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Medical registries and their use for research projects

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Registries provide important real-world data about public health and thus have a major impact on far-reaching political health decisions and medical patient care. In addition, registries contribute to transparency and comparability of medical services and are the basis for epidemiological and clinical research. Last but not least, they play a key role for quality assurance and the development of medical services (Mathis-Edenhofer and Piso 2011). It is therefore hardly surprising that the number of registries in Switzerland is steadily increasing. In order to effectively operate registries and use them for research purposes, it is essential to ensure the quality of the collected data and their compliance with regulatory requirements. This article provides an overview of medical registries by discussing four related questions.

What are medical registries?

A commonly used and broadly applicable definition of the term “registry” is provided by Mathis and Wild (2008): “A registry is a systematic collection of population or patient-related, but also quality-related medical and/or health economic data in a predefined workspace, and its evaluation, which fulfils a defined purpose, but for which variability for different questions is allowed.” The landscape of medical registries in Switzerland is highly diverse and constantly growing. As of August 2020, 103 registries have been recorded on the online platform of the Swiss Medical Association (FMH) (DE; FR) (see also section **Medical registries in Switzerland**). These registries collect health data for epidemiological and/or clinical purposes and cover all fields of medical care and a huge variety of indications.

Registries can be classified as mandatory or voluntary. Mandatory registries are required by public health policy and serve a variety of purposes. For example, they can be used to monitor evolutions of communicable diseases, organ donations, or cancer, or they can help to assure the quality required for the professional certification needed to receive a performance mandate for highly specialised medicine. Applicable legislation (e.g. Cancer Registration Act or Transplantation Act) is issued by the federal or a cantonal government or is decreed by intercantonal agreements from the Swiss Conference of the Cantonal Ministers of Public Health.

Most registries, however, are voluntary and initiated by medical specialists, medical associations, industries, or even patient groups. The aims and purposes of these registries vary widely and cover a broad range of indications. Voluntary registries have different geographical reaches: some focus on a specific region, while others have a nationwide focus or involve international collaboration. Health data collection might also be restricted to one or only a few institutions.

What are the operational and regulatory requirements for registries?

Setting up a registry may sound easy, but it requires much more than just developing an electronic database and collecting health-related data. In fact, managing a registry is a tremendous and ongoing task. Both establishing and maintaining a medical registry require substantial professional expertise, human resources, infrastructure, and financial resources.

So why make the effort to set up a registry? The overarching aim of medical registries is to accurately and consistently collect high-quality, reliable data over a long period of time and then use this data to improve care and treatments of patients and for research purposes. Associated benefits for patients and society include increasing the transparency and comparability of treatments, establishing or monitoring quality management, detecting problems, and, ultimately, improving health care. In order to fulfil this aim, registries have to comply with certain quality requirements. The ANQ (Swiss National Association for Quality Development in Hospitals and Clinics), FMH (Swiss Medical Association), H+ (the association of Swiss hospitals), SAMS (Swiss Academy of Medical Sciences), and unimedsuisse (an association of university medicine in Switzerland) jointly issued recommendations to help ensure that registries are established and operated in accordance with essential quality criteria (see **Table 1**,
source: https://www.anq.ch/wp-content/uploads/2018/02/Registries_Recommendations.pdf)

	Quality criteria
1	Registry design
2	Expertise required for registry management
3	Data protection and data ownership
4	Data collection
5	Quality assurance
6	Data use
7	Change of purpose and dissolution

Table 1: Quality criteria for medical registries

Additional aspects that need to be considered when setting up a registry are discussed below.

Legal framework

The legal framework that applies to a medical registry should be clarified before setting it up since this determines the operational requirements to maintain it (see Table 2 for an overview of regulatory requirements). Depending on their purpose and field of interest, medical registries are subject to various federal and cantonal regulations that govern data protection, data collection, data transfer, confidentiality, and other applicable areas. In general, voluntary registries collecting previously recorded routine clinical data for future research purposes are also regulated by the Human Research Act (HRA) and chapter 3 of the Human Research Ordinance (HRO). If a medical registry is supplemented by a concomitant biobank that collects additional body fluids and tissue, it is also subject to the HRA and chapter 2 of the HRO. The same applies if additional health-related data are collected beyond clinical routine procedure.

