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ORCHID (Outcome Registry for CHIldren with severe congenital heart Disease) a Swiss, nationwide, prospective, population-based, neurodevelopmental paediatric patient registry: framework, regulations and implementation

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Summary

INTRODUCTION: Congenital heart disease (CHD) is the most frequent birth defect. As survival has significantly improved, attention has turned to neurodevelopmental outcomes of children undergoing heart surgery in early infancy. Since multiple risk factors contribute to neurodevelopmental alterations, a nationwide registry collecting data on medical characteristics, interventions, clinical course and neurodevelopment until school-age is needed to improve the quality of management, identify risk- and protective factors affecting neurodevelopment, and facilitate multicentre trials.

METHODS AND ANALYSIS: The Swiss Outcome Registry for CHIldren with severe congenital heart Disease (ORCHID) is a nationwide, prospective, population-based patient registry developed (1) to collect baseline characteristics and clinical data of CHD patients operated with bypass-surgery or hybrid procedures in the first 6 weeks of life in Switzerland, (2) to monitor long-term neurodevelopment, and (3) to relate clinical characteristics and neurodevelopment to identify risk and protective factors in these children. This registry started data collection relating to pregnancy, birth, preoperative course, catheter-based and surgical treatment, postoperative course and reinterventions in 2019. The primary outcome includes standardised neurodevelopmental assessments at 9 to 12 months, 18 to 24 months and 5.5 to 6 years. We expect to include 80 to 100 children per year. Correlation and regression analyses will be used to investigate risk- and protective factors influencing neurodevelopment.

ETHICS AND DISSEMINATION OF RESULTS: Swiss ORCHID received support by the Accentus Charitable Foundation, the Anna Mueller Grocholoski Stiftung, the Swiss Society of Paediatric Cardiology, the Verein Kinderherzforschung, and the Corelina – Stiftung für das Kinderherz, and was approved by the cantonal ethics committees. Findings will be presented at national and international scientific meetings, and published in peer-reviewed journals. Results will also be shared with patient organizations, primary health care providers, and public health stakeholders to ensure a widespread dissemination of the results.

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Introduction

Congenital heart disease (CHD) is the most frequent birth defect, affecting almost 1% of live births [1]. One in four will have critical CHD and need surgery in the first year of life [2]. Improvement in surgical techniques, catheter-based interventions and perioperative intensive care have made it possible to perform corrective and/or palliative surgery for most severe CHD in the first weeks of life with a gradual drop in perioperative mortality [3–5]. Meanwhile, more than 95% of children born with CHD will survive into adulthood with an at least acceptable quality of life [6]. Therefore, there is nowadays more focus on follow-up, especially to the neurological development of these children [7–9].

Risk factors for brain anomalies and neurodevelopmental impairment in children with severe CHD

Studies have shown that there is a high prevalence of neurodevelopmental impairment in numerous domains but the severity of these problems are low [5, 10]. Up to 50% of children born with severe CHD may show some type of deficit persisting until adolescence and adulthood, including intellectual, behavioural, motor and higher-order cognitive difficulties (executive functions, memory, learning disabilities) [7, 9]. Children requiring cardiac surgery in the neonatal period or as young infants have a higher incidence of neurodevelopmental impairment than children operated on later in childhood [3, 11, 12]. Causes of neurodevelopmental disabilities in children with CHD are multifactorial, involving pathophysiological and medical factors related to the altered fetal brain development, the perinatal adaption, the perioperative course, as well as genetic [9], or environmental factors such as low socioeconomic status of the family [3, 13]. Structural brain anomalies may occur in children with CHD owing to a genetic comorbidity. In addition, cerebral blood flow, oxygen delivery or both may be altered due to fetal haemodynamic changes related to the CHD, affecting brain growth, connectivity [14] and central nervous system development in utero [15–18]. In the case of severe CHD, impaired brain development may result in a small brain volume and acquired brain injuries are similar to those seen in preterm neonates [4, 19, 20], most often in the form of white matter injury or cerebral stroke that may be identified after birth pre- or postoperatively, and has shown to be associated with impaired neurodevelopmental outcome [4]. Early diagnosis of CHD (preferably prenatal) allowing an optimised management of the delivery and the perinatal period, is therefore of great importance to avoid prolonged systemic hypoxaemia or cerebral hypoperfusion after birth [3, 21]. Preoperative risk factors for neonatal brain injury include male sex, intravenous prostaglandin infusion, intubation and mechanical ventilation, sedation [22], hypoxaemia and invasive procedures such as balloon atrial septostomy [3, 23]. Intraoperative risk factors are multiple, including duration of cardiac surgery, cardiopulmonary bypass [24], aortic clamping and deep hypothermic cardiac arrest, depth of body and brain cooling temperature, time of rewarming, reperfusion injury and inflammation, glycaemic control, pH and haematocrit management, and have all been described to play a role in neurodevelopmental outcome [3, 15, 17]. Similarly, perioperative management of low cardiac output [25] and thus oxygen delivery, as well as sedation, the risk of paradoxical embolism in presence of right to left shunt, infection, sepsis [26], hyper- or hypoglycaemia, changes in cerebral blood flow due to acute changes in ventilation can all have a prominent impact on the developing brain [27]. The above-mentioned factors are closely related, and most likely lead to a longer duration of hospital stay, which is the strongest surrogate marker for adverse neurodevelopmental outcome [28].

