <5 patients atteints de SMA ont participé à l'étude Jewelfish et <5 patients atteints de SMA à l'étude Sunfish. <5 patients atteints de SMA ont participé à une étude d'observation à l'hôpital universitaire de Zürich sur l'implication cardiaque et musculaire dans la SMA. En plus, <5 patients atteints de DMD traités en Suisse ont participé à un essai clinique à l'étranger en 2020.

En plus de faciliter l'inclusion de patients dans les essais cliniques, le registre vise à évaluer l'efficacité et les effets secondaires des nouveaux médicaments après leur autorisation de mise sur le marché. Nous voulons également en savoir plus sur la santé, les soins et les besoins des personnes atteintes d'une maladie neuromusculaire en Suisse. Cela nécessite la collecte de données médicales clairement définies. En 2020, nous avons finalisé la nouvelle base de données pour la DMD/BMD et toutes les données déjà existantes ont été saisies. Nous avons défini l'ensemble des données médicales pour LAMA2 qui sont collectées dans le registre. Pour atteindre les patients qui ne connaissent pas les langues locales, nous avons traduit en anglais le formulaire d'information et de consentement du patient.
Enfin, nous avons formalisé la structure organisationnelle du Swiss-Reg-NMD et défini les règles de partage des données et de diffusion des informations du Swiss-Reg-NMD.

En 2020, le Swiss-Reg-NMD a reçu un financement de la 'Schweizerische Muskelgesellschaft', de l'Association suisse romande intervenant contre les maladies neuro-musculaires', de l'Associazione malattie genetiche rare della svizzera italiana', de 'SMA Suisse', de 'Duchenne Suisse' et de la Fondation suisse pour la recherche sur les maladies musculaires', de Biogen Suisse, de PTC Therapeutics, de Sarepta International et de Pfizer Suisse. Nous remercions ces organisations et entreprises pour leur soutien.

2. Introduction

Neuromuscular disorders (NMDs) are diseases that affect the functioning of the first motoneuron (CNS) and of the peripheral nervous system (motor neurons, nerves, neuromuscular transmission and muscle). Most have a genetic origin and all NMDs are rare diseases with few patients scattered across the country. Symptoms vary depending on the disease but commonly include muscle weakness, delayed motor development and/or functional impairment. In addition, patients may also suffer from chronic pain, intellectual impairment, problems with eating or communication. Hence they require multi-disciplinary care. Symptoms often begin in childhood but can occur throughout life.

In 2008, a national registry for NMD was launched at the Centre hospitalier universitaire vaudois (CHUV) in Lausanne to give patients access to new therapies and to facilitate the identification of patients for clinical trials in Switzerland. In 2017, the registry moved to the Institute of Social and Preventive Medicine (ISPM) in Bern and was modernized to meet current and future data quality and security standards and satisfy the needs of patient organisations, health authorities and research organisations. Its long-term goal is to improve the care and well-being of people with neuromuscular diseases in Switzerland.

This report provides an overview of the Swiss-Reg-NMD and its activities in 2020.

3. Description of the Swiss-Reg-NMD

3.1. Organisational structure

On a daily basis, the Swiss-Reg-NMD is run by a clinical lead and an executive office. The registry has a steering group which meets a few times per year. This board is intended to be small and consists of both paediatric neurologists as well as neurologists working across different neuromuscular centres in Switzerland. The overall lead of the registry is shared between the clinical lead and a legal representative at the ISPM. Nine neuromuscular centres report regularly to the registry. The organisational structure of the Swiss-Reg-NMD is displayed in Table 1.

