Annual Report 2022
Swiss Rare Disease Registry

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1 Summary

EN:

The Swiss Rare Disease Registry (SRDR) collects medical data from persons with a rare disease living and/or being treated in Switzerland. The SRDR is located at the Institute of Social and Preventive Medicine (ISPM) at the University of Bern and is maintained by SwissRDL (Medical Registries and Data Linkage).

The goals of the SRDR are:

- Collection of epidemiological data (incidence, prevalence, progression, survival, mortality).
- Collection of essential health care data (diagnostic centers, treatment centers)
- Facilitate the participation of patients in clinical studies
- Harmonization of data and linkage of existing disease-specific registries
- Interoperability and collaboration with international registries
- Establishment of a communication network for affected persons and healthcare providers

This report describes the progress of the SRDR in 2022.

During the past year, the SRDR has finalized its organization structure consisting of the patronage of kosek (Nationale Koordination Seltene Krankheiten), a Steering Board and the supporting entities, Data Provider Board and Patient Board. A detailed description of the organization structure can be found here.

By the end of 2022, the SRDR has initiated the collaboration with nine institutions and discussed first steps with eleven more (see Appendix I). By August 2022, in total 46'386 patients had been ORPHA coded by the institutions, an increase of 13'816 from the previous year. Of these, 3'100 patients had been informed about the SRDR, and 1'334 of them consented.

Automatic data transfer was initially considered the primary modality of data transfer. But internal clarifications at most participating institutions revealed that the budget for developing the technical framework was lacking, or that a changeover to a new hospital information system was pending. Therefore, until the automatic data transfer is implemented at participating institution, data is transferred by manual entry through the SRDR online application. Hospitals transferred 331 data sets to the SRDR database by the end of 2022.

DE:

Das Schweizer Register für seltenen Krankheiten (SRSK) erfasst medizinische Daten von Personen mit einer seltenen Krankheit, die in der Schweiz leben und/oder behandelt werden. Das SRSK befindet sich am Institut für Sozial- und Präventivmedizin (ISPM) an der Universität Bern und wir von SwissRDL (Medical Registries and Data Linkage) unterhalten.

Die Ziele des SRSK sind:

- Erfassen von epidemiologischen Daten (Inzidenz, Prävalenz, Verlauf, Überlebenszeit, Mortalität)
- Erheben von essenziellen Daten zur Gesundheitsversorgung (diagnostische Zentren, Behandlungszentren)
- Erleichterung der Teilnahme von Betroffenen an klinischen Studien
- Harmonisierung der Daten und Verknüpfung von bestehenden krankheitsspezifischen Registern
- Interoperabilität und Kollaboration mit internationalen Registern
- Aufbau eines Kommunikationsnetzwerkes für Betroffen und Gesundheitsdienstleister

Dieser Bericht beschreibt die Fortschritte des SRSK im Jahr 2022.

Im vergangenen Jahr hat das SRSK seine Organisationsstruktur, bestehend aus der Schirmherrschaft der kosek (Nationale Koordination Seltene Krankheiten), dem Vorstand und den unterstützenden Einheiten, dem Data Provider Board und dem Patienten Board, ausgearbeitet. Eine detaillierte Beschreibung der Organisationsstruktur finden Sie hier.

Bis Ende 2022 hat das SRSK die Zusammenarbeit mit neun Institutionen definiert und erste Schritte mit elf weiteren diskutiert (siehe Anhang I). Bis August 2022 wurden insgesamt 46’386 Patientinnen und Patienten durch die Institutionen ORPHA kodiert, ein Anstieg von 3’816 im Vergleich zum Vorjahr. Davon wurden 3’100 Patientinnen und Patienten über das SRSK informiert, wovon 1’334 ihr Einverständnis gaben.