There is not only a high socioeconomic burden on the healthcare system of children with CHD, but also a high individual burden to patients and families. Thus, developing multicentre and/or nationwide registers is crucial. To date, many registries have focused on assessing cardiac diagnoses and treatments: examples from the US, Canada, Germany, and Scandinavian countries clearly prove the value of a nationwide, or multicentric data collection to monitor and improve quality of care in patients with CHD [29–35]. However, only few publications report on registries developed to assess long-term neurodevelopmental outcomes and to identify risk-factors for adverse consequences.

Recognising the importance of assessing neurodevelopmental outcome in this population, the American Heart Association issued a scientific statement in 2012, endorsed by the American Academy of Pediatrics, that proposes a framework for assessing neurodevelopmental outcomes [7]. In addition, specific guidelines for the neurodevelopmental evaluation of children with severe CHD from birth to 5 years of age have recently been published [36]. Nevertheless, a systematic nationwide paediatric patient registry for CHD patients in Switzerland, although clearly needed, was lacking until 2019.

Neurodevelopmental follow-up programmes for high-risk neonates in Switzerland

Center-based neurodevelopmental follow-up programmes and registries have been recommended for children with CHD [4, 7, 36]. Neurodevelopmental follow-up programmes allow the early detection of neurodevelopmental delay and the initiation of early interventions for improving outcomes [37]. Neurodevelopmental follow-up includes age-adjusted and standardised tests performed at defined ages during child development. In Switzerland, specific neurodevelopmental follow-up programmes for high-risk newborns (i.e., premature born and neonates with hypoxic-ischaemic encephalopathy) are conducted by the Swiss Neonatal Network and Follow-Up Group (SwissNeoNet). Sixteen follow-up centres across the country perform assessments at 6 to 12 months, 18 to 24 months and 5.5 to 6 years, and enter data in a centralised registry database. SwissNeoNet, inaugurated in 1995, serves as the national medical quality register of the Swiss level III and level IIB neonatal units, and as a collaborative research platform [38] (https://www.neonet.ch/swissneonet). It was therefore an ideal platform, which could be easily adapted for another high-risk population (i.e., CHD neonates). Neurodevelopmental follow-up of children with CHD requiring open-heart surgery has been introduced stepwise since the year of 2000 in only a few of the above-mentioned centres, which collected data locally. ORCHID allows standardised neurodevelopmental follow-up and fo-

cusses on the most complex CHDs and neonatal heart surgery.

Paediatric cardiac centres in Switzerland, creation of a nationwide registry

Around 800 neonates are born annually with CHD in Switzerland. Approximately 80 to 120 are operated on in the first 6 weeks of life. Cardiopulmonary bypass surgery is performed in four paediatric heart centres (Zurich, Bern, Lausanne and Geneva). Until 2019, no nationwide centralised data collection was in place, and neurodevelopmental outcome data were only collected locally by each follow-up centre.

In 2013, the process of establishing a nationwide patient registry was initiated by paediatric cardiologists and developmental paediatricians from the four paediatric heart centres in Switzerland. This core group decided that there was a need for national data collection of neurodevelopmental outcome in children operated on in early life, similar to the follow-up programmes for neonates born preterm or with asphyxia. The network was therefore extended to include a multidisciplinary group of paediatric cardiologists, paediatric intensive care physicians, neonatologists, paediatric cardiac surgeons, paediatric neurologists and developmental paediatricians from the four paediatric heart centres and the follow-up centres, and the existing SwissNeoNet platform was extended and adapted accordingly. In 2018, the Swiss neurodevelopmental Outcome Registry of CHIldren with severe congenital heart Disease (ORCHID) was founded as a collaborative, clinical and scientific research platform.

