SCTO PLATFORMS

ISSUE 7, JUNE 2022

Data privacy and data sharing in clinical research

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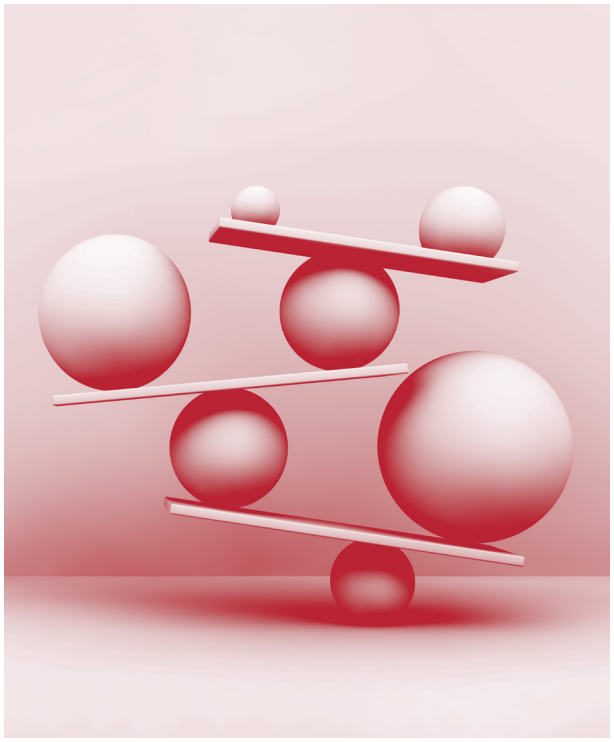
EDITORIAL



KEEPING A BALANCE BETWEEN DATA PRIVACY AND DATA SHARING IN CLINICAL RESEARCH

Achieving balance in our frantic daily lives is not easy. Weighing up pros and cons requires time and information on the risks involved and the potential consequences of doing – or not doing – something. This balancing act also takes place in clinical research, especially when considering the immanent pressure on researchers to "publish or perish".

Sharing research data that are new, of interest to the scientific community, of good quality, and that favour reproducible research is a welcome call. However, clinical research by nature deals with sensitive data that, if disclosed, can potentially have huge consequences on an individual's life. On top of legislation aimed at protecting citizens' data in general, additional laws, ordinances, guidelines, and guidance provide the clinical research community with a full framework aimed at protecting individuals' privacy and health and respecting their dignity. In addition, the Swiss National Science Foundation (**SNSF**) has created practical documents such as guidelines and a template for creating a data management plan (**DMP**), and the Swiss Clinical Trial Organisation (**SCTO**) has published a guidance document on sharing data from clinical research projects in order to help researchers anticipate the life cycle of their research data and make appropriate decisions when sharing research data.

When managing research data, researchers can face a series of dilemmas: How to respect privacy and share data at the same time? How to responsibly balance protection and the use of clinical research data? It is not ethical to publish personal data, even when anonymised, without consent (with a few exceptions). But it is also not ethical to *not* share data that could facilitate medical progress and help other human beings. Therefore, should a researcher favour the individual or the community? In the end, it is all a matter of perspective. Perception will vary between individuals, depending on their age, education, health condition, and many other personal factors that can tip the scales one way or the other. The scales can even tip in opposite directions throughout a person's life, reflecting changes in the factors that influence a person's decision-making in any given situation. Therefore, researchers need to be continually informed about the relevant regulatory background and the ethical and practical factors to consider when thinking about how to make decisions about data sharing and data protection.

Our initial aim for this issue of *Regulatory Affairs Watch* was to focus exclusively on clinical research data, meaning data obtained from clinical studies or clinical trials. However, we decided we also needed to address the elephant in the room: the further use of health data

from routine clinical activities. The articles in this *RA Watch* lead you through different factual aspects of data sharing and data protection, present various opinions and points of view, and contain examples and experiences related to the topic. This *RA Watch* is intended to help inform your opinion on this tricky topic.

- **DEEP DIVE:** As a starting point, the Regulatory Affairs Platform (RA Platform) team provides an overview of the various requirements that apply to data privacy and data sharing in clinical research conducted in Switzerland.

- **VIEWS AND OPINIONS:** Diverse approaches are reported here: a regulatory analysis from the Cantonal Ethics Committee Zurich, a legal view of the topic from a specialised lawyer, and a perspective from industry about the challenges and opportunities of data sharing.

- **NEWS FROM:** The news corner covers the approach and concepts governing the initiation and provision of data sharing services of one of the best known Swiss data repositories (Zenodo at CERN) and offers advice on preparing data to be shared. Two ways of taking advantage of the scientific benefits of shared data are also presented: the highest level of evidence through meta-analyses by an epidemiological expert at the University of Bern and the research on research (**RoR**) approach by the STEAM working group.

- **CASE STUDY:** Last but not least, an illustration of a researcher's experience with sharing real-world data is shared by the man behind the data of one of Switzerland's greatest successes in observational research: the CoLaus|PsyCoLaus cohorts.

After almost one year of coordinating the RA Platform *ad interim*, it is time for me to hand over *RA Watch* to a new, permanent RA Platform coordinator and pursue other opportunities. It was truly a pleasure to prepare this new issue. I hope that you enjoy reading it and that it will help you keep your balance!

Isabelle Guilleret, Interim *RA Watch* Editor and Interim Regulatory Affairs Platform Coordinator at the Clinical Research Centre (CRC) Lausanne

Opinion

Data sharing and data privacy: what an inherently antithetical, self-contradictory topic! How and why should researchers share what one would normally rather keep undisclosed – especially in the context of clinical research, which by nature deals with sensitive health-related data? The difficult nature of this topic was reflected by some pushback the *RA Watch* team experienced when requesting contributions for this issue (it is too controversial, it is too early to have a (publishable) opinion or policy, it is too much of a work in progress, etc.). While most experts in our field take a more cautious approach to data sharing, some other more confident stakeholders consider the existing data protection policies and systems to be sufficiently safe to upscale data sharing across multiple sources, from sport watches to genomic data to health records. Is there any zero-defect system? What about cyber-attacks? And while the UK's National Health Service (**NHS**) demonstrated to the world the power of data sharing in COVID-related research, it has also been challenged by a BMJ audit detecting hundreds of data privacy breaches. And should we openly share data in a world in which Switzerland's Federal Data Protection and Information Commissioner (**FDPIC**) joined the Court of Justice of the European Union (**CJEU**) in invalidating their Privacy Shield data transfer pacts with the US? What protections for data privacy are possible without impairing research?

These questions on data privacy and data sharing do not have easy answers. In this issue of