Die automatische Datenübertragung wurde zunächst als primäre Übertragungsmodalität in Betracht gezogen. Interne Abklärungen in den meisten teilnehmenden Institutionen ergaben, dass entweder das Budget für die Entwicklung der technischen Rahmenbedingung fehlte oder ein Wechsel auf ein neues Klinikformationssystem anstand. Bis zur Einführung der automatischen Datenübertragung bei den teilnehmenden Institutionen, erfolgt die Datenübertragung daher momentan vorwiegend manuell über die SRSK-Online-Anwendung. Die Krankenhäuser übertrugen bis Ende 2022 331 Datensätze an die SRSK-Datenbank.

FR:

Le Registre suisse des maladies rares (RSMR) recueille les données médicales des personnes atteintes d'une maladie rare qui vivent et/ou sont traitées en Suisse. Le RSMR est situé à l'Institut de médecine sociale et préventive (ISPM) de l'Université de Berne et est géré par SwissRDL (Medical Registries and Data Linkage).

Les objectifs du RSMR sont:

- La collecte de données épidémiologiques (incidence, prévalence, progression, survie, mortalité).
- Collecte de données essentielles sur les soins de santé (centres de diagnostic, centres de traitement).
- Faciliter la participation des patients aux essais cliniques
- Harmonisation des données et mise en relation des registres existants spécifiques à une maladie.
- Interopérabilité et collaboration avec les registres internationaux
- Mise en place d'un réseau de communication pour les personnes concernées et les prestataires de soins.

Le présent rapport décrit les progrès réalisés par le RSMR en 2022.

Au cours de l'année écoulée, le RSMR a finalisé sa structure organisationnelle, qui comprend le patronage de la kosek (Coordination nationale des maladies rares) le comité directeur et les entités de soutien, le comité des fournisseurs de données et le comité des patients. Une description détaillée de la structure organisationnelle est disponible ici.

A la fin de l'année 2022, le RSMR a établi une collaboration avec neuf institutions et a discuté des premières étapes avec onze autres (voir Annexe I). En août 2022, 46’386 patients au total avaient été codés ORPHA par les institutions, soit une augmentation de 13’816 par rapport à l'année précédente. Parmi eux, 3’100 patients ont été informés du SRDR, et 1’334 d'entre eux ont donné leur consentement.

Le transfert automatique des données était initialement considéré comme module de transmission primaire. Des clarifications internes dans la plupart des institutions participantes ont révélé que soit le budget pour développer le cadre technique faisait défaut, soit un changement vers un nouveau système d'information clinique était en cours. Par conséquent, pour le moment, les données seront principalement transférées par saisie manuelle via l'application en ligne du RSMR. Fin 2022, les hôpitaux avaient transféré 331 ensembles de données dans la base de données du RSMR.

2 Background

A disease is considered rare when less than one of 2'000 people are affected. Evidence-based understanding of rare diseases is limited due to lack of clinical and epidemiological studies. The International Statistical Classification of Diseases and Related Health Problems (ICD-10 and earlier versions), used for hospital and mortality statistics, is not specific for rare diseases, making individuals with rare diseases invisible in routine statistics, and causing lack of data for researchers, practitioners, health authorities, and policy makers.

To improve the evidence base, many countries have established rare disease registries. The Swiss Rare Disease Registry (SRDR) was established in 2016/2017 by an interdisciplinary working group in collaboration with the Federal Office of Public Health (FOPH) and was approved by the Ethics Committee of the Canton of Bern in 2018. The SRDR is financially supported by the FOPH and the medical faculty of the University of Zurich. Matching funds are contributed by participating institutions. Further information on the SRDR can be found here.

3 Achievements of the SRDR in 2022

3.1 Finalization of the SRDR organizational structure

In February - April 2022, the Steering Board finalized and approved the organizational structure of the SRDR (Figure 1). This structure outlines the roles and responsibilities of each body involved in the SRDR, as well as the regulations for finance, confidentiality and data protection. The corresponding document entitled "Collaboration Agreement on the Swiss Rare Disease Registry" can be found here.