Aims and hypotheses of the registry

Swiss ORCHID serves as a nationwide, population-based, prospective registry of neurodevelopmental outcome of CHD patients with severe types of CHD, and has the following aims and hypotheses:

– To monitor on a population basis, clinical characteristics of patients with a severe type of CHD operated on in Switzerland within the first 6 weeks of life. Hypotheses: the epidemiological and clinical characteristics will be comparable within the four paediatric heart centres all over Switzerland; centre-specific differences in treatment strategies may potentially affect long-term outcome.
– To monitor the neurodevelopment of this population at 6 to 12 months, 18 to 24 months and 5.5 to 6 years of age. Hypothesis: neurodevelopmental outcome may be more closely related to the severity of the treated type of CHD (and the associated invasiveness of treatments) than to the potential variety of management strategies across centres.
– To identify risk and protective factors for mid-to-long-term neurodevelopment. Hypothesis: due to the large number of patients to be included in Swiss ORCHID and the longitudinal design of the study, data will enable determination of factors predictive of long-term outcome.

Swiss ORCHID enables quality control and improvement, management monitoring, and permits the comparison of cohorts between centres (e.g., if new intervention strategies are implemented). It also constitutes a framework that facilitates patient recruitment for pharmacological and non-pharmacological intervention trials and other prospective collaborative multicentre studies.

Methods and data analysis

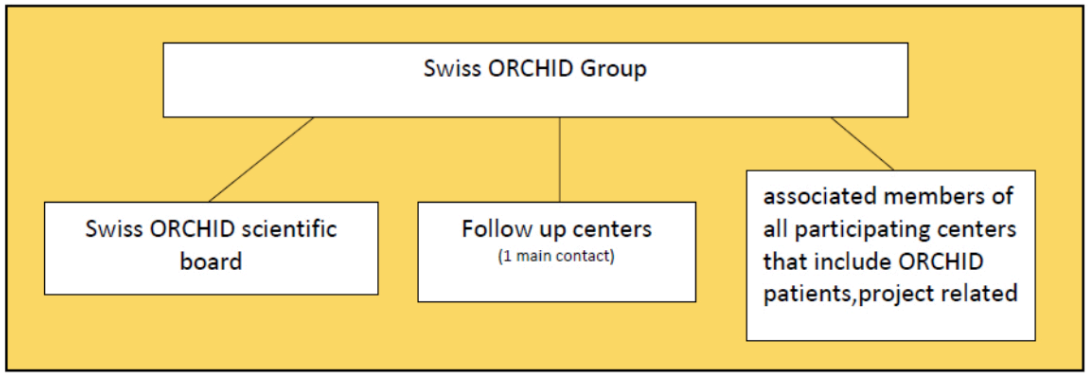
Registry design

Swiss ORCHID (CRC-Trial code: ORCHID) is a prospective multicentre observational data collection (registry) for all children with severe CHD in Switzerland who require a cardiac intervention within the first 6 weeks of life. The registry includes clinical, surgical and neurodevelopmental variables, and has been presented to the cantonal ethics committees (Req-2019-00089). The registry is operated by the Swiss ORCHID group, which consists of a scientific board (representatives of paediatric cardiology, paediatric intensive care and developmental paediatrics from the associated cardiac centres), the follow-up-centres and associated members from all participating centres (fig. 1).

Inclusion criteria, recruitment and number of participants

All neonates (including preterm born children) with severe CHD requiring an intervention within the first 6 weeks

Figure 1: Swiss ORCHID structure.



of life (cardiac surgery with cardiopulmonary bypass, hybrid procedure or surgery in preparation for later univentricular palliation surgery with cardiopulmonary bypass) at one of the cardiac centres in Switzerland are included in the Swiss ORCHID registry (table 1). Types of surgery included definitive neonatal repair, staged repair or staged palliation leading toward the Fontan procedure. Exclusion criteria are neonates having cardiac surgery or catheter intervention not meeting inclusion criteria (i.e., patent ductus arteriosus, coarctation of the aorta) due to low burden on neurodevelopmental outcome [7, 39] (table 1).

Furthermore, children have to be born and living in Switzerland. To ensure that only children who meet the inclusion criteria are included, registration of participants is restricted to the paediatric heart centres. As no other centres take care of this paediatric population of patients with severe CHD in Switzerland, the Swiss ORCHID registry is designed to be fully population based. We aimed to include 80–100 patients per year but our preliminary data since 2019 shows that we will be including between 50–60 patients per year. For registration and full data entry into the Swiss ORCHID registry, signed informed consent of the parents is necessary. If consent cannot be obtained, or a child dies before the intervention, only a minimal data set is entered into the database.

