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Annual Report 2023
Swiss Pediatric Inflammatory Brain Disease Cohort Study

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1 Summary

EN:

«The Swiss Pediatric Inflammatory Brain Disease Cohort Study: A nationwide population-based registry to enhance knowledge and improve care of pediatric-onset MS and related disorders»

The Swiss Pediatric Inflammatory Brain Disease Cohort Study (Swiss-Ped-IBrainD) has a registry at its core. Since its establishment in 2019, it has been hosted at the Institute of Social and Preventive Medicine (ISPM) of the University of Bern. Its purpose is to systematically collect medical data of people with a pediatric-onset inflammatory brain disease (IBrainD).

The Swiss-Ped-IBrainD aims to collect and evaluate data on the diagnosis, course, and treatment of people with pediatric-onset IBrainDs. The gained knowledge can help improve the healthcare of children with an IBrainD in Switzerland. The registry further aims to clarify which areas of daily life are affected by IBrainDs and to what extent.

However, the registry is not just a simple data collection. It is also a platform that promotes the communication and collaboration of the participating clinics. The registry fosters a network of specialists in the field of IBrainDs. They do not only help gather knowledge but also implement the acquired knowledge in the best interest of their patients. **The overall goal of the Swiss-Ped-IBrainD is to improve the medical care and the quality of life of children with IBrainDs**.

In 2023 we focused on:

- Collecting and analyzing data and presenting first epidemiological results at an international conference
- Preparing and launching the first survey study
- Publishing a methodological manuscript
- Continuing international collaborations

DE:

«Die Schweizerische Pädiatrische Kohortenstudie zu entzündlichen Hirnerkrankungen: Ein landesweites Register mit dem Ziel, Multiple Sklerose und verwandte Erkrankungen bei Kindern besser zu verstehen und zu behandeln»

Die schweizerische pädiatrische Kohortenstudie zu entzündlichen Hirnerkrankungen (Swiss-Ped-IBrainD) hat als Kernstück ein Register. Dieses wurde 2019 gegründet und wird seither am Institut für Sozial- und Präventivmedizin (ISPM) der Universität Bern geführt. Das Register erfasst systematisch medizinische Informationen über Menschen, die als Kind an einer entzündlichen Hirnerkrankung (IBrainD) erkrankt sind.

Das Swiss-Ped-IBrainD hat zum Ziel, umfassende Daten zur Diagnose, zum Verlauf und zur Behandlung von Menschen mit einer pädiatrischen IBrainD zu sammeln und auszuwerten. Die so gewonnenen Erkenntnisse können dazu beitragen, die Gesundheitsversorgung von Kindern mit einer IBrainD in der Schweiz zu verbessern. Ausserdem soll das Register klären, wie sich die Krankheiten auf das tägliche Leben auswirken und in welchem Ausmass.

Das Swiss-Ped-IBrainD ist aber nicht nur eine einfache Datensammlung. Es ist auch eine Plattform, die die Kommunikation und Zusammenarbeit zwischen den teilnehmenden Kliniken fördert. Das Register pflegt ein Netzwerk von Fachleuten im Gebiet der IBrainDs. Diese helfen dabei Wissen zu schaffen und setzen es im besten Interesse ihrer Patienten um. **Das ultimative Ziel des Swiss-Ped-IBrainD ist die Verbesserung der medizinischen Versorgung und Lebensqualität von Kindern mit IBrainDs.**

Im Jahr 2023 haben wir uns auf folgende Themen konzentriert:

- Sammeln und Analysieren von Daten und Präsentation erster epidemiologischer Resultate an einem internationalen Kongress
- Vorbereitung und Lancierung der ersten Fragebogenstudie
- Publizieren eines methodologischen Manuskripts
- Weiterführen internationaler Kollaborationen

FR :

« L'étude de cohorte suisse sur les maladies inflammatoires du cerveau à l'âge pédiatrique : Un registre national pour mieux comprendre et traiter la sclérose en plaques et maladies apparentées chez les enfants ».

L'étude de cohorte suisse sur les maladies inflammatoires du cerveau à l'âge pédiatrique (Swiss-Ped-IBrainD) repose sur un registre. Depuis sa fondation en 2019, ce registre est géré à l'Institut de Médecine Sociale et Préventive (ISPM) de l'Université de Berne. Le registre recueille des données médicales de patients atteints de maladies cérébrales inflammatoires d'origine pédiatrique (IBrainDs).

Le Swiss-Ped-IBrainD a pour objectif de recueillir et d'évaluer des informations détaillées relatives au diagnostic, à l'évolution de la maladie et au traitement des personnes atteintes d'une IBrainD d'origine pédiatrique. Les connaissances acquises peuvent contribuer à améliorer la prise en charge des personnes atteintes en Suisse. En plus, le registre devrait permettre de mieux comprendre quels domaines de la vie quotidienne sont affectés par les IBrainDs et dans quelle mesure.

Le registre n'est toutefois pas un simple recueil de données, mais aussi une plateforme qui facilite la communication et la collaboration entre les cliniques participantes. Il favorise un réseau de spécialistes du domaine, qui contribueront non seulement à rassembler les connaissances, mais aussi à les mettre en œuvre dans le meilleur intérêt de leurs patients. **L'objectif global du Swiss-Ped-IBrainD est d'améliorer les soins médicaux et la qualité de vie des enfants atteints de IBrainDs.**

En 2023, nous nous sommes concentrés sur :

- Recueillir et analyser des données et présenter premiers résultats épidémiologiques à une conférence internationale
- Préparer et lancer la première étude d'enquête
- Publier un manuscrit méthodologique
- Continuer les collaborations internationales

IT:

"Lo studio svizzero di coorte sulle malattie cerebrali infiammatorie in età pediatrica: Un registro nazionale per aumentare le conoscenze epidemiologiche e migliorare la cura della sclerosi multipla e delle patologie correlate nei bambini."