Ethics committees (approval, information, and advice)

The HRA does not require authorisation for collecting already existing data and samples per se, provided participants have given their consent or have been informed accordingly. Approval from an ethics committee (EC) is needed only when data or samples are used for research projects. However, researchers can voluntarily request an EC's opinion when setting up a registry or a biobank. This gives them the certainty that ethical, legal, and technical requirements have been met and research projects based on that registry or biobank will have a smooth approval process. A form has recently been introduced on the BASEC (Business

Administration System for Ethics Committees) portal for this purpose (cf. article from swissethics in this issue).

Taking additional samples of tissue, blood, or other body fluids for research purposes represents a research project itself (HRO, chapter 2), even if taken during a routine procedure (e.g. taking an extra tube of blood during routine blood sampling). Therefore, before additional samples can be taken, EC approval and patients' consent must be obtained in advance. The same applies if additional data are collected (e.g. questionnaires on aspects of quality of life which are not routinely assessed).

Informed consent

Generally, patients must give their consent or be informed about their right of objection before their data can be used for research purposes. Either a registry-specific or a general consent form can be used. Depending on the degree of traceability (uncoded, coded, or anonymised) and the type of data (genetic or non-genetic), stricter data protection rules may apply (see HRO, art. 28–32). For example, while informing the patient about his or her right of objection is sufficient for the further use of coded non-genetic data, the further use of coded genetic data for research requires the (written) consent of the patient. In exceptional cases, where it is impossible or requires disproportionate effort to obtain consent or inform the patient, the EC may authorise the further use of data even without the patient's consent or information. However, this is reserved for special situations and requires a case-by-case assessment by the EC (HRA, art. 34).

For further information on points 2b and 2c, see the document Guiding Principles for Registries in Human Research on swissethics' website (in German and French).

Registries' internal regulations

The quality, transparency, and focus of a registry are pivotal success factors. To put a medical registry into operation, it is vital to establish internal regulations that define the registry's aims and tasks and that cover all the essential aspects of the above-mentioned registry recommendations (see Table 1). Additional documents describing the registry's organisation, orientation, and activities might be necessary and should be regularly updated (organigrams, flow charts, annual reports, etc). In essence, the documents should provide a comprehensive and binding description of the registry and should be kept current (Lübbeke-Wollf, Clerc, and Kern 2019).

Agreements

The relationship to stakeholders (e.g. financial donors, participating institutions involved in data exchange, and external service providers) has to be defined by appropriate agreements. Contracts should be in place which define not only the roles and responsibilities but also the rights to data usage for all involved parties. It has to be stressed that special attention should be paid to regulate the data exchange for research projects. swissethics provides academic institutions with a Data Transfer and Use Agreement (DTUA) template issued by the Swiss Personalized Health Network (SPHN).

Finances

A long-term financial concept has to be in place in order to run a registry for a long period of time and gain high-quality data sets from which meaningful results can be generated. Moreover, registries require, amongst other things, professional staff and systems for data collection, validation, and cleaning.

Governance of patient data

The governance of patient data has to be clarified and regulated in advance: how data are stored and processed in the registry (non-coded, pseudonymised, or anonymised), how the traceability of data is maintained, where and by whom data are stored, how data protection requirements are maintained, which software is used, how data access and exchange are regulated, etc. In addition, the administrative, technical, and physical safeguards for storing, processing, and exchanging data have to be defined. Although data storage and processing may be outsourced to specialised service providers, the holder of the registry is responsible for adhering to legal requirements and contractual agreements.