Data collection and data management

Swiss ORCHID complies with all regulatory standards of good clinical practice. Technically, the Swiss ORCHID database is set up as an extension to the SwissNeoNet and follow-up database (www.swissneonet.ch). The SwissNeoNet web application fulfils information technology security standards with respect to confidentiality, accountability, data integrity and availability. Confidentiality is achieved by restricted access (qualified password protection, centre- and person-specific user rights, encrypted transactions using Transport Layer Security), accountability by access logs, data integrity by recording when a dataset was first setup and each time that it was changed (date, user, field changed, content changed) and availability by performing continuous backups, updating and renewing the infrastructure cyclically, as well as by possessing a disaster recovery and business continuity process plan. The SwissNeoNet data collection is monitored for population coverage, dataset completeness, plausibility and reliability. Data are centrally stored on a secure server in Switzerland.

Patient recruitment, data collection and use of data of the Swiss ORCHID registry is displayed in figure 2. Each of the four paediatric heart centres is accountable for registering new patients, entering baseline data and subsequently referring the patient and family to the follow-up centre closest to their home. If families give consent to enter their child`s data into the registry, data entry includes date of birth, and a patient identifier in order to be able to find individual datasets and to add additional data on clinical course and neurodevelopmental outcome. For all other patients, despite those who definitely refused consent, an anonymised minimal data set is entered. Centralised mon-

Table 1:
Cardiac diagnostic criteria for patients included in the ORCHID registry.

Cardiac ventricle	**Biventricular CHD (staged or definite repair)**	
Primary cardiac diagnosis	Class I: two ventricles without arch obstruction	
	Class II: two ventricles with arch obstruction	
CHD	D-Transposition of the great arteries (simple/complex)	
	Aortic arch hypoplasia / complex coarctation of the aorta/ interrupted aortic arch	
	Truncus arteriosus communis	
	Total anomalous pulmonary vein return	
	Severe (neonatal) Ebstein anomaly	
	Pulmonary atresia ventricular septum defect (major aorto-to-pulmonary collateral artery)	
	Severe aortic stenosis	
	Others (ALCAPA and other coronary anomalies, aorto-pulmonary window, severe vascular rings and slings)	
Procedure (examples)	Arterial switch	
	Aortic arch surgery	
	Primary repair or right ventricular to pulmonary artery Sano shunt	
	Total anomalous pulmonary venous return repair	
	Repair or shunt procedure	
	Shunt procedure (unifocalisation, …)	
	Aortic valve repair / Ross	
Cardiac ventricle	**Univentricular CHD (staged procedure)**	
Primary cardiac diagnosis	Class III: single ventricle without arch obstruction	pulmonary duct-dependent perfusion / pulmonary overflow / systemic duct-dependent perfusion
	Class IV: single ventricle with arch obstruction	
CHD	Right heart hypoplasia: tricuspid atresia with pulmonary stenosis / pulmonary atresia +ventricular septum defect/ pulmonary atresia+interventricular septum / double inlet left ventricle +transposition of great arteries / others/ tricuspid atresia without pulmonary stenosis / others	
	Left heart hypoplasia: hypoplastic left heart syndrome/complex / Shone complex / dysbalanced atrioventricular septal defect + aortic arch hypoplasia / borderline left ventricle / others	
Procedure (examples)	Shunt procedure or ductstenting or RVOT opening	
	Pulmonary artery banding, central or bilateral	
	Norwood stage I or Hybrid (patent ductusarteriosus stent / bilateral pulmonary artery banding)	
	Damus-Kaye-Stansel procedure + aortic arch enlargement	

ALCAPA: anomalous left coronary artery from the pulmonary artery; CHD: congental heart disease; RVOT: right ventricular outflow tract

itoring is provided by a data management team. All data exports from the registry are coded and secured.

The start of data collection was 01 January 2019. Preliminary data are summarised at the end of the manuscript.

Anonymised data can be made available to ORCHID investigators for research projects when legal requirements are met. These include approval of the study protocol by one cantonal ethics review board, which is then also valid for (national) multicentre use. Currently, data usage by regional, national or international research projects is not planned. Researchers interested in collaborative work can contact the authors to discuss planned projects or analyse existing data. The decision on collaboration is made by the scientific board of the Swiss ORCHID.