Table 1. People involved in the registry

Lead		
Andrea Klein, PD MD	Clinical Lead	Inselspital, Bern; UKBB, Basel; CHUV, Lausanne
Claudia Kuehni, Prof. MD	Legal representative	ISPM, Bern
Steering Board		
Andrea Klein, PD MD	Clinical Lead, Pediatric Neurologist	Inselspital, Bern; UKBB, Basel; CHUV, Lausanne
David Jacquier, MD	Vice Clinical Lead, Pediatrician	CHUV, Lausanne
Paolo Ripellino, MD	Neurologist	EOC, Lugano
Georg Stettner, PD MD	Pediatric Neurologist	Kinderspital, Zürich
Olivier Scheidegger, PD MD	Neurologist	Inselspital, Bern
Executive Office		
Claudia Kuehni, Prof. MD	Legal representative	ISPM, University of Bern
Anne Tscherter, PD PhD	Project coordination	ISPM, University of Bern
Dominique Baumann, PhD	Project coordination	ISPM, University of Bern
Nadine Lötscher, Nrs	Data manager	ISPM, University of Bern
Advisors		
F. Joncourt, PhD	Genetic curator	Previously Genetic Laboratory University Hospital Bern
Participating centres		
Aarau, Basel, Bern, Geneva, Lausanne, Luzern, St. Gallen, Ticino, Zürich, and some private practices.		

3.2. Objectives

The main objective of the Swiss-Reg-NMD is to facilitate the inclusion of Swiss patients in therapeutic trials and to improve, on the basis of a better knowledge, the current and future care and well-being of individuals with NMDs. In addition, it offers a platform to observe the overall outcome of patients receiving new drugs and to improve communication and collaboration.

The specific aims of the registry are therefore:

1. Provide epidemiological data:
    - Incidence
    - Prevalence
    - Clinical spectrum at diagnosis
    - Disease progression / prognosis
    - Survival rates and mortality

2. Provide a platform for clinical research and Post-Marketing Follow-up:
    - Recruitment of patients into therapeutic trials
    - Collection of outcome data during treatment
    - Facilitation of observational studies
      e.g. on healthcare, education and quality of life
3. Provide a platform for communication:
    - Promotion of the exchange of knowledge between clinics, researchers, therapists and health authorities
    - Facilitation of national and international collaborations

3.3. Inclusion criteria

The Swiss-Reg-NMD includes children, adolescents and adults living or treated in Switzerland who are diagnosed with a NMD. The diagnosis needs to be confirmed, whenever possible, by genetic testing, or at least by biopsy and/or electroneuromyography, according to international standards for the diagnosis of the given NMD. Once the diagnosis is established, there are no specific exclusion criteria.

Currently, patients with DMD/BMD/IMD, SMA and patients with a congenital muscular dystrophy (CMD) due to mutations in the laminin-α-2 gene (LAMA2 also named MDC1A) or collagen VI (COL6) genes are included in the registry. In the future, patients with other NMDs may also be included.

Duchenne Muscular Dystrophy (DMD) is an X-linked progressive muscular dystrophy affecting one in every 3’600-10'000 live male births (Mah et al. 2014). Becker Muscular Dystrophy (BMD) is the less severe form affecting about one in every 18’000 live male births (Emery et al. 1991). Patients with a less severe form than DMD but more severe than BMD are classified as intermediate form (IMD). These disorders are caused by mutations in the dystrophin gene. Boys present delayed motor development and muscle weakness and progress to loss of ambulation, and, in the more severe cases, respiratory and heart failure.

Spinal Muscular Atrophy (SMA) is a disease affecting motor neurons in the spinal cord and the brain stem. It is an autosomal recessive disease affecting about one in every 10'000 live births (Faravelli et al. 2015). It is caused by mutations in the ‘survival motor neuron 1’ gene (*SMN1*). SMA patients present with progressive motor weakness and weakness of bulbar and respiratory muscles. Conventionally, SMA is divided into four clinical subtypes, from type I with onset before 6 months and, if untreated, death before the second birthday to type IV with adult onset, weakness and a slowly progressing course. Recently, the first treatment for SMA, Nusinersen (Spinraza®), has been approved by Swissmedic.