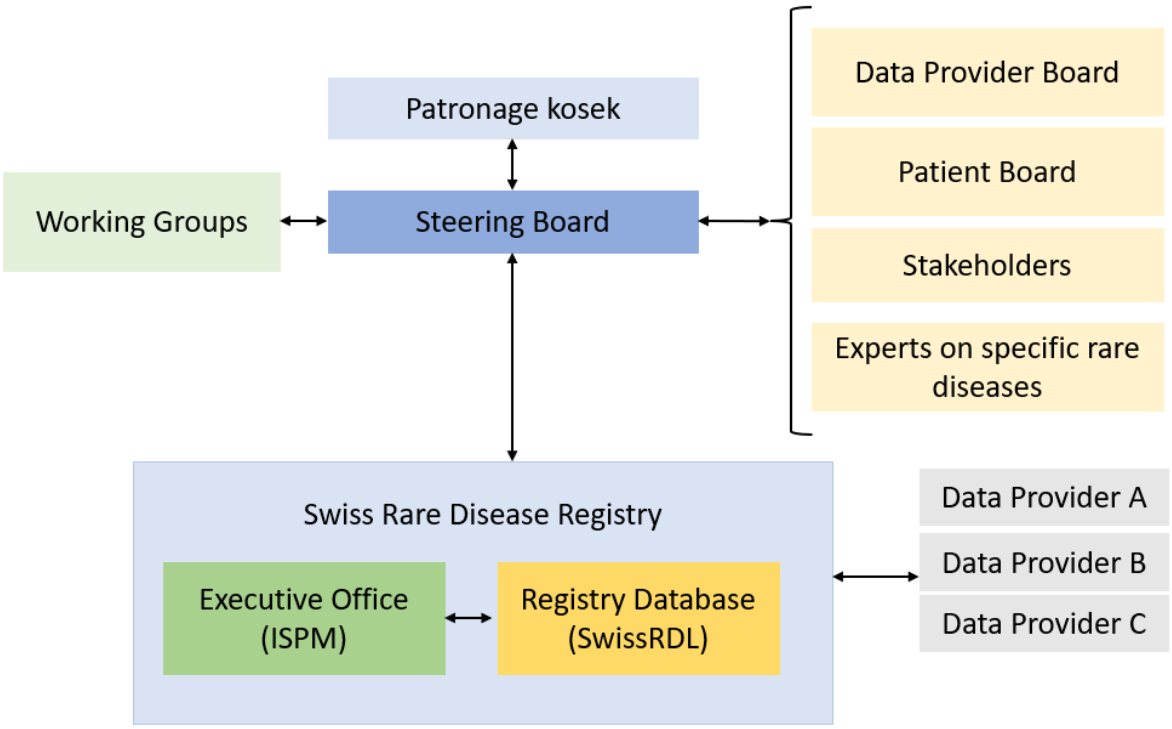

***Figure 1**: Overview of the SRDR organization structure*

The organizational structure is as follows:

Patronage: The Coordination Rare Diseases Switzerland (kosek) has the patronage of the SRDR.

Steering Board: The Steering Board includes representatives of the five Swiss university hospitals, Orphanet Switzerland, patient organizations, SwissRDL and the Institute for Social and Preventive Medicine (ISPM) of the University of Bern. (Appendix II).

Council of the Steering Board: Within the Steering Board, there is a working group (Council of the Steering Board) consisting of the President, the Vice-President of the Steering Board, a representative of ISPM, a representative of SwissRDL and other 1-2 members (Appendix III).

Executive Office: The Executive Office is located at Institute for Social und Prevention Medicine (ISPM) at the University of Bern.

SwissRDL: SwissRDL (Medical Registries and Data Linkage) is responsible for the development and maintenance of the database.

Supporting bodies: A patient board and a board of data providers are planned as supporting bodies, replacing the Registry Advisory Board. The members of the two boards will be appointed in 2023.

Experts on rare diseases will be consulted as needed.

Working Groups: The Steering Board forms working groups as needed. A working group on ORPHA coding has been active since July 2021. Members are persons involved in medical coding at university hospitals and cantonal hospital.

