Swiss-Reg-NMD

UNIVERSITÄT BERN

Swiss Registry for Neuromuscular Disorders

Annual report for 2021

Swiss-Reg-NMD

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Bern, 22 February 2022, Swiss Registry for Neuromuscular Disorders

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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), LAMA2-related muscular dystrophy (LAMA2) or Collagen-VI-related myopathy (COL-6). 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 31.12.2021, a total of 332 patients with neuromuscular disorders were registered in the Swiss-Reg-NMD, (not reported as deceased): about 189 patients with dystrophin associated muscular dystrophy (DMD/BMD/IMD), 129 patients with SMA, about 10 patients with LAMA2 and less than 5 patients with COL-6.

In 2021, a few DMD patients participated in the TAMDMD study and some patients were screened for the Ciffreo study. A few SMA patients participated in the Jewelfish or Sunfish trial or in an observational study at the University Hospital Zürich investigating cardiac and muscle involvement in SMA. Additionally, a few DMD and SMA patients treated in Switzerland participated in clinical studies abroad.

As in previous years, the registry answered requests from multiple stakeholders in 2021. In particular, we answered several questions from TREAT-NMD, researchers at Swiss University Hospitals and from pharmaceutical companies about the feasibility of clinical studies.

The registry collects medical data to learn more on the health, care and needs of people with a neuromuscular disease in Switzerland. To stay up to date with international standards, we revised our DMD/BMD and SMA datasets based on TREAT-NMD guidelines. We updated the SMA dataset with regard to the new disease-modifying treatments. This allows us to investigate the effectiveness and side effects of all three currently approved SMA therapies. We also defined the medical dataset that will be collected from LAMA2 patients starting in 2022.

The collected data were used for several research projects. We submitted an article entitled "Evaluation of Real-Life Outcome Data of Patients with Spinal Muscular Atrophy Treated with Nusinersen in Switzerland" to the journal Neuromuscular Disorders; it was accepted and will be published in early 2022. A Master's thesis in Public Health analysed hospitalization data of patients treated with Nusinersen. Further, we conducted a survey on the education and social participation of young DMD patients in Switzerland. The aim of this survey is to understand the current situation and identify opportunities for improvement in Switzerland. We supported the CARE-NMD-CH study by inviting all eligible patients of the registry to participate in a survey on the care situation of people with neuromuscular diseases. Also, we supported a project from a Swiss University Hospital investigating the access to dental care for children and adolescents with motor disabilities.

We continued to collaborate closely with TREAT-NMD, and, following an extensive application process, became a Core Member Registry for DMD and SMA and an Affiliated Member Registry for congenital muscular dystrophy (CMD).

In 2021, 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, Novartis Gene Therapies Inc., Pfizer AG Switzerland, PTC Therapeutics International, Roche Pharma AG Switzerland and Sarepta International. 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 befindet sich am Institut für Sozial- und Präventivmedizin (ISPM) in Bern. Das Register erfasst in der Schweiz lebende Kinder und Erwachsene, bei denen Duchenne-Becker-Muskeldystrophie (DMD/BMD), Spinale Muskelatrophie (SMA), LAMA2-assoziierte Muskeldystrophie (LAMA2) oder Collagen VI-assoziierte Myopathie (COL6) 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 31.12.2021 waren im Swiss-Reg-NMD insgesamt 332 Patienten mit neuromuskulären Erkrankungen registriert (und nicht als verstorben gemeldet): etwa 189 Patienten mit einer Dystrophin-assoziierten Muskeldystrophie (DMD/BMD/IMD), 129 Patienten mit SMA, etwa 10 Patienten mit LAMA2 und weniger als 5 Patienten mit COL-6.

Im Jahr 2021 nahmen einige DMD-Patienten an der TAMDMD-Studie teil und einige Patienten wurden für die Ciffreo-Studie geprüft. Mehrere SMA-Patienten nahmen an der Jewelfish- oder Sunfish-Studie oder an einer Beobachtungsstudie am Universitätsspital Zürich teil, in der die Beteiligung des Herzens und der Muskeln bei SMA untersucht wurde. Außerdem nahmen wenige DMD- und SMA-Patienten, die in der Schweiz behandelt wurden, an klinischen Studie im Ausland teil.