Congenital muscular dystrophies (CMD) are a group of diseases that are mostly inherited in an autosomal recessive fashion. The prevalence has been estimated at 7×10^{-6} (Mostacciuolo et al. 1996). LAMA2-related muscular dystrophy and COL6-related muscular dystrophy are the two most frequent forms of CMD. Both forms lead to marked weakness of skeletal muscles, the tendency to develop contractures and rigidity of the spine as well as respiratory muscle weakness. A phase I study with Omigapil was conducted in the US and other therapeutic compounds showing promising results in preclinical studies are in development. It is therefore important to include these forms for natural history data and trial readiness.

3.4. Registration of patients and collection of medical data

In general, a paediatric or adult neurologist diagnoses an individual with a NMD. The physician then informs the patient and/or their parents (or other legal representative) about the Swiss-Reg-NMD during a routine medical consultation. The physician also gives them printed information about the registry and a form that they can sign if they want to participate in the registry (informed consent form). This information can be taken home so that a decision can be made after careful deliberation.

If consent is given, the physician reports the patient to the Swiss-Reg-NMD, and provides data on the clinical status of the patient at regular intervals (once per year or, for SMA, 2-3 times per year for Post-Marketing Follow-up). At the ISPM (the Institute of Social and Preventive Medicine of the University of Bern where the registry is hosted), this information is then entered into a secured database.

If consent is not given, the patient can still be reported, but with very minimal non-identifying data (diagnosis, gender, birth year, death) to allow a proper estimate of the incidence and prevalence of the diseases in Switzerland to be made. No further information is collected.

3.5. Data protection / Ethics approval

The Human Research Act (HFG) sets the framework conditions for medical research. The Swiss-Reg-NMD is subject to this Act. In 2008, the old registry for DMD/BMD and SMA received ethics approval in the different cantons. In 2018 approval for the new, improved Swiss-Reg-NMD was obtained from the Cantonal Ethics Committee of Bern (#2018-00289). This approval allows the collection of data all over Switzerland.

If consent is given, the Swiss-Reg-NMD is authorised to collect the medical data as long as these data are collected routinely in the course of the treatment and follow-up of the patient. It is permitted to use these data for reports and in-depth research studies. In addition, the registry is allowed to initiate questionnaire studies on quality of life, development, health and health care use. Finally, the registry can inform patients directly about clinical trials.

Study information and consent forms are available in four different languages (French, German, Italian and English). All data made available to the Swiss-Reg-NMD is stored in a secure IT environment at the University of Bern. This data is kept strictly in accordance with the requirements of the Data Protection Acts. All staff members of the Swiss-Reg-NMD are bound to professional secrecy. Only coded data (without names or identifying data) is used for research purposes.

3.6. Funding

During 2020, major efforts have been made to obtain the necessary funds to finalise the restructuring of the registry and improve data quality.

In 2020, the Swiss-Reg-NMD has received unconditional funding from the ‘Schweizerische Muskelgesellschaft’, the ‘Association Suisse Romande Intervenant contre les Maladies neuro-Musculaires’, the ‘Associazione malattie genetiche rare della svizzera italiana’, from ‘SMA Schweiz’, from ‘Duchenne Schweiz’ and from the ‘Schweizerische Stiftung für die Erforschung der Muskelkrankheiten’. Furthermore, Biogen Switzerland AG, PTC Therapeutics International, Pfizer Switzerland and Sarepta International have supported the work of the Swiss-Reg-NMD.

We are very grateful to all these organisations and companies for their support.

4. Registered cases

On 31.12.2020, a total of 285 patients with neuromuscular disorders were registered in the Swiss-Reg-NMD, (not reported as deceased, Table 2 and Table 3): 172 patients are affected by a dystrophin associated muscular dystrophy (DMD/BMD/IMD), 104 patients by SMA and 9 patients by LAMA2. This is 38 patients more than a year ago.