Other stakeholders: Other stakeholders such as federal bodies, medical societies, and research platforms are informed about the SRDR once a year.

3.2 Participating institutions

Participating institutions are named in Appendix I.

3.3 Determination of the regulation of further use of SRDR data and publication

The SRDR seeks to create a research platform and provide data to health policy makers so they can identify areas of need. Data from the SRDR can be requested by research institutions, industry, public agencies and federal bodies, patient organizations and the media. To ensure transparent and efficient data-sharing, the Steering Board and Executive Office drafted the document "SRDR: Regulations for research, collaborations, data sharing, and publications". This document was unanimously approved in August 2022 and is now being revised based on feedback from the University Hospitals.

3.4 Data set and data structure of the SRDR database

The SRDR dataset, based on the "Set of Common Data Elements for Rare Diseases Registration" published by the EU RD Platform on Rare Disease, was revised through discussions with data reporting institutions.

3.5 Status of ORPHA coding, obtaining patient consent forms and data collection from participating institutions

The status of ORPHA coding, obtaining patient consent forms, and data transfer is described in the following sections.

3.5.1 ORPHA Coding

The Orphanet nomenclature of rare diseases (ORPHAcodes) has been recognized as the most appropriate nomenclature for clinical coding of rare diseases. 18 of the 20 participating institutions have already implemented ORPHA coding, resulting in 46’386 ORPHA-coded patients as of August 2022. This represents an increase of 13’816 ORPHA-coded patients compared to 2021.

3.5.2 Obtaining patient consent forms

Each institution determines the modalities of the process of obtaining patient consent forms itself. Table 1 summarizes the status of obtaining patient consent forms as of August 2022. The SRDR has provided the necessary documents and informed the participating institutions about the process. Five institutions already determined the modalities of obtaining patient consent forms.

Table 1 Status of obtaining patient consent forms

	Informed patients	Consent to participate	Participation refused	No feedback
Total	3’100	1’334	21	1’779

By the end of August 2022, 1’334 patient consent forms had been obtained - a tenfold increase compared to the year before. This is an extremely positive development, considering the significant time and financial resources needed to obtain written consent from all 580’000 patients in Switzerland and 6’000 new patients per year. This increase is thanks to the adoption of the process of obtaining patient consent so that only the patient or legal representative's signature is required, and the treating physician's signature is no longer necessary.

3.5.3 Data transfer

Data reporting institutions can transfer the data automatically or manually to the SRDR. Automatic transfer via an application interface (API) between the clinical information systems of the university hospitals and the SRDR is possible if the technical framework conditions are met.

For personnel, financial and structural reasons, automatic data transfer was not possible yet for some institutions. Therefore, the SRDR concept also enables manual data entry using an online application which is available since April 2022. Table 2 shows the number of participating institutions that transfer data automatically, are in the process of setting up/intending to set up an interface, enter/intend to enter data manually, or did not yet define the modality of data transfer.

Table 2: Modalities of data transfer

Automatic data transfer		**Manual data entry**		**Not yet defined**
in place	in planning	in place	in planning	
1	11	6	7	1

Note. Overall, 20 institutions. The same institution can be listed twice.

3.6 Possibility for self-registration by affected persons

Since March 2022, the SRDR offers a paper form for self-registration, approved by Ethics on 09.03.2022. So far, 56 affected persons have self-registered via paper form. Their medical data will now be validated with their treating physicians before being added to the SRDR database.

3.7 Number of registered patients

4 of the 20 institutions (Appendix I) reported data in 2022. Of the 1'334 affected persons who consented, **364** data sets were transferred to the SRDR data base (automatic data transfer: 207; manual data entry: 130; self-registration: 27).

3.8 Launch of national information campaigns

At the start of 2022, we finalized and launched the SRDR website (https://www.raredisease.ch/) with information for patients, professionals and researchers. To inform the public, we sent out a media release to 142 different stakeholders. Additionally, PD Dr. Michaela Fux and Dr. Natalie Bayard-Guggisberg provided further details about the SRDR at key events (Appendix IV).