Lo Studio svizzero di coorte sulle malattie cerebrali infiammatorie in età pediatrica (Swiss-Ped-IBrainD) ha un registro al suo centro. Dalla sua fondazione nel 2019, è ospitato presso l'Istituto di medicina sociale e preventiva (ISPM) dell'Università di Berna. Il suo scopo è quello di raccogliere sistematicamente i dati medici delle persone affette da una malattia infiammatoria del cervello (IBrainD) di origine pediatrica.

Lo Swiss-Ped-IBrainD ha l'obiettivo di raccogliere e valutare i dati relativi alla diagnosi, al decorso e al trattamento delle persone affette da IBrainD a esordio pediatrico. Le conoscenze acquisite possono contribuire a migliorare l'assistenza medica dei bambini con IBrainD in Svizzera. Inoltre, il registro ha l'obiettivo chiarire quali aree della vita quotidiana sono influenzate dalle IBrainD e in che misura.

Tuttavia, il registro non è solo una semplice raccolta di dati. È una piattaforma che promuove la comunicazione e la collaborazione tra le cliniche partecipanti. Il registro promuove una rete di specialisti nel campo delle IBrainD. Essi non contribuiscono solo a raccogliere le conoscenze, ma anche a metterle in pratica nell'interesse dei loro pazienti. **L'obiettivo ultimo dello Swiss-Ped-IBrainD è quello di migliorare l'assistenza medica e la qualità di vita dei bambini affetti da IBrainD.**

Nel 2023 ci siamo concentrati su:

- Raccolta e analisi dei dati e presentazione dei primi risultati epidemiologici a una conferenza internazionale
- Preparazione e lancio del primo studio di indagine basato su il registro.
- Pubblicazione di un manoscritto metodologico
- Continuazione delle collaborazioni internazionali

2 Background

Pediatric-onset multiple sclerosis (MS) and other IBrainDs are severe diseases which affect children and adolescents in a period of critical brain development. This may lead to a variety of focal neurological deficits as well as early cognitive impairment. In turn, cognitive impairment can cause additional difficulties in daily life and affect school performance and vocational achievements.

Timely diagnosis and treatment initiation as well as individually tailored management are important for a favorable disease course. However, the diagnosis of the different IBrainDs can be challenging, especially in young children, since their first acute inflammation is often accompanied by unspecific symptoms common to all IBrainDs. Creating guidelines for physicians based on a systematic assessment of similarities and differences between clinical signs, symptoms, and diagnostic work-up of different IBrainDs would enable a faster and more reliable diagnosis.

Furthermore, neither epidemiological data nor information on health care management and disease outcomes of people with a pediatric-onset IBrainD exist in Switzerland. Therefore, we have set up a national registry with the aim of understanding the epidemiology, clinical presentation, and management of pediatric-onset IBrainDs. Ultimately, the registry aims to improve the care of children and adolescents with an IBrainD in Switzerland.

3 Description of the Swiss-Ped-IBrainD

3.1 Organizational Structure

The Swiss-Ped-IBrainD consists of three governing bodies: the Steering Board, the Executive Office, and the participating clinics (university and cantonal hospitals). The Steering Board members, Executive Office staff, and participating clinics are listed in Table 1. In 2023, Claudia Kuehni stepped down from the Steering Board and Oliver Maier was elected to fill the vacancy.

Steering Board		
Sandra Bigi, PD MD	President	Department of Child Neurology, Luzerner Kantonsspital, Kinderspital Zentralschweiz, Luzern; ISPM, University of Bern, Bern
Stéphanie Garcia-Tarodo, PD MD	Vice president	Department of Child Neurology, University Hospitals of Geneva, University of Geneva, Geneva
Barbara Goeggel Simonetti, PD MD	Member	Department of Child Neurology, Pediatric Institute of Southern Switzerland, Ospedale San Giovanni, Bellinzona
Oliver Maier, MD	Member	Children's Hospital of Eastern Switzerland, St Gallen
Executive Office		
Sandra Bigi, PD MD	Clinical lead	Department of Child Neurology, Luzerner Kantonsspital, Kinderspital Zentralschweiz, Luzern; ISPM, University of Bern, Bern
Claudia Kuehni, Prof. MD	Legal representative	ISPM, University of Bern, Bern
Anne Tscherter, PD PhD	Project advisor	ISPM, University of Bern, Bern
Lorena Hulliger, MSc	Project manager	ISPM, University of Bern, Bern
Susanne Hofer, MSc	Data manager	ISPM, University of Bern, Bern
Isabella Christen, BSc	Research assistant	ISPM, University of Bern, Bern
Clinics		
University Hospital Bern, University of Bern, Bern		
Luzerner Kantonsspital, Kinderspital Zentralschweiz, Luzern		
Kantonsspital Aarau, Clinic for Children and Adolescents, Aarau		
University Children’s Hospital Basel, University of Basel, Basel		
University Hospitals of Geneva, University of Geneva, Geneva		
Paediatric Institute of Southern Switzerland, Ospedale San Giovanni, Bellinzona		
University Children’s Hospital of Zurich, University of Zurich, Zurich		
University Children's Hospital Lausanne, Lausanne		
Children's Hospital of Eastern Switzerland, St Gallen		
Kantonsspital Winterthur, Social Pediatric Centre, Winterthur		
Kantonsspital Graubünden, Department of Child and Adolescent Medicine, Chur		

Table 1: Swiss Pediatric Inflammatory Brain Disease Cohort Study staff and participating clinics; ISPM: Institute of Social and Preventive Medicine

Figure 1 illustrates the organizational structure of the registry including the interactions between the governing bodies.