Registry classification	Mandatory	Voluntary	
Initiation	Federal or cantonal authorities (Federal Office of Public Health, Swiss Federal Statistical Office)	Medical specialist associations, investigators, industries, patient associations	
Examples	Notification of observations on communicable diseases (HIV, measles, tuberculosis, etc.), Swiss Organ Living-Donor Health Registry, cantonal cancer registries, SIRIS (Swiss National Joint Registry)	Swiss HIV Cohort Study, SCQM (Swiss Clinical Quality Management in Rheumatic Diseas-es)	
Category	Routine data only	**Routine** data/samples	**Additional** data/samples
Regulatory requirements (as applicable)	Federal and cantonal data protection acts, legislation on the electronic patient dossier, Federal Act on Medicinal Products and Medical Devices, Swiss Criminal Code (art. 321), Medical Professions Act, Psychology Professions Act, and others as applicable		
	Swiss Federal Health Insurance Act, Cancer Registra-tion Act, Epidemics Act, Transplantation Act, etc	Human Research Act Human Research Ordinance, chapter 3	Human Research Act Human Research Ordinance, chapter 2
Patient information and consent	Exemption example: Swiss National Cancer Registry – information and opt-out	Written patient information and consent (registry-specific or general)	Patient consent (registry-specific) and EC approval
Ethics approval of data/sample analysis	n/a	EC approval for any further use	EC approval for any further use not already included in the initial project

Table 2: Overview of regulatory requirements for mandatory and voluntary medical registries

How can research projects use data from medical registries?

Research projects based on data from medical registries complement clinical trials in an important way. Registries gather data from real-world daily clinical practice and thus from a larger and more heterogeneous

population (with comorbidities) over a longer period of time. By comparison, in clinical trials new treatments are usually investigated under strictly defined conditions for highly selected populations. Registries are therefore valuable data sources for supporting evaluations of safety and effectiveness and for other issues, such as treatment compliance and disease risk factor recognition. Meaningful results from such research projects may only be derived if the registries used were carefully designed to reflect the current medical and scientific contexts, need, and state of knowledge. Further, it is essential that the collected data are valid, accurate, complete, and comprehensive, and that bias is minimised as much as possible. When planning a research project, attention should be paid to the hypothesis and formulation of appropriate plausible research questions. In addition, it is worth examining in advance whether the data from the registry are suitable to answer the research questions. This pre-check allows the quality of the data-set to be determined and thus can expose limitations of the data which can be considered with regard to study design, data analysis, and finally the evaluation of the results (Psoter and Rosenfeld 2013).

Before data from registries can be analysed, a research project has to be defined and EC approval has to be sought (see Section 2b above). The research application for an EC requires certain study documents – for example, a research protocol and informed consent form. Detailed guidelines and templates for required regulatory documents are available on swissethics' website (see **Table 3**). In addition, Clinical Trial Units (CTUs) at university or cantonal hospitals support clinicians performing research projects by providing advice and assistance on fulfilling regulatory requirements.

What can we learn from a successful medical registry?

The Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry illustrates how a medical registry can be successfully managed in the long term and benefit both patients and physicians. Established in 1997, the SCQM registry is a voluntary national registry for various inflammatory rheumatic diseases. It is managed by a non-profit foundation that closely collaborates with the Swiss Society of Rheumatology (SGR). Various industrial sponsors as well as the SGR secure the registry's long-term financing.

One aim of the registry is to improve quality management and the treatment of patients with rheumatic diseases. This is achieved by providing an immediate feedback system to follow up the course of the disease and the treatment available to the treating physician and patient. Additional objectives are to enable research using the collected data to investigate the tolerability and efficacy of treatments in everyday clinical routine, to evaluate disease assessments, and to gain new insights into the pathogenesis of the investigated diseases. To do this, physicians record data from annual control (follow-up) and interim visits in a highly structured database. In order to keep the registry attractive for the contributing patients and physicians, various innovations have been introduced over the years. Feedback reports summarise the data at the level of the individual patient. They include graphical overviews and tabular listings displaying physician and patient reported outcome measures, lab and other follow-up parameters, and anti-rheumatic medication over time. These overviews are extremely valuable to physicians when they prepare for patient visits, when they aim to treat to target, or when they make treatment evaluations and decisions together with their patients. In addition, patients can retrieve the graphical overviews at any time, which makes their treatment and the course of the disease as transparent as possible. Moreover, an app enables patients to report on-demand drug use, drug compliance, and patient reported disease activity between visits to the doctor. These updates provide additional data and more precise documentation without increasing the workload for the physicians. The integrated registry for pregnant patients supports quality management in this critical period of women with inflammatory rheumatic diseases and may provide new insights and opportunities for research.