Two projects have recently been submitted to the scientific board of the Swiss ORCHID and are currently being evaluated: (1) neurodvelopmental outcome in patients with preoperative levosimendan infusion and (2) the impact of necrotising enterocolitis on neurodevelopmental outcome.

Data collected

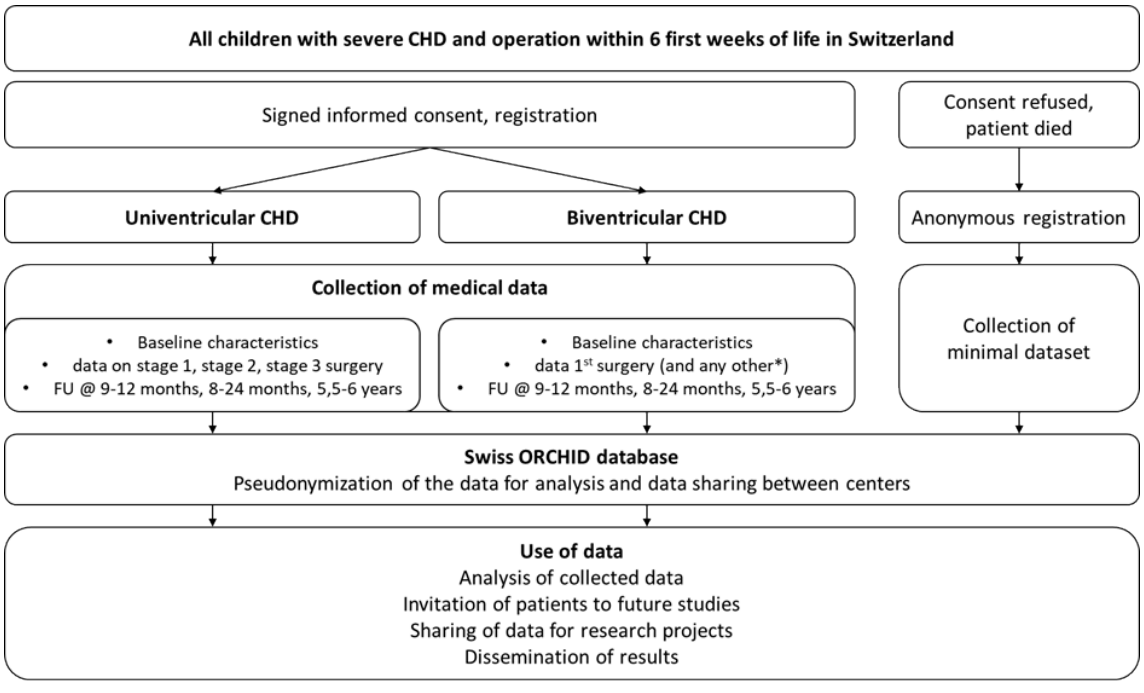
The type of data collected at different time points for different groups of patients is displayed in table 2; detailed information on all collected variables is provided in tables 3 and 4. If a child dies before the first intervention, only an anonymous, minimal dataset is entered into the database, consisting of the primary cardiac diagnosis and cardiac diagnosis group, sex, year of birth, birth location and cause of death. For all registered children whose data are fully entered, different procedures are followed depending on the type (univentricular or biventricular) of CHD. Data are entered after the first surgery for all children, after any other consecutive surgeries (depending on the type of CHD in children with biventricular CHD), and after stage 2 and stage 3 surgery for patients with univentricular CHD (tables 2 and 3). Follow-up data are entered for all children following routine visits at 9–12 months, 8–24 months, and 5.5–6 years of age (tables 2 and 4).

Outcome measures

Primary outcome measures: neurodevelopmental follow-up

Routine neurodevelopmental follow-up is at three different ages: 9–12 months, 18–24 months and 5.5–6 years. Assessments take place at the 16 follow-up centres all over Switzerland, which are also responsible for follow-up and data entry for other at-risk groups within the SwissNeoNet [40] framework. Up to an age of 42 months (3½ years), neurodevelopmental assessments are performed using the Bayley Scales for Infant and Toddler Development, 3rd Edition (BSID-III) [41], which comprises cognitive, language and motor subscores. In addition, neurological examination allows detection of cerebral palsy, which is graded according to the Gross Motor Function Classification System (GMCFS) [42]. At 5.5–6 years of age, the Kaufman Assessment Battery for Children, 2nd Edition (KABC-II) is used for cognitive evaluation [43]. This test includes five subscales that explore several aspects of intelligence including simultaneous and sequential fluid reasoning, visual processing, short term memory, planning, learning, and knowledge. In addition, a neuro-orthopaedic examination and the Zurich Neuromotor Assessment, 2nd Edition (ZNA-2) [44] are performed. The latter assesses motor functions during this early school age visit, evaluating quality of movement, motor coordination, balance and