3.9 Necessary steps on the political level

Currently, Switzerland has no specific legal basis for compulsory registration of patients with rare diseases, as there is for cancer registration. The cooperation of the institutions is voluntary. This requires intensive information work on the part of the SRDR with the data reporting institutions. Obtaining the patients' consent is extremely time-consuming. Furthermore, the institutions that transmit the data must bear the costs incurred by data collection and registration. These costs might even increase in the future, since suitable framework conditions for the development of the web service must be created or, in the case of manual data entry, appropriate staff must be made available. The legal framework conditions are therefore not optimal for efficiently driving the SRDR forward. The recently adopted motion 21.3978 *"For sustainable financing of public health projects of the National Concept Rare Diseases"* promises to improve this situation. A legal basis along the lines of the Cancer Registration Act would be the best approach to drive the SRDR forward efficiently and sustainably.

4 Outlook for 2023

4.1 Regulatory framework

There will be changes in the regulatory framework of the SRDR concept:

1. The SRDR was approved by the ethics committee of Bern as a monocentric study. But discussions with university and cantonal hospitals have revealed that this study design does not meet the corporate compliance of most participating institutions. To address this issue the SRDR will be transformed into a multicentric study.
2. The concept of the SRDR involves collecting data from affected persons who have been informed about the SRDR but have not actively refused consent within 6 weeks. This procedure has been approved by the ethics commission Bern. For data protection reasons, the SRDR will for the time being dispense with this so-called opt-out system.

4.2 Involvement of institutions

With the adjustments to the legal framework and thus the hospitals' corporate compliance, the SRDR hopes that hospitals will now have the appropriate conditions to participate in the SRDR in the coming year. The SRDR will mainly focus on initiating and boosting data collection from the hospitals.

4.3 Funding for the online application for self-registration

The desire of affected persons to be able to register themselves with the SRDR is clearly noticeable. Until now, however, the financial means to develop an online application for self-registration have been lacking. The paper form is only intended as a temporary solution. The SRDR is currently writing an application for financial support to the Lotteriefond Bern. The SRDR plans to involve affected persons in the development of the online application.

4.4 Dissemination

The SRDR plans to publish an article for professionals and an article for affected persons about the registry. By doing so, the SRDR hopes to further increase its visibility and the motivation of physicians and affected persons to participate.

4.5 Collaboration with PPI (Patient and Public Involvement)

The SRDR aims to foster the patient and public involvement (PPI). The SRDR has worked with patients and patient organizations in the past. In order to find out what expectations and concerns patients have about the registry, the SRDR has organized a workshop in fall 2021. In a further collaboration with patients, the SRDR developed a flyer for patients with the most important information about the registry. For 2023, the SRDR plans to replace the paper form for self-registration with an online platform. The online platform will be tested by patients in a pilot project. The SRDR is also planning a patient board to support the registry on important issues. To implement these two project the SRDR needs to raise additional funding.

4.5 Necessary steps on the political level

Since there is currently no specific legal basis for compulsory registration of patients with rare diseases, the cooperation of the institutions remains voluntary and requires intensive information work. Obtaining patient consent is time-consuming, and the data reporting institutions must bear the costs incurred by the SRDR. The recently adopted 21.3978 *"For sustainable financing of public health projects of the National Concept Rare Diseases"* promises to improve the overall situation. The SRDR will further engage in political activity to ensure the independence and sustainability of the registry.

5 Acknowledgements

We want to thank all the children, adolescents, and adults with a rare disease and their families for agreeing to participate in the SRDR. We are further very thankful to all participating hospitals and physicians for their support and effort in data collection.
We thank all patient organizations for their outstanding efforts in making the SRDR known among affected persons.

We are very grateful to all funding bodies for their financial support. In 2022 the SRDR was financially supported by the FOPH and the medical faculty of the University of Zurich and the University of Bern. The participating institutions contributed with matching funds.