Wie in den Vorjahren beantwortete das Register auch im Jahr 2021 Anfragen von verschiedenen Interessengruppen. Insbesondere beantworteten wir mehrere Anfragen von TREAT-NMD, von Forschenden an Schweizer Universitätsspitälern und von Pharmaunternehmen zur Durchführbarkeit klinischer Studien.

Das Register sammelt medizinische Daten, um mehr über den Gesundheitszustand, die Versorgung und die Bedürfnisse von Menschen mit einer neuromuskulären Erkrankung in der Schweiz zu erfahren. Um auf dem neuesten Stand der internationalen Standards zu bleiben, haben wir unsere DMD/BMD- und SMA-Datensätze auf der Grundlage der TREAT-NMD-Richtlinien überarbeitet. Wir haben auch den SMA-Datensatz im Hinblick auf die neuen Therapien aktualisiert. Dies ermöglicht uns, die Wirksamkeit und die Nebenwirkungen aller drei derzeit zugelassenen SMA-Therapien zu untersuchen. Wir haben auch den medizinischen Datensatz definiert, der ab 2022 von LAMA2-Patienten erhoben werden soll.

Die gesammelten Daten wurden für mehrere Forschungsprojekte verwendet. Wir haben einen Artikel mit dem Titel "Evaluation of Real-Life Outcome Data of Patients with Spinal Muscular Atrophy Treated

with Nusinersen in Switzerland" bei der Zeitschrift Neuromuscular Disorders eingereicht; er wurde akzeptiert und wird Anfang 2022 publiziert. Eine Masterarbeit im Bereich Public Health analysierte die Hospitalisierungsdaten von Patienten, die mit Nusinersen behandelt wurden. Darüber hinaus haben wir eine Umfrage zur Bildung und sozialen Teilhabe von jungen DMD-Patienten in der Schweiz durchgeführt. Ziel dieser Umfrage ist es, die soziale und schulische Situation der Teilnehmenden zu verstehen und Verbesserungsmöglichkeiten in der Schweiz zu identifizieren. Wir unterstützten zudem die CARE-NMD-CH-Studie, indem wir alle in Frage kommenden Patienten des Registers einluden, an einer Umfrage über die Versorgungssituation von Menschen mit neuromuskulären Erkrankungen teilzunehmen. Auch unterstützten wir ein Projekt eines Schweizer Universitätsspitals, das den Zugang zu zahnärztlicher Versorgung für Kinder und Jugendliche mit motorischen Beeinträchtigungen untersucht.

Wir arbeiteten auch im Jahr 2021 eng mit TREAT-NMD zusammen und wurden nach einem umfangreichen Bewerbungsverfahren als ‘Core Member Registry’ für DMD und SMA und als ‘Affiliated Member Registry’ für kongenitale Muskeldystrophie aufgenommen.

Im Jahr 2021 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 Schweiz, Novartis Gene Therapies Inc, Pfizer AG Schweiz, PTC Therapeutics International, Roche Pharma AG Schweiz und Sarepta International. Wir danken diesen Organisationen und Unternehmen 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), de dystrophie musculaire liée à LAMA2 (LAMA2) ou de myopathie liée au collagène VI (COL-6). 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 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 31.12.2021, un total de 332 patients atteints de maladies neuromusculaires étaient enregistrés dans le Swiss-Reg-NMD (non déclarés comme décédés) : environ 189 patients sont atteints d’une dystrophie musculaire (DMD/BMD/IMD), 129 patients d’une SMA, environ 10 patients de LAMA2 et moins de 5 patients de COL-6.

En 2021, quelques patients atteints de DMD ont participé à l'étude TAMDMD et certains patients ont été sélectionnés pour l'étude Ciffreo. Quelques patients atteints de SMA ont participé à l'étude Jewelfish ou Sunfish ou à une étude d'observation à l'hôpital universitaire de Zurich sur l'implication cardiaque et musculaire dans la SMA. En outre, quelques patients atteints de DMD ou SMA traités en Suisse ont participé à des études cliniques à l'étranger.

Comme les années précédentes, le registre a répondu en 2021 aux demandes de multiples acteurs. En particulier, nous avons répondu à plusieurs questions de TREAT-NMD, de chercheurs des hôpitaux universitaires suisses et de sociétés pharmaceutiques sur la faisabilité d'études cliniques.