In 2020, <5 SMA I patients included in the Swiss-Reg-NMD were reported as deceased and <5 patients have moved abroad.

To ensure patient confidentiality we mask small numbers with "<5" in our annual report.
Not all patients with a NMD living or treated in Switzerland are registered in the Swiss-Reg-NMD. The participation is voluntary and some patients do not want to participate.

Table 2. Total number of patients alive[a] by neuromuscular disorder and age (status as at 31.12.2020).

	Age 0-20	Age 20-65	Total
DMD-Duchenne	95	41	**136**
BMD-Becker	17	14	**31**
IMD-Intermediate	<5	<5	**5**
SMA type 1	18	0	**18**
SMA type 2	27	20	**47**
SMA type 3	11	28	**39**
LAMA2	8[b]	<5	**9**
Total	**179**	**106**	**285**

DMD: Duchenne Muscular Dystrophy; BMD: Becker Muscular Dystrophy; IMD: Intermediate form; SMA1-3: Spinal Muscular Atrophy type 1-3; LAMA2: *LAMA2*-related Muscular Dystrophy.
[a] Not reported as deceased; [b] Approximate value to ensure patient confidentiality

Table 3. Total number of patients alive[a] by centers (status as at 31.12.2020).

Centre	DMD/IMD/BMD	SMA	LAMA2	Total
Aarau	7	0	0	**7**
Basel	27	<5	6	**36[b]**
Bern	17	25	<5	**44[b]**
Genève	<5	<5	<5	**8**
Lausanne	36	21	0	**57**
Luzern	5	<5	0	**7[b]**
St. Gallen	<5	21	0	**25[b]**
Ticino	12	5	0	**17**
Zürich	47	28	0	**75**
Other	13	<5	0	**15[b]**

Note that some SMA patients are seen in two centres. DMD: Duchenne Muscular Dystrophy; BMD: Becker Muscular Dystrophy; IMD: Intermediate form; SMA: Spinal Muscular Atrophy; LAMA2: *LAMA2*-related Muscular Dystrophy.
[a] Not reported as deceased; [b] Approximate value to ensure patient confidentiality

5. Achievements of the Swiss-Reg-NMD in 2020

The Covid-19 pandemic also affected the work of the Swiss Reg-NMD. The members of the executive office have worked most of the time from their home offices. Communication with each other and with the stakeholders was mostly virtual.

5.1. Requests to the registry

The registry always replies to requests in a way that no identifying information is disclosed. Conclusions about individual persons are not possible under any circumstances. The identity of the enquirer is confidential and is not disclosed either.

Requests on the feasibility for studies and recruitment for clinical trials

- We have responded to a request from a Swiss University Hospital to provide aggregated information on DMD patients eligible for potential exon skipping trials.
- We have answered a request on the feasibility of a trial in SMA in Switzerland. We have provided aggregated information about treated SMA patients with a specific age range eligible for a clinical study.

Further requests

- We have answered a request from a Swiss patient organization wishing to complete their annual report by sending them the Registry Annual Report 2019.
- Following an initial request to TREAT-NMD regarding Non-Dystrophic Myotonias, we have compiled a list of all neuromuscular disorders for which the registry collects patient data.
- We have responded to a request from TREAT-NMD on behalf of a British University. We have provided aggregated information about DMD patients with specific medical characteristics.
- We have answered an enquiry from TREAT-NMD on behalf of a non-profit European SMA umbrella organization (SMA Europe). We have provided aggregated information about SMA patients with a specific genetic background.

Post-Marketing Follow-up

- We have completed a report for the Federal Social Insurance Office, which provides information for assessing the effectiveness of Nusinersen in treating SMA patients. This report contains aggregated data on motor functions and no identifying information. Identification of single patients is not possible.