6 Appendixes

6.1 Appendix I: Participating Institutions

The following hospitals are already working with the SRDR:

- Inselspital, Universitätsspital Bern
- Inselspital, Zentrum für Seltene Krankheiten in Bern (ZSK-Bern)
- Hôpitaux Universitaires de Genève (HUG)
- Universitäts-Kinderspital Zürich – Das Spital der Eleonorenstiftung
- Centre Maladies Rares des Hôpitaux universitaires de Genève
- Kantonsspital Aarau (KSA)
- Zentrum für seltene Krankheiten, Aarau (ZSK-Aarau)
- Centre Hospitalier Universitaire Vaudois (CHUV)
- Centre Maladies Rares du Centre hospitalier universitaires vaudois (CMR-CHUV)

Initial collaboration steps have been taken with the following hospitals:

- Zentrum für seltene Krankheiten, Zürich (ZSK-ZH)
- Universitätsspital Zürich (USZ)
- Universitätsklinik Balgrist
- Centro per le Malattie Rare della Svizzera Italiana (EOC)
- Kantonsspital St. Gallen (KSSG)
- Ostschweizer Kindespital (Kispi SG)
- Ostschweizer Zentrum für seltene Krankheiten (ZSK-O)
- Universitätsspital Basel (USB)
- Universitäts-Kinderspital beider Basel (Kispi Basel)
- Universitätszentrum für Seltene Krankheiten Basel (ZSK-Basel)
- Luzerner Kantonsspital

6.2 Appendix II: Members of the Steering Board

- President: Prof. Dr. med. Matthias Baumgartner, University Children's Hospital Zurich
- Vice-President: Agnes Nienhaus, kosek
- SRDR Director: Prof. Dr. med. Claudia Kühni, University of Bern
- Dr. med. Loredana D'Amato Sizonenko, Hôpitaux Universitaires de Genève (HUG), Coordinatrice Orphanet Suisse
- Prof. Dr. med. Hans H. Jung, University Hospital Zurich
- Prof. Dr. med. Jean-Marc Nuoffer, Center for rare diseases, University Hospital, Inselspital Bern
- Dr. Adrian Spörri, SwissRDL, University of Bern

- Dr. med. dent. Alfred Wiesbauer, ProRaris
- Dr. med. Andreas Wörner, University Children's Hospital Basel (UKBB)
- Dr. med. Christel Tran, Centre hospitalier universitaire vaudois (CHUV)

6.3 Appendix III: Members of the Council of the Steering Board

- Prof. Dr. med. Matthias Baumgartner, University Children's Hospital Zurich
- Agnes Nienhaus, kosek
- Prof. Dr. med. Claudia Kühni, University of Bern
- Dr. Adrian Spörri, SwissRDL, University of Bern
- Dr. med. dent. Alfred Wiesbauer, ProRaris
- Dr. med. Loredana D'Amato Sizonenko, Hôpitaux Universitaires de Genève (HUG)

6.4 Appendix IV: National Information Campaigns

PD Dr. Michaela Fux and Dr. Natalie Bayard-Guggisberg provided detailed information about the SRDR at the following events and congresses:

- European Conference on Rare Diseases - 27. June - 01. July 2022
- Center for Rare Diseases Continuing Education Series, Berne - 04. November 2021
- ITINERARE Symposium - 12. November 2021
- Presentation of the SRDR at the Centre Hospitalier Universitaire Vaudois (CHUV) - 23. November 2021
- Patient organization Morbus Wilson - 12. March 2022
- Patient organization Schweizer Gesellschaft für Porphyrie - 14. May 2022
- Half-year meeting of patient organizations and foundations ASRIMM, Muskelgesellschaft, Associazione Malattie Genetiche Rare Svizzera italiana (MGR), FSRMM – 05. April 2022
- Presentation of the SRDR at the Hôpitaux Universitaires de Genève (HUG) - 16. June 2022
- Participation in a full day workshop of the Screen4Care project (www.screen4care.eu) - 21. April 2022
- Meetings of the coordination group of the centers for rare diseases - regularly