Besides the advantages the SCQM registry brings to daily clinical practice, it also serves as a data source for research projects for participating physicians. For this purpose, the SCQM registry has established an application process together with rules governing collaboration and research with data from the registry. To

ensure high data quality, automated processes and appropriate software support data plausibility and completeness by conducting data checks directly during data entry.

To minimise data gaps and to increase data quality, minimal quality requirements have been defined and various measures have been implemented. Monthly status reports that provide an overview about the data quantity and data quality of an institution's data records are generated for and issued to each participating institution. This supports physicians by providing a minimal and meaningful data set.

Further, SCQM staff and physicians at larger institutions train and support participating physicians. To manage the complexity and huge extent of data and adhere to data protection requirements, the electronic database is continuously developed.

Not only its professional, very well-structured database contributes to the success of the SCQM registry, but its highly organised staff and working structures also play an important role. The registry's first pillar, the SCQM board, is responsible for its strategic orientation and the approval of research project applications. The second pillar, the registry's scientific committees, is responsible for ensuring that the registry corresponds to the latest scientific and medical state of the art essential for collecting data of scientific relevance. The scientific committees are also responsible for evaluating research applications. The third pillar of the registry, an administrative team, organises all structures and processes within the registry for fundraising, finance administration, service provision, stakeholder management, marketing and communication, and human resources management. A scientific team is responsible for data requests, applications for research projects, study management and coordination, planning analysis of research projects, supporting publications, etc. Over many years, the registry has continuously increased patient numbers and produced a remarkable output, including many peer-reviewed publications each year.

The SCQM registry clearly demonstrates that a successful registry cannot be run by simply providing a database from which data may be derived. A substantial investment is needed to maintain a high-quality standard for acquiring complete and correct data and to develop a registry according to new needs and changing requests.

Table 3: Summary of guidelines, information, templates, and checklists for establishing registries and related research projects

Guidelines and information

Recommendations for the development and operation of health-related registries from ANQ, FMH, H+, SAMS, and unimedsuisse
https://www.anq.ch/en/publications/register-recommendations/
https://swissethics.ch/en/themen/biobanken

Guiding principles for registries in human research (in German and French)
https://swissethics.ch/en/themen/biobanken

Guideline on the retention period of data and samples for further use projects without consent (in German, French, and Italian)
https://swissethics.ch/en/themen/biobanken

Ethical Framework for Responsible Data Processing in Personalized Health Research, Version 2
https://sphn.ch/services/documents/ethics-legal-governance/

Templates and checklists

Template for the Data Transfer and Use Agreement (DTUA)
https://swissethics.ch/en/themen/biobanken
https://sphn.ch/services/documents/ethics-legal-governance/

Checklist for health-related registries from ANQ, FMH, H+, SAMS, and unimedsuisse
https://www.anq.ch/en/publications/register-recommendations/
https://swissethics.ch/en/themen/biobanken

Study protocol template for further use with consent (in German, French, and Italian)
https://swissethics.ch/en/templates/studienprotokollvorlagen

Study protocol template for further use without consent (HRA, art. 34 and HRO) (in German, French, and Italian)
https://swissethics.ch/en/templates/studienprotokollvorlagen

Template for a patient information/informed consent according to the HRA and HRO art. 28 (in German, French, and Italian)
https://swissethics.ch/en/templates/studieninformationen-und-einwilligungen

General consent template for the general re-use of coded (genetic) personal data and coded material for research purposes (in German, French, and Italian)
https://swissethics.ch/en/templates/studieninformationen-und-einwilligungen

Conclusion and outlook

Medical registries are highly valuable sources of health information. They can be used for many purposes – for example, as tools for quality assurance and improvement in medical care or as sources for research projects. Research projects from medical registries are less expensive and less complex logistically compared to clinical trials and are thus an inexpensive and relatively quick option for answering research questions. However, data quality must be ensured, and both the appropriate organisation and adequate financing need to be in place. In the last few years, the regulatory and operational frameworks for medical registries and research projects have been very clearly defined by various stakeholders with guidelines, recommendations, and templates. Moreover, the SPHN is currently working to build up an appropriate infrastructure to facilitate the pooling and accessibility of health-related data from multiple Swiss healthcare institutions for research purposes. Further guidance on how to ensure data protection and regulate data sovereignty will be helpful.

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