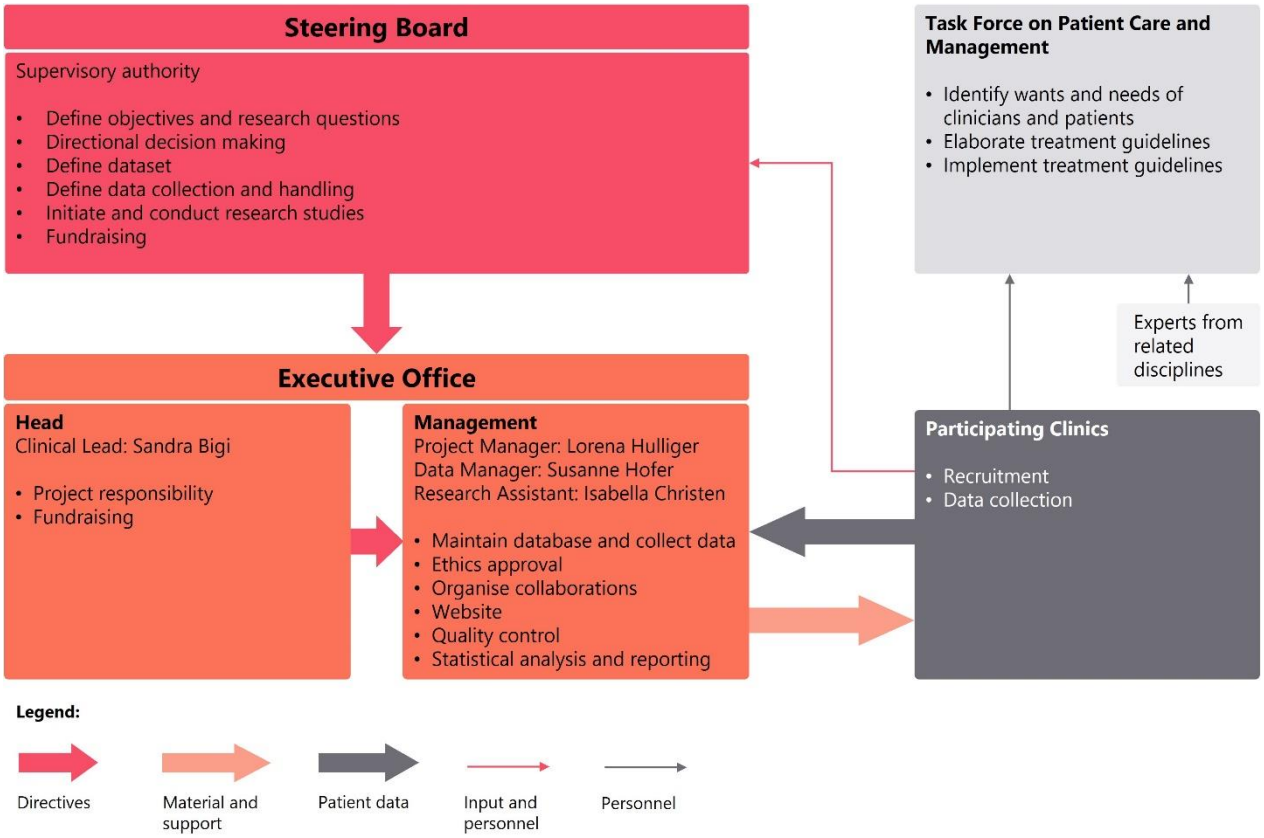

Figure 1: Organizational structure of the Swiss-Ped-IBrainD.

The Steering Board supervises the Swiss-Ped-IBrainD, takes directional decisions and has steering function. It defines the objectives of the Swiss-Ped-IBrainD and protects its interests towards third parties. Other fields of responsibility include management and legal issues, database and data collection, communication (e.g., with stakeholders, funding agencies), finances, research, and data sharing and inquiries.

The Executive Office represents the operative part of the Swiss-Ped-IBrainD. It is headed by the clinical lead who has the project responsibility and is strongly involved in funding acquisition.

The Executive Office management, which is comprised of the project and data managers, organizes a variety of tasks such as the development and of documents (study plan, patient information, case report forms, standard operating procedures, etc.), set-up of the electronic database (REDCap), collection of data, submission of documents to the ethics committee, organization collaborations, management of finances, preparation of legal documents (e.g., study agreements), dissemination of study results.

The clinics have the fundamental task of recruiting patients for the Swiss-Ped-IBrainD and providing data/data access to the Executive Office.

The constitution, rights and responsibilities of the Steering Board and Executive Office are recorded in the governance document «Collaboration Agreement on the Swiss Paediatric Inflammatory Brain Disease Cohort Study».

At the end of 2021, the «Swiss-Ped-IBrainD Task Force» was founded. The task force consists of the local principal investigators (PIs) of the participating clinics and additional members from related disciplines such as pediatric neuroradiology and neuropsychology.

The purpose of the task force is to discuss challenging cases from the clinics and to develop and implement treatment guidelines. The pediatric IBrainD patients that are currently being cared for benefit directly from the knowledge exchange within this expert panel.

In 2023, the task force met every two months. During these hybrid meetings, challenging cases from different neuropediatric clinics were discussed. The task force meetings were further used as a networking opportunity and a platform to discuss pressing matters in the field of IBrainDs such as the organization of the participation in large international studies.