5.2. Promotion of national centres and inclusions in clinical trials

In 2020, three trials involving **DMD patients** were conducted in Switzerland:

- TAMDMD is an international placebo controlled trial lead by Prof. Dirk Fischer at the UKBB Basel, investigating Tamoxifen in DMD patients. Screening for this study started in 2018, when 15 Swiss patients were screened. In 2020, no new patient was enrolled in this study. Currently, 11 Swiss patients are enrolled in the trial.
- The SIDEROS study is an international study run by Santhera, which investigates the effect of Idebenone on lung function evolution in patients with DMD receiving steroids. Screening and inclusion for this study started in 2017, when 6 patients were screened and 5 included at the site in Basel (UKBB, principal investigator PD Andrea Klein). In October 2020, Santhera stopped the SIDEROS study because of insufficient effect. <5 patients were still included until the study was terminated.

- An observational study was conducted at the University Children's Hospital Zürich investigating cardiac involvement in DMD/BMD. In 2019, <5 patients started this study. In 2020, <5 patients were enrolled.
- Additionally in 2020, <5 DMD patients treated in Switzerland participated in a clinical study abroad investigating Vamorolone (Santhera) in the care of patients with DMD.

There are currently three trials involving **SMA patients** from Switzerland:

- The Jewelfish trial conducted by Roche investigates the effect of Risdiplam, a small molecule that enhances the functioning of the SMN2 gene, in different groups of SMA patients. In 2020, no new patient was enrolled in this study, currently <5 Swiss patients are participating in this trial (UKBB, principle investigator Prof. Dirk Fischer).
- The Sunfish trial conducted by Roche investigates the effect of Risdiplam in comparison with a placebo group in SMA 2 and 3 patients. Currently, <5 Swiss patients are included.
- An observational study started in 2020 at the University Hospital Zürich investigating cardiac and muscle involvement in SMA. <5 SMA patients are enrolled in this study.

Note: the above mentioned numbers include only the patients registered in Swiss-Reg-NMD.

5.3. Collaboration with TREAT-NMD (www.treat-nmd.eu)

TREAT-NMD is a network for the neuromuscular field that provides an infrastructure to ensure that the most promising new therapies reach patients as quickly as possible. Since its launch in January 2007 the network's focus has been on the development of tools that industry, clinicians and scientists need to bring novel therapeutic approaches through preclinical development and into the clinic, and on establishing best-practice care for neuromuscular patients worldwide.
Dr. Andrea Klein is an elected member of the TREAT-NMD Global Database Oversight Committee (TGDOC) for the international registry for SMA and DMD. The TGDOC is responsible for reviewing all requests for data from the global database.

Collaboration with TREAT-NMD in 2020:

- We have been involved in the review of the TREAT-NMD SMA Core Dataset version 1, contributing with our feedback to the finalization of the second version of the TREAT-NMD SMA Core Dataset.
- We have actively participated in the DMD expanded dataset pilot project contributing to the finalization of the TREAT-NMD DMD Expanded Dataset.
- We have updated the information on the registry completing the TREAT-NMD Registries Review 2020 survey.
- Dr. Andrea Klein, as a member of the TGDOC, has given her vote on several requests for data from the global database.

5.4. Development of the registry

Main steps in 2020

- The new database for DMD/BMD has been finalized and tested in spring 2020. All already existing data have been entered.
- The medical dataset for LAMA2 that is collected in the registry has been defined.
- We have formalized the organizational structure of the Swiss-Reg-NMD and defined the rules for data sharing and dissemination of Swiss-Reg-NMD information.
- The patient information and consent form are now available also in English language.

Next steps in 2021

- We will place a focus on the registration of adult patients and on the collection of their medical data.
- We will build a new database (REDCap) for the collection of medical data on LAMA2.
- Genetic diagnosis DMD/BMD: Dr. Franziska Joncourt, genetic curator of the registry, will update the genetic data according to the newest international HGVS rules as also required by TREAT-NMD.
- We will define the data collection of children treated with Risdiplam or Onasemnogene abeparvovec.