Figure 2: Schematic chart of patient recruitment, data collection, and use of data of the Swiss ORCHID. Stage 1: Norwood or Hybride procedure, Stage 2: Bidirectional cavopulmonary anastomosis, Stage 3: Total cavopulmonary connection, FU: follow-up, * other consecutive surgeries depending on type of congenital heart disease (CHD)



adaptive fine and gross motor tasks. For timepoints and instruments used, see tables 2 and 4.

Secondary outcome measures

Secondary outcome measures will be defined in the context of future study protocols, based on the Swiss ORCHID registry. They could include functional cardiac variables, as well as assessments of health-related quality of life, behaviour, executive functions, attention, parenting style, parental satisfaction, parental needs, or others.

Endorsement or collaboration

ORCHID members are key stakeholders in the fields of Swiss paediatric cardiology, cardiac surgery, paediatric intensive care, paediatric anesthesia, and developmental paediatrics. ORCHID is cooperating with the "Verein Kinderherzforschung" (VKHFS) and is in close contact with patient and parent associations. The Swiss ORCHID will provide a large amount of prospectively collected data on the clinical characteristics of, and surgical strategies used to treat, CHD patients in Switzerland and their relationship with the neurodevelopment outcome of this vulnerable population. By gathering a large number of patients, the registry will enable an increase in the sample size for multicentre studies and allow more robust statistical analyses.

Swiss ORCHID is endorsed by the Swiss Society of Paediatric Cardiology (SSCP), and the Swiss Society of Developmental Pediatrics (SGEP). ORCHID representatives are also members of scientific societies (e.g., Swiss Heart Foundation, European Society of Paediatric Research, Cardiac Neurodevelopmental Outcome Collaborative, Newborn Brain Society, Swiss Society of Intensive Care Medicine [SSIGM], European Society of Paediatric and Neonatal Intensive Care [ESPNIC]). All of the above-mentioned channels are important to disseminate our findings.

Patient and public involvement

Patient and parent associations were not directly involved in the ORCHID registry conception. However, patient representatives will be invited as consultants in the future in order to integrate their perspectives into development of future research questions, study design, choice of outcome measures, as well as to facilitate recruitment.

Statistical analyses

After a patient's data has been checked by our database manager for completeness, plausibility and consistency, we randomly perform control checks to detect systematic mistakes during data entry. In addition, selected data points are cross-checked for plausibility with previously entered data. Descriptive statistics will include means with standard deviations (SD), and interquartile ranges (IQRs) for continuous variables, and number and percentage for categorical variables. T-tests will be used for continuous variables and $\chi 2$ tests for categorical variables. Associations between potential risk factors and neurodevelopmental outcome will be investigated using linear regression analyses. For these models, potential confounders will be included in the models. For these and further statistics, appropriate data analyses will be selected based on the research question and performed using dedicated programs (STATA, R, SPSS). All analyses will be conducted with an alpha level of 0.05. Bonferroni or false discovery rate correction will be applied if needed. In the case that the data do not meet the assumptions of linearity and normality, nonparametric tests will be performed.

Ethics and dissemination of results

The Swiss ORCHID registry has been reviewed by the cantonal ethics committees in charge of each of the paediatric heart centres (Req-2019-00089). Oral and written information about the registry is given to the patient's parents or legal guardians in either the pre- or postoperative period. If consent cannot be obtained prior to discharge

Table 2:
ORCHID data collection during follow up.

Data variables	Timepoint patient group	
	Registered uni- or biventricular CHD patients	Death prior to consent
Minimal dataset	x	x
Baseline characteristics		
Patient information, baseline medical data, pregnancy, presurgical	x	
Data after stage 1, or first surgery		
Surgery/intervention, postoperative, discharge at end of stage	x	
Data after any other biventricular surgery or after stage 2 and 3 (univentricular CHD)		
General data, presurgical, surgery, postoperative, discharge	x	
Neurodevelopmental assessment at 9–12 months		
Socioeconomic status, medical history, somatic growth parameters, physical examination	x	
BSID-III cognitive, language and motor scales	x	
Neurodevelopmental assessment at 18–24 months		
Socioeconomic status, medical history, somatic growth parameters, physical exam	x	
BSID-III cognitive, language and motor scales	x	
Neurodevelopmental assessment at 5.5–6 years		
Socioeconomic status, medical history, somatic growth parameters, physical exam	x	
K-ABC II general intelligence composite score	x	
ZNA-2 motor performance	x	