Le registre recueille des données médicales pour en savoir plus sur la santé, les soins et les besoins des personnes atteintes d'une maladie neuromusculaire en Suisse. Pour rester à jour avec les normes internationales, nous avons révisé nos ensembles de données DMD/BMD et SMA sur la base des directives TREAT-NMD. Nous avons aussi adapté l'ensemble de données SMA en tenant compte des nouveaux traitements. Cela nous permet d'étudier l'efficacité et les effets secondaires des trois thérapies SMA actuellement approuvées. Nous avons également défini l'ensemble des données médicales qui sera collecté des patients atteints de LAMA2 à partir de 2022.

Les données collectées ont été utilisées pour plusieurs projets de recherche. Nous avons soumis un article intitulé "Evaluation of Real-Life Outcome Data of Patients with Spinal Muscular Atrophy Treated with Nusinersen in Switzerland" à la revue Neuromuscular Disorders; cet article a été accepté et sera publié au début 2022. Un travail de master en santé publique a analysé les données d'hospitalisation des patients traités par Nusinersen. En outre, nous avons mené une enquête sur l'éducation et la participation sociale des jeunes patients atteints de DMD en Suisse. L'objectif de cette enquête est de comprendre la situation actuelle et d'identifier les possibilités d'amélioration en Suisse. Nous avons soutenu l'étude CARE-NMD-CH en invitant tous les patients éligibles du registre à participer à une enquête sur la situation des soins aux personnes atteintes de maladies neuromusculaires. Nous avons également soutenu un projet d'un hôpital universitaire suisse sur l'accès aux soins dentaires pour les enfants et les adolescents souffrant de handicaps moteurs.

Nous avons continué à collaborer activement avec TREAT-NMD et, après une procédure de candidature extensive, nous sommes devenus un 'Core Member Registry' pour DMD et SMA et un 'Affiliated Member Registry' pour la dystrophie musculaire congénitale.

En 2021, le Swiss-Reg-NMD a reçu un financement de '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 Novartis Gene Therapies Inc, de Pfizer Suisse, de PTC Therapeutics International, de Roche Pharma Suisse et de Sarepta International. 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 2021.

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 board which meets a few times per year. This board consists of paediatric neurologists, neurologists and since 2021 also of a pulmonologist 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
Bettina Schreiner, PD MD	Neurologist	Universitätsspital Zürich
Esther Irene Schwarz, PD MD	Pulmonologist	Universitätsspital Zürich
Executive Office		
Claudia Kuehni, Prof. MD	Legal representative	ISPM, University of Bern
Dominique Baumann, PhD	Project manager	ISPM, University of Bern
Anne Tscherter, PD PhD	Project manager	ISPM, University of Bern
Nadine Lötscher, Nrs	Data manager and research assistant	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 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) 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. In recent years, three treatments for SMA have been developed and approved by Swissmedic. The first was Nusinersen (Spinraza®), followed by Risdiplam (Evrysdi®) and Onasemnogene abeparvovec-xioi (Zolgensma®).

Congenital muscular dystrophies (CMD) are a group of diseases that are mostly inherited in an autosomal recessive manner. 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, date and cause of 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 2021, efforts have been made to obtain the necessary funds to finance the running of the registry, to conduct the DMD questionnaire study and to report on SMA disease modifying treatments.

In 2021, 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, Novartis Gene Therapies Inc., Pfizer AG Switzerland, PTC Therapeutics International, Roche Pharma AG 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 31.12.2021, a total of 332 patients with neuromuscular disorders were registered in the Swiss-Reg-NMD, (not reported as deceased, Table 2 and Table 3): about 189 patients with dystrophin associated muscular dystrophy (DMD/BMD/IMD), 129 patients with SMA, about 10 patients with LAMA2 and less than 5 patients with COL-6. 43 patients have newly signed an Informed Consent in 2021.

In 2021, <5 SMA I patients and <5 DMD 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. Since the new ethics approval of 2018, less than 5 people have declined to participate in the registry.

Table 2. Total number of patients alive[a] by neuromuscular disorder and age (status as at 31.12.2021).