3.2 Objectives

The Swiss-Ped-IBrainD has the following objectives:

1) Gathering representative, population-based epidemiological data on pediatric-onset IBrainDs in Switzerland.

2) Monitoring treatment, clinical course, education, social aspects, and outcomes of pediatric IBrainD patients.

3) Providing a platform to facilitate research, national and international collaboration, and exchange of knowledge between experts.

3.3 Inclusion/Exclusion Criteria

The following patients qualify for inclusion: All patients living and/or treated in Switzerland living with an IBrainD specified in Table 2 with an onset before the age of 18.

Demyelinating diseases
Optic neuritis
Transverse myelitis
Acute disseminated encephalomyelitis
Multiple sclerosis
Neuromyelitis optica spectrum disorders
Antibody-associated diseases
MOG-antibody disease
Anti-NMDA-R associated autoimmune encephalitis
Anti-GAD65 associated autoimmune encephalitis
Anti-AMPA-1/2 associated autoimmune encephalitis
Anti-Lgi-1 associated autoimmune encephalitis
Anti-CASPR-2 associated autoimmune encephalitis
Anti-GABA-1/2 associated autoimmune encephalitis
Onconeuronal antibody (Hu, Ri, Yo, Amphiphysin, CRMP-5, Ma-1, Ma-2, SOX-1) associated autoimmune encephalitis
Hashimoto encephalopathy
Other IBrainDs
CNS vasculitis
CNS sarcoidosis

CNS Lupus
Rasmussen's encephalitis

Table 2: Included inflammatory brain diseases

Excluded are patients with:

1) Neurological symptoms due to infectious diseases of the CNS

2) Genetic/metabolic causes of central demyelinating diseases

3) Neurological symptoms due to Guillain-Barré-Syndrome

3.4 Registration of Patients and Collection of Medical Data

The local PIs and their teams at the participating clinics are responsible for identifying children with the listed IBrainDs (see Table 2) during regular medical consultations. They inform patients and their parents/legal representatives orally and in writing about the Swiss-Ped-IBrainD. Patients who cannot be informed because they are e.g. no longer treated for their IBrainD, have transitioned to adult care, or have relocated, are sent an invitation to participate by post. Once a patient (and/or their legal representative[s]) consents to participate, their medical data is collected and entered into the registry's database. The data collection focuses on diagnostic data, follow-up data, and data on relapses.

Medical data is sourced from medical records and reports, oral/written information from treating physician(s), oral/written information from patient/family, routine statistics, and other medical registries as well as questionnaires for patients and their families.

The patients' diagnostic workup and treatment continue as usual and are independent from participation; no examination is carried out specifically for the Swiss-Ped-IBrainD.

If informed consent is not obtained after informing a patient and their family, the patient is registered in the Swiss-Ped-IBrainD with a minimal dataset. This minimal dataset consists of the following variables:

- Birth year
- Sex
- Status (alive, dead, unknown)
- Diagnosis
- Year of diagnosis

The minimal dataset is essential to properly calculate the incidence and prevalence of pediatric-onset IBrainDs in Switzerland. Furthermore, collecting the minimal dataset prevents a systematic bias by not excluding very mild cases and very severe cases of pediatric-onset IBrainDs with fatal consequences.

3.5 Ethics Approval / Data Protection

The Swiss-Ped-IBrainD project (title: «Swiss Pediatric Inflammatory Brain Disease Cohort Study», project number: 2019-00377) has been approved by the ethics committees of Bern, the Ethikkommission Nordwest- und Zentralschweiz (EKNZ), the Ethikkommission Ostschweiz (EKOS), the ethics committee of Zürich and the ethics committees of Lausanne, Geneva, and Bellinzona.

In November 2023, ethics approval was granted for the first registry-based survey study as a sub-project of the main cohort study under the same project number.

The transmission, storage, and analysis of health-related personal data within this project follow the current Swiss legal requirements for data protection and the Human Research Ordinance Art. 5. Data is always pseudonymized for analysis.

Health-related personal data are strictly confidential. They are handled with utmost discretion and are only accessible to authorized personnel. Direct access to source documents for purposes of monitoring, audits, or inspections is permitted. The data protection concept of the ISPM ensures the secure handling of all sensitive data at ISPM and within the Swiss-Ped-IBrainD. All employees are subject to a confidentiality agreement.

3.6 Funding

The Swiss-Ped-IBrainD is financed through third-party funds. We differentiate between peer-reviewed funding, funding provided by the pharmaceutical industry and funding from other sources (see Table 3).

Peer-reviewed funding

Our peer-reviewed support comes from the **Swiss MS Society** and the **Anna Mueller Grocholski-Stiftung.** The Swiss MS Society has supported the Swiss-Ped-IBrainD since its inception, providing more than a third of our total funding. **The Anna Mueller Grocholski-Stiftung** has provided the financial resources to hire staff for the registry-based survey study (See section 4). Their contribution makes up almost a tenth of our total funds.

Pharmaceutical industry funding

Roche Pharma (Switzerland) Ltd, **Novartis Pharma Schweiz AG**, and **Sanofi-Aventis (Schweiz)** are further sponsors of the Swiss-Ped-IBrainD. In 2022, we added **Biogen Switzerland AG** to our list of supporters from the pharmaceutical industry. To date, the pharmaceutical industry has provided Swiss-Ped-IBrainD with almost half of its total funding.

Other funding

The **PedNet Bern** supported the Swiss-Ped-IBrainD in its beginning with start-up aid. Additionally, the **Fondation Johanna Dürmüller-Bol** has donated money to the Swiss-Ped-IBrainD for the coverage of material costs.