5.5. Dissemination and Networking

Information about the registry is always available on our website 'www.swiss-reg-nmd.ch', where also the information leaflets and consent forms can be downloaded.
We have prepared a short description of the registry with information about its purpose and structure. This text has been provided to the supporting patient organisations for dissemination to provide consistent information.

Due to the Covid-19 pandemic, several conferences were held virtually or postponed to 2021. Members of the Steering Board and/or of the executive office represented the registry in the following meetings in 2020:

- 53. Pädiatrischer Fortbildungskurs Obergurgl 2020, Neuromuskuläre Erkrankungen, «Differentialdiagnosen des floppy infant», Obergurgl (A), 30.01.2020
- Vorlesung, Master of Science in Physiotherapie, ZHAW, «Diagnostik: Neuromuskuläre Erkrankungen», 06.03.2020
- Rare Disease Action Forum (RDAF), Multistakeholder Expert Forum, «Registries for rare diseases in Switzerland – Opportunities and Challenges», 08.04.2020
- Interchange between FSIO, FOPH, Pharma on «Postmarketing surveillance of expensive medicines through national registries», Bern, 18.08.2020
- Meeting of the 'fachlicher Beirat Muskelgesellschaft und Myosuisse', Zürich and virtual, 20.08.2020
- Swiss Public Health Conference, «From Evidence to Public Health Policy and Practice», virtual, 02./03.09.2020
- Training for physiotherapists, SMA Care, organized by Biogen Switzerland, Bern and virtual, 18.09.2020
- Pediatric Neurology Junior Class, Schweizerische Gesellschaft für Neuropädiatrie SGNP, «Neuromuskuläre Erkrankungen», Kloster Kappel, 26.09.2020
- Spinale Muskelatrophie: Care Standards und neue Therapiemöglichkeiten, Pädiatrie Update Refresher, Technopark Zürich,28.10 2020
- Seminar Neurologische Probleme des Neugeborenen, «Floppy Infant Syndrom», Klinik für Neonatologie, Universitätsspital Zürich, 12.11.2020
- Swiss Academy of Childhood Disability, Webinar - Kontroversen, 12.11.2020
- SwissPedNet Board F2F, Bern, 15.06.2020 and 29.10.2020 and General Assembly, Bern, 20.11.2020
- TREAT- NMD Conference, Annual Curators' Meeting, virtual, 30.11.-02.12.2020

5.6. Research

- The first questionnaire study to assess education, leisure activities and quality of life in young patients with DMD in Switzerland has been approved by the Cantonal Ethics Committee of Bern at the end of 2019. However, we could not send out the questionnaires because of the outbreak of the Covid-19 pandemic. It would have been difficult for the families to answer the questions on school and leisure time activities during 2020. We have now adjusted several questions regarding school and leisure time because of the Covid-19 pandemic. As soon as these changes have been approved by the Ethics Committee, this questionnaire will be sent to children aged 8-18, who are known in the registry as having DMD.
- The quality of medical data collected from patients with SMA was optimized in view of a scientific publication on motor functions, speech, chronic ventilation and the need of nutritional support.

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7. References

Emery AE. Population frequencies of inherited neuromuscular diseases-a world survey. Neuromuscul Disord. 1991; 1: 19-29.

Faravelli I, Nizzardo M, Comi GP, Corti S. Spinal muscular atrophy-recent therapeutic advances for an old challenge. Nat Rev Neurol. 2015 Jun; 11: 351-9.

Mah JK, Korngut L, Dykeman J, Day L, Pringsheim T, Jette N. A systematic review and meta-analysis on the epidemiology of Duchenne and Becker muscular dystrophy. Neuromuscul Disord. 2014; 24: 482-91

Mostacciuolo ML, Miorin M, Martinello F, Angelini C, Perini P, Trevisan CP. Genetic epidemiology of congenital muscular dystrophy in a sample from north-east Italy. Hum Genet. 1996 Mar;97(3):277-9.