	Age 0-20	Age 20-65	Total
DMD-Duchenne	104	45	**149**
BMD-Becker	20	16	**36**
IMD-Intermediate	<5	<5	**<5**
SMA type 1	25	0	**25**
SMA type 2	32	23	**55**
SMA type 3	11	38	**49**
LAMA2	8	<5	**10[b]**
COL-6	<5	0	**<5**
Total	**206**	**126**	**332**

DMD: Duchenne Muscular Dystrophy; BMD: Becker Muscular Dystrophy; IMD: Intermediate form; SMA1-3: Spinal Muscular Atrophy type 1-3; LAMA2: *LAMA2*-related Muscular Dystrophy, *COL-6:* Collagen-VI-related myopathy.
[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 31.12.2021).

Center	DMD/IMD/BMD	SMA	LAMA2	COL-6	Total
Aarau	5	0	0	0	**5**
Basel	23	<5	6	<5	**34**
Bern	20	34	<5	<5	**57**
Geneva	6	<5	<5	0	**10**
Lausanne	41	24	0	0	**65**
Luzern	6	<5	0	0	**9[b]**
St. Gallen	<5	24	0	0	**27[b]**
Ticino	14	5	<5	<5	**22**
Zürich	60	34	0	0	**94**
Other	11	6	0	0	**17**

Note that some SMA patients are seen and therefore listed in two centres. DMD: Duchenne Muscular Dystrophy; BMD: Becker Muscular Dystrophy; IMD: Intermediate form; SMA: Spinal Muscular Atrophy; LAMA2: *LAMA2*-related Muscular Dystrophy; *COL-6:* Collagen-VI-related myopathy.
[a] Not reported as deceased; [b] Approximate value to ensure patient confidentiality

Clinical Trials

In 2021, two 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. Currently, <5 Swiss patients are enrolled in the trial. In 2021, no new patient was enrolled in this study.
- Ciffreo is an international placebo controlled trial investigating the safety and effectiveness of gene therapy in DMD patients. In 2021, <5 patients were re-screened for this study after the study had been paused due to safety concerns.

Additionally, in 2021 <5 DMD patients treated in Switzerland participated in a clinical study abroad investigating Vamorolone (ReveraGen BioPharma) in the care of patients with DMD.

In 2021, several **SMA patients** were participating in trials conducted in 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 2021, 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.
- Additionally, in 2021 <5 SMA patients treated in Switzerland participated in a clinical study abroad investigating the safety and efficacy of Zolgensma®.

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

5. Achievements of the Swiss-Reg-NMD in 2021

The coronavirus pandemic has continued to have an impact on the work of the Swiss-Reg-NMD. The members of the executive office have repeatedly worked from their home offices. Communication with each other and with stakeholders then took place virtually.

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 clinical trials

- Following a request from TREAT-NMD regarding exon deletion in DMD patients, we provided data about all deletions registered in our dataset.
- We have responded to a request from a Swiss University Hospital to provide aggregated information about ambulation and steroid treatment of DMD patients eligible for two potential clinical studies.

- We have answered a request from a Swiss University Hospital on the feasibility of a clinical study in SMA in Switzerland. We have provided aggregated information about SMA patients without full-time ventilation and with a specific age range.
- We have answered another request from a Swiss University Hospital asking to provide aggregated data about non-ambulant SMA patients eligible for a research study.
- We have responded to a request by a pharmaceutical company providing aggregated data on DMD patients with a non-sense mutation.

Further requests and collaborations

- We have answered an enquiry from a Swiss University Hospital to provide aggregated data on SMA patients currently on full-time ventilation.
- We have responded to a request from an international research center and provided aggregated data on therapy availability in Switzerland to be used for research purposes.
- The study 'Caring for Patients with Neuromuscular Diseases in Switzerland' (CARE-NMD-CH) investigates the care situation of people with neuromuscular disorders and their families in Switzerland. We have invited all eligible patients of the registry to participate in an online survey conducted by CARE-NMD-CH.
- We are currently supporting a project from a Swiss University Hospital investigating the access to dental care for children and adolescents with motor disabilities.

5.2. Collaboration with TREAT-NMD (treat-nmd.org)

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 2021

- We have completed the extensive application process and have become a Core Member Registry for DMD and SMA and an Affiliate Member Registry for Congenital Muscular Dystrophy (CMD).
- We were among the first registries to implement the TREAT-NMD Duchenne Muscular Dystrophy core dataset; we regularly share our experiences with the DMD team on data collection and implementation of TREAT-NMD DMD Core Dataset version 1.2.
- We have updated the information on the registry completing the TREAT-NMD Registries Review 2021 and the SMA Year 2 Report Survey.
- Dr. Andrea Klein, as a member of the TGDOC, has given her vote on several requests for data from the global database.