CHD: Congenital Heart Disease; BSID-III: Bayley Scales for Infant Development, 3rd Edition; KABC-II: Kaufman Assessment Battery for Children, 2nd Edition; ZNA-2: Zurich Neuromotor Assessment, 2nd Edition.

from hospital, families can be asked to give their consent at the first follow-up visit. Parents or legal guardians sign a written consent form to make anonymised registry data of their child accessible for further scientific use. To enrol patients for future studies, each particular research project based on the registry has to undergo another, specific

Table 3:
Medical and surgical variables of ORCHID.

	Data variables		**TimepointPatient group**	
			Registered uni- or biventricular CHD patients	**Death prior to consent**
Minimal dataset	Cardiac centre entering the data, place of birth, year of birth, sex, cardiac diagnosis, type of CHD, year of death*, cause of death*		X	X
Baseline characteristics	Patient information	Swiss ORCHID-ID-Nr., cardiac centre entering the data[1], informed consent, place of birth, date/year[1] of birth, sex[1], gestational age	X	
	Baseline medical data	Cardiac diagnosis[1], type of CHD[1], weight, length, head circumference, year of death[1,*], cause of death[1,*]	X	
	Presurgical	Delivery mode, birth adaptation (Apgar score, umbilical artery cord pH, lactate), feeding, intubation, respiratory support, cardiac medication, preductal saturation, haematocrit, creatinine, lactate, need for resuscitation, seizures, cerebral MRI or cranial ultrasound (classification of results if performed)	X	
Data after stage 1 or first surgery	Surgery/intervention	Age at time of catheter, age at surgery with cardiopulmonary bypass, type of interventional cardiac catheter, cardiac surgery type, RACHS score, CICU discharge day, cardiopulmonary bypass time, aortic cross clamp time, circulatory arrest time, antegrade cerebral perfusion, lowest temperature, ultrafiltration	X	
	Postoperative	Lactate peak value within 24 first hours, need for repeat surgery with or without cardiopulmonary bypass, cardiac catheter, resuscitation, ECMO and type of ECMO, drugs and duration, arrhythmias or block and treatment, duration of intubation, noninvasive ventilation, nitric oxide, oxygen, highest postoperative creatinine value, renal replacement therapy, complications after surgery (infection, diaphragmatic paralysis, chylothorax…), cerebral MRI or cranial ultrasound (date and classification of results if performed), death within 30 days postoperative	X	
	Discharge at end of stage	Day of discharge, overall number of days in CICU, destination at discharge, medication at discharge, growth parameters, transcutaneous saturation, tube feeding	X	
Data after any other biventricular surgery, or after stage 2 and 3 (univentricular CHD)	General data	Age, day of admission or surgery if still hospitalised, growth parameters	X	
	Presurgical	Repeat surgery between stage 1 discharge and stage 2 with or without cardiopulmonary bypass, cardiac catheter intervention between stage 1 and 2, preoperative intubation and duration, other respiratory support and its duration, preductal saturation, haematocrit, NYHA classification, need for resuscitation, medications, preoperative feeding, seizures	X	
	Surgery	Age at surgery, cardiac surgery with cardiopulmonary bypass, type of surgery, cardiac surgery shunt procedure, RACHS, CICU discharge day, cardiopulmonary bypass, aortic cross clamp and circulatory arrest durations, antegrade cerebral perfusion, lowest temperature, ultrafiltration	X	
	Postoperative	Lactate peak value within first 24 hours, repeat surgery with or without cardiopulmonary bypass, cardiac catheter intervention, need for resuscitation and duration, ECMO and type of ECMO, medications and duration, arrhythmias or block and treatment, duration of intubation, noninvasive ventilation, nitric oxide, oxygen, highest postoperative creatinine value, renal replacement therapy, complications after surgery (infection, diaphragmatic paralysis, chylothorax…), death within 30 days postoperative	X	
	Discharge	Day of discharge, overall number of days in CICU, destination at discharge, medication at discharge, growth parameters, transcutaneous saturation, tube feeding	X	

[1] Part of minimal data set, * if applicable

CHD: congenital heart disease; CICU: cardiac intensive care unit; ECMO: extracorporeal membrane oxygenation; MRI: magnetic resonance imaging; NYHA: New York Heart Association; ORCHID: Outcome Registry for CHIldren with complex congenital heart Disease; RACHS: risk adjustment for congenital heart surgery

Table 4:
Neurodevelopmental outcome variables of ORCHID.