Source	Contribution to total funding
Peer-reviewed funding	50%
Pharmaceutical industry	49%
Other funding	2%

Table 3: Funding contributions in percent by source

4 Achievements of the Swiss-Ped-IBrainD 2023

In 2023 we focused on:

- Collecting and analyzing data and presenting first epidemiological results at an international conference
- Preparing and launching the first registry-based survey study
- Publishing a methodological manuscript
- Continuing international collaborations

Collecting and analyzing data and presenting first epidemiological results at an international conference

The data manager, hired in 2022 to oversee data collection, regularly visits clinics to update the medical records of IBrainD patients enrolled in the registry. This relieves the PIs and their teams of the burden of data extraction from the clinic information system and entry into the registry database. Ongoing data collection for patients with extensive medical histories dating back to 2005 can be a time-consuming process. Establishing a secure remote access to some clinic information systems has greatly accelerated the data collection process and improved its cost effectiveness.

We are now up to date with the collection of baseline data for all patients enrolled in the registry. Baseline data includes information on patient demographics, initial symptoms, diagnosis, hospitalization, acute management, and long-term management if indicated. From these baseline data, and the data from the Federal Office of Statistics, we were able to approximate the incidence of IbrainDs in Switzerland for the first time (see section 5.3).

We presented these data under the title «The Swiss Pediatric Inflammatory Brain Disease Cohort Study: First insights into epidemiology» at the 48th Annual Conference of the German Neuropediatric Society (GNP) in Dortmund. The submitted abstract was published as a conference abstract in «Neuropädiatrie in Klinik und Praxis» [1].

Preparing and launching the first registry-based survey study

After hiring a research assistant at the beginning of the year, the first registry-based survey study was launched in November. It consists of two parts: a questionnaire on the quality of life (QoL) and a questionnaire on the perception of the diagnostic process of patients with pediatric-onset MS and other IBrainDs. Some of the milestones we have reached include selecting and acquiring a validated instrument (PedsQL^{TM}) to evaluate the QoL of children with MS and other IBrainDs, securing funds for a dedicated research assistant, adapting the questionnaire on the perception of the diagnostic process for different age groups, completing a pilot study to validate the questionnaire and adjusting the questionnaires accordingly.

As of the 31. December 2023, 28 patients and/or their families have responded to the survey. We are expecting around 40 responses. The first reminder will be sent out in January. We will stop sending reminders once our target of a 60% response rate has been met.

Writing and publishing a methodological manuscript

The study protocol manuscript is undergoing peer review and was submitted to PLOS ONE in June 2023. It is currently being reviewed after revisions were implemented. A preprint of the manuscript has been published on MedRxiv [2].

Continuing international collaborations

We successfully collaborated with Prof. Kevin Rostásy MD of the Witten/Hardeck University, Children's Hospital Datteln, Germany, in his project «Diagnostische Bedeutung von Biomarkern in der Differentialdiagnose und Langzeitverlauf von Kindern mit einer ersten demyelisierenden ZNS Erkrankung». Part of the Results from the project have been presented under the title «Long-time follow up of children with pre- and (post)pubertal MS» by Franziska Kauth at the 48th Annual Conference of the German Neuropediatric Society (GNP) in Dortmund. Ms. Kauth received the prize for the best abstract and her work was published in the journal «Neuropädiatrie in Klinik und Praxis» [3]. Further results of the project have been submitted for publication and are currently under review.

We initiated a collaboration with Mag. Dr. Christian Lechner from the Pediatric University Clinic in Innsbruck, Austria to conduct the survey on patient/family perception of the diagnostic process and quality of life with an Austrian cohort. This collaboration will continue in 2024.

Further achievements

As part of a university institution, the Swiss-Ped-IBrainD Registry fulfils its teaching mission by promoting young talent. In 2023, a student of human medicine started her master thesis on the diagnostic work-up of children with suspected IBrainD. The thesis is led by PD Dr. med. Sandra Bigi and supervised by Lorena Hulliger.

5 Numbers

5.1 Population and Demographics

As of the 31. December 2023, 282 eligible patients with a pediatric-onset IBrainD in 11 Swiss clinics have been identified (see Table 4). Of these, 116 patients have agreed to participate in the Swiss-Ped-IBrainD (consented). By signing the informed consent form, they allow us access to their medical data and collect the full dataset. The demographics of these participants are shown in Table 5. An additional 113 patients have been informed of the registry but have not responded (informed, not consented). Most of these patients are adults who are no longer treated by their neuropediatricians and can therefore not be informed orally in a face-to-face setting, which may explain the response rate. Fifty-three eligible patients remain to be informed (eligible, not informed). No patient/family has refused participation yet (refused).

The minimal dataset of both the patients who have agreed to participate (consented) and those who were informed but did not consent (informed, not consented) have been collected. These patients' demographics are shown in Table 6.

Population as per 31.12.2023, n=282	**n (increase/decrease compared to 2022)**
Consented	116 (+28)
Informed, not consented	113 (+11)
Eligible, not informed	53 (+3)
Refused	0

Table 4: Categories of study population

Demographics of participants (consented), n=116	
	n (%)
Sex	
Female	72 (62)
Male	44 (38)
Language region of Switzerland	
German speaking	91 (79)
French speaking	17 (15)
Italian speaking	4 (3)
Other regions	4 (3)
Age	
0-4	3 (3)
5-9	14 (12)
10-14	30 (26)
15-19	37 (32)
20-24	16 (14)
25-29	11 (9)
≥30	5 (4)

Table 5: Demographics of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland who have agreed to participate in the Swiss Pediatric Inflammatory Brain Disease Cohort Study.

Demographics of patients in the minimal dataset (consented + informed, not consented), n= 229	
	n (%)

Sex	
Female	142 (62)
Male	87 (38)
Language region of Switzerland	
German speaking	190 (83)
French speaking	31 (13)
Italian speaking	4 (2)
Other regions	4 (2)
Age	
0-4	3 (1)
5-9	16 (7)
10-14	45 (20)
15-19	60 (26)
20-24	60 (26)
25-29	28 (12)
≥30	17 (7)

Table 6: Demographics of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland of whom the minimal dataset has been collected and registered.

5.2 Diagnoses and Initial Symptoms

Among the 116 participants who have consented, pediatric-onset MS (41, 35%) was the most common diagnosis, followed by myelin oligodendrocyte glycoprotein antibody-associated disease (20, 17%) and acute disseminated encephalomyelitis (15, 13%). See Figure 2 for more details.

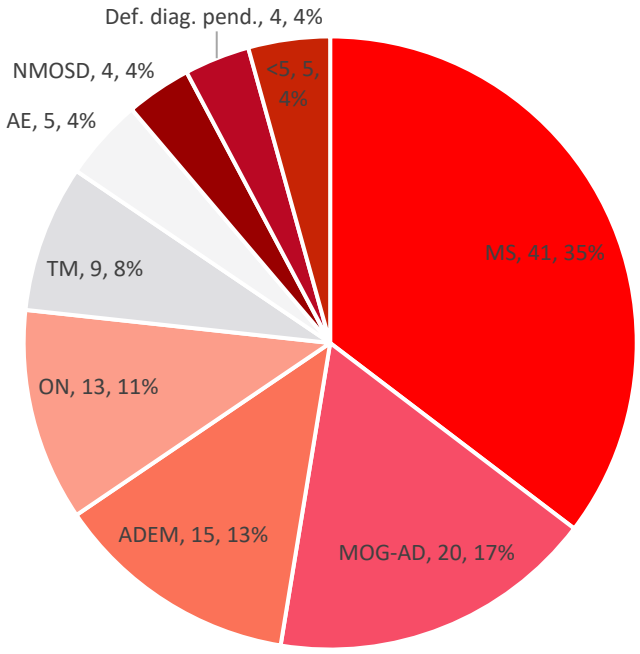

Figure 2: Diagnoses of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland who have consented to participation in the Swiss Pediatric Inflammatory Brain Disease Cohort Study (n=116). MS: multiple sclerosis; MOG-AD: myelin oligodendrocyte glycoprotein antibody-associated disease; ADEM: acute disseminated encephalomyelitis; ON: optic neuritis; TM: transverse myelitis; AE: autoimmune-encephalitis; NMOSD: neuromyelitis optica spectrum disorders; Def. diag. pend.:

inflammatory brain diseases with definitive diagnosis still pending; <5: inflammatory brain diseases diagnosed in fewer than 5 patients

The most frequent initial symptoms among the 116 participants (consented) were visual impairment (40), nausea/vomiting (39), and headaches (36). See Figure 3 for more details.

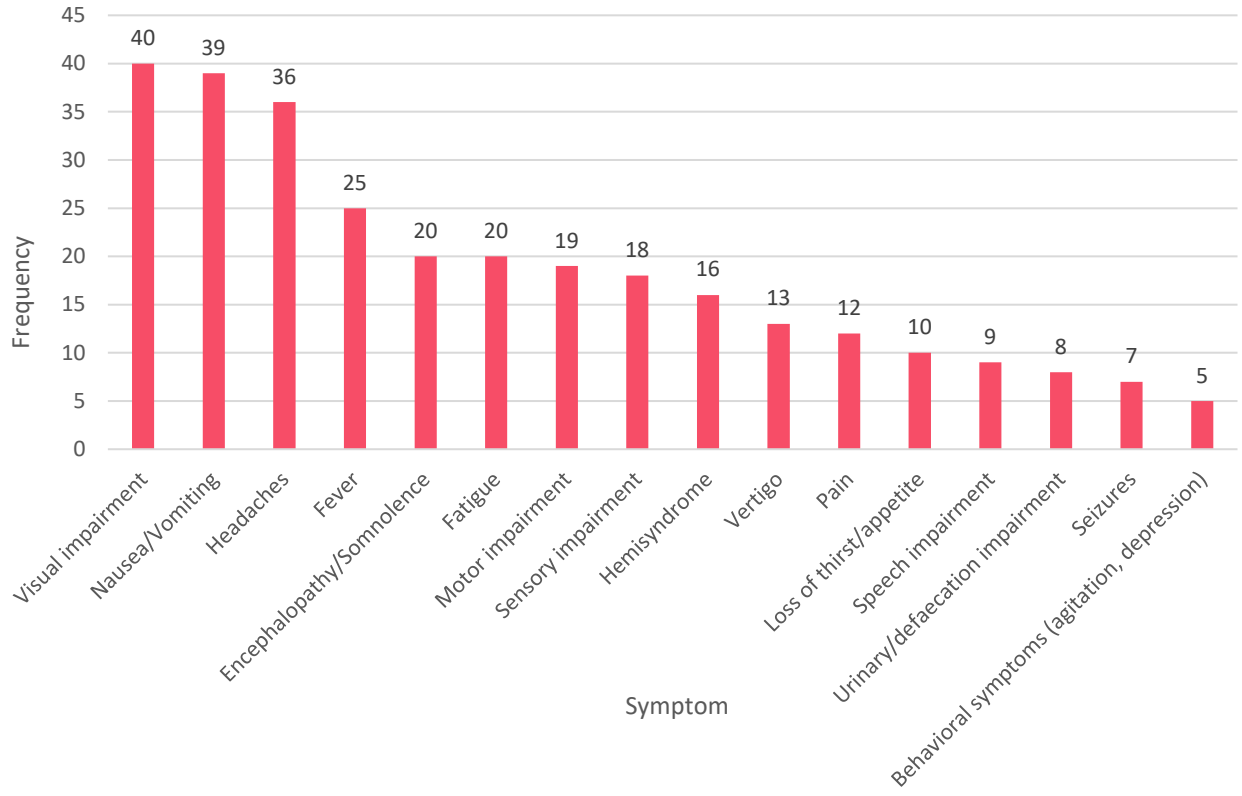

Figure 3: Frequency of initial symptoms of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland who have consented to participation in the Swiss Pediatric Inflammatory Brain Disease Cohort Study (n=116).

The minimal dataset (n=229) revealed pediatric-onset MS (108, 47%) to be the most common pediatric-onset IBrainD diagnosis, followed by acute disseminated encephalomyelitis (26, 11%), and myelin oligodendrocyte glycoprotein antibody-associated disease (22, 10%). See Figure 4 for more details.

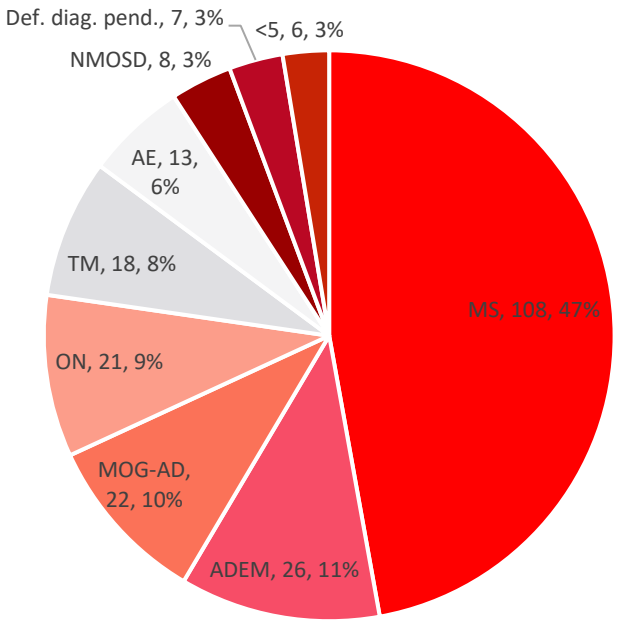

Figure 4: Diagnoses of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland of whom the minimal dataset has been collected and registered (n=229). MS: multiple sclerosis; ADEM: acute disseminated encephalomyelitis, MOG-AD: myelin oligodendrocyte glycoprotein antibody-associated disease; ON: optic neuritis; TM: transverse myelitis; AE: autoimmune-encephalitis; NMOSD: neuromyelitis optica spectrum disorders; Def. diag. pend.: inflammatory brain diseases with definitive diagnosis still pending; <5: inflammatory brain diseases diagnosed in fewer than 5 patients

5.3 Epidemiology

From the minimal dataset (and baseline data) gathered over the last three years we were able to determine 2019-2021 as the years with the most reported diagnoses. Despite our nationwide coverage and close monitoring of the participating clinics, it is probable that we missed a minor part of the cases (also because children with relatively mild attacks might not be seen by a specialist). Therefore, the calculated incidences and incidence rates are to be perceived as an approximation. However, these are the first and only epidemiological data on IBrainDs in Switzerland. They also compare well to incidences reported for other European countries.

The incidence rate of pediatric-onset IBrainDs in Switzerland is 0.74 per 100’000 person years over three years (2019-2021) and the incidence of pediatric-onset MS is 0.27 per 100’000 person years over three years (2019-2021). This translates into a pediatric-onset IBrainD incidence rate of 1.48 per 100’000 children and year and a pediatric-onset MS incidence rate of 0.56 per 100’000 children and year.

5.4 MS versus other Inflammatory Brain Diseases

During cursory analysis of baseline data, we found notable differences between patients with IBrainDs other than MS (non-MS) and those with MS, including age at symptom onset and lesion distribution across different brain areas at first presentation.

The median age at symptom onset of patients with MS was 14.4 years (15.3-12.4) and the median age of patients with other IBrainDs (non-MS) was 8.9 years (12.7-5.7; see Figure 5). The difference between the two means is highly significant (T-test, $p < 1.24e-09$).

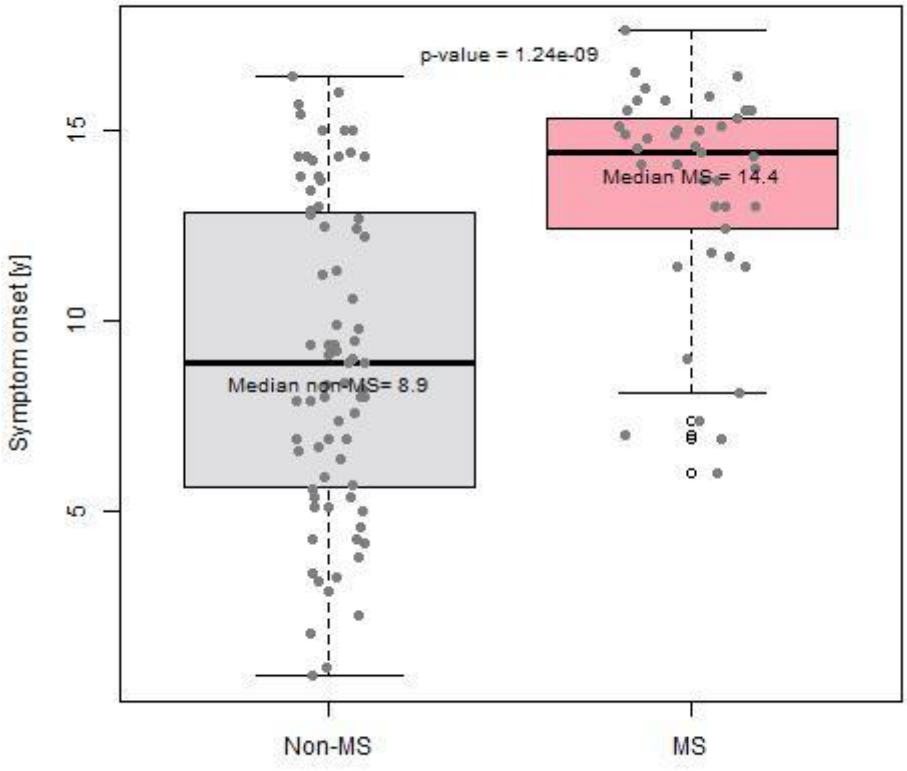

Figure 5: Distribution of age at symptom onset of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland who have consented to participation in the Swiss Pediatric Inflammatory Brain Disease Cohort Study (n=116) stratified by diagnosis into Non-MS and MS patients. MS: multiple sclerosis.

The lesion distribution at first presentation shows differences of more than 20% in the following areas: periventricular (52%), white matter (40%), juxtacortical (30%), spinal cord (23%; see Figure 6). Lesions in these areas were more common in children with MS than in children with another IBrainD. Although differences were not as large, thalamic lesions and lesions in the basal ganglia were more common in children with IBrainDs other than MS than in children with MS.

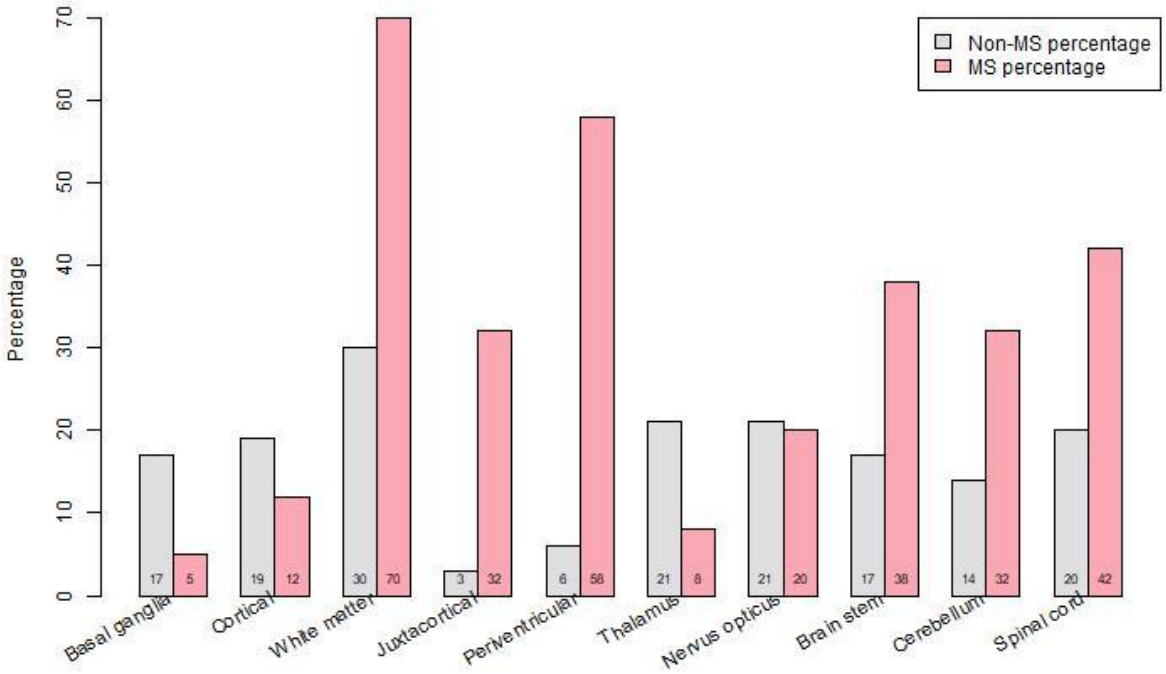

Figure 6: Distribution of lesions across different brain areas at first presentation of patients with a pediatric-onset inflammatory brain disease living or treated in Switzerland who have consented to participation in the Swiss Pediatric Inflammatory Brain Disease Cohort Study and have complete MRI data (n=110) stratified by diagnosis into Non-MS (n=70) and MS patients (n=40). MS: multiple sclerosis.

6 Outlook

In 2024 we will focus on the following activities:

- Continuing recruitment and data collection
- Creating a dataset comprised of baseline, one- and five-year follow-up data
- Preparing manuscript on epidemiology and spectrum of Ped-IBrainD diagnoses in Switzerland
- Analyzing the survey on quality of life and perception of the diagnostic process and preparing a manuscript
- Planning a second quality of life survey
- Transitioning from retrospective and prospective patient recruitment to prospective recruitment
- Continuing fundraising to secure the further existence of the Swiss-Ped-IBrainD
- Continuing the collaboration with Austria on the diagnostic process survey study

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Previous publications

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