5.3. Development of the registry

Main steps in 2021

- We could push forward our set focus on adult patient registration and data collection, with 15 adult SMA patients and <5 adult DMD and LAMA-2 patients newly registered in 2021.

- Together with the registry steering board, we revised the DMD/BMD dataset, based on the latest version of the TREAT-NMD Core Dataset (version 1.2).
- We also adapted the SMA dataset, based on the latest version of the TREAT-NMD Core Dataset for SMA (version 2.1); this was done also with regard to new developments in disease-modifying treatment. The SMA data to be collected in case of treatment with Evrysdi® or Zolgensma® have been defined.
- With international collaboration, we defined a first version of the dataset for the collection of LAMA2 medical data. We created the corresponding case report forms (CRF).
- Dr. Franziska Joncourt, genetic curator of the registry, has updated the genetic data of DMD/BMD patients according to the newest international HGVS rules.

5.4. Dissemination and Networking

On our website “www.swiss-reg-nmd.ch”, we provide the information leaflets and consent forms as downloads and news on the work of the registry. Further information can also be found on the clinicaltrials.gov website (NCT05102916).

Due to the ongoing coronavirus pandemic, several conferences were again held virtually or postponed. Members of the Steering Board and/or of the executive office represented the registry at the following meetings in 2021:

- Conference Österreichische Muskel Forschung, «UpDate Muskelforschung 2021», virtual, 26./27.02.2021.
- Virtual Symposium, Inselspital Bern, «Pediatric and Adult Neuromuscular Diseases», virtual, 01.04.2021.
- Peripheral Nerve Society annual meeting, virtual, 12.-13.06.2021/25.-27.06.2021.
- Jahrestagung der Schweizerischen Gesellschaft für Neuropädiatrie, «Future Aspects in Diagnostics and Therapy in Neuropediatrics», virtual, 16./17.06.2021.
- European Academy of Neurology congress, virtual, 19.-22.06.2021.
- Multi-stakeholder workshop, Rare Disease Action Forum RDAF, «Registries of rare diseases in Switzerland», virtual, 30.06.2021.
- Jahrestreffen des fachlichen Beirats Myosuisse, Bern, 26.08.2021.
- International Conference and Course on NeuroMuscular Imaging, virtual, 22.-24.09.2021.

5.5. Research and Post-Marketing Follow-up

- In 2021, we analysed the relevant registry data and, together with the data providers, submitted an article entitled “Evaluation of Real-Life Outcome Data of Patients with Spinal Muscular Atrophy Treated with Nusinersen in Switzerland” to Neuromuscular Disorders. The article was accepted and will be published in 2022.
- Based on registry data, a master student completed her master thesis on hospitalizations of patients with Spinal Muscular Atrophy under Nusinersen treatment in Switzerland.
- In early summer 2021, together with researchers at University Children’s Hospital Basel (UKBB), we conducted the DMD survey entitled "Neurocognitive functions, education, participation and quality of life in children and adolescents with Duchenne muscular dystrophy in Switzerland". Our aim is to gain knowledge about education and social participation of young DMD patients (8-18 years) in Switzerland and about the impact of the Covid 19 pandemic on these aspects. We have achieved an excellent response rate. We are currently evaluating the responses.

- To investigate the safety and effectiveness of all three currently approved SMA therapies even after their market introduction, we have adapted the SMA dataset and collect data regarding therapy administration, motor function, motor assessments, nutrition, respiration and side effects. This collection of real world medical data from people diagnosed with SMA is crucial for patients and treating physicians to optimize future care.

6. Outlook for 2022

- We will continue our efforts to improve data collection especially for adult patients. To support the data providers and in agreement with them, a new member of the executive office will collect the medical data in the clinics and enter it into the registry database.
- We will promote the collection of LAMA2 data in patients up to 20 years of age and build the correspondent new database (REDCap).
- We will analyse the responses to the DMD questionnaire survey and publish the results.
- A research article on the structure and functioning of the registry is in preparation.
- Fundraising will continue to be a significant part of the work next year.

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