Data category	**Data variables**	**Age at assessment**	
		9 to 12 and 18 to 24 months	**5.5 to 6 years**
Socioeconomic status	Parents' education and current occupation	X	X
Medical history	Cardiac medication, hospitalisation during the first year, interventions during the first year (repeat cardiac surgery, catheter intervention or other interventions), tube feeding	X	X
	Current therapy (early intervention, physiotherapy, occupational, psychology, other…)		
Somatic growth parameters, physical exam	Height, weight, head circumference	X	X
	Cerebral palsy and GMCFS, non-cerebral-palsy neuromotor abnormalities		
	Sensory assessment (visual impairment, hearing impairments)		
	Other neurodevelopmental abnormalities (fetal alcohol syndrome, genetic disorder, congenital infection, attention-deficit hyperactivity disorder, autistic spectrum disorder, speech impairment, epilepsy, …)		
Assessment tools	BSID-III cognitive, language, and motor standard scale	X	
	K-ABC II general intelligence composite score / ZNA-2 motor performance		X

BSID-III: Bayley Scales for Infant Development, 3rd Edition; GMCFS: Gross Motor Function Classification System; KABC-II: Kaufman Assessment Battery for Children, 2nd Edition; ZNA-2: Zurich Neuromotor Assessment, 2nd Edition

approval procedure by the cantonal ethics committees. The registry fosters national collaboration and standardisation of practices, and will form the basis of research projects aiming at improving management and monitoring outcome after new intervention strategies. Annual reports go to all participating centres and collaborators for quality control purposes, as well as to the funders, parent organisations, healthcare stakeholders and the endorsing medical associations. Findings will also be presented at national and international scientific meetings, and published in peer-reviewed journals to ensure a widespread dissemination of the results.

Preliminary data

Between 2019 and 2021, 161 patients met the inclusion criteria. Of these, we received informed consent of 138 families and could record complete data sets. Reasons for patients not fulfilling the inclusion criteria were no consent given (n = 3), death before available consent (n = 12), or incomplete dataset (n = 8).

The most common type of CHD was transposition of the great arteries, (n = 50, 31.1%) followed by single ventricle CHD (n = 32, 19.9%), the latter requiring a 3-stage surgical management (table 5.)

Discussion

The neurodevelopmental Outcome Registry for CHIldren with severe congenital heart Disease (ORCHID) is based on an interdisciplinary network of collaborating paediatric cardiologists, developmental paediatricians, paediatric intensive care and anaesthesiologists, neonatologists, and paediatric cardiac surgeons, to ensure a wide range of viewpoints and contributions to new research projects that will use registry data. Standardised neurodevelopmental outcome assessment after early invasive surgical or catheter-interventional treatment of neonates affected by a severe form of CHD in a nationwide registry facilitates quality improvement, allows comparison of strategies of care, and lowers the threshold for multicentre trials. Utilising the structure and established protocols of a pre-existing registry (SwissNeoNet) along with discussion with the involved centres and experts as a basis for ORCHID proved to be cost effective and time saving. The data collection will enable a better understanding of clinical risk factors for neurodevelopmental impairments, although direct comparisons of participating centres will remain limited due to the variety of differences in treatment procedures between paediatric heart centres.

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Author contributions: JN and JS wrote the first draft. BL and WK conceived and initiated the registry. NS, CBT, JB, MB, KF, MG, DH, JK, CL, MP, AP, MvR, and WK are steering committee members of the Swiss ORCHID, who designed and developed the registry, and gave valuable input to the manuscript. MvR, WK, and NS critically revised the manuscript. VR and MA added many details and proof-read the text.

Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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Table 5:
Preliminary data 2019-2021.

Cardiac diagnosis	Number of patients	Percentage
Hypoplastic left heart syndrome	20	12.4%
Single ventricle, other	12	7.5%
Transposition of great arteries	50	31.1%
Aortic coarctation / hypoplastic aortic or interrupted aortic arch	15	9.3%
Common arterial truncus	10	6.2%
Pulmonary atresia + ventricular septum defect / tetralogy of Fallot	6	3.7%
Pulmonary atresia + interventricular septum	6	3.7%
Total anomalous pulmonary venous return / partial anomalous pulmonary venous return	11	6.8%
Other	27	16.8%
Unknown (incomplete data so far)	4	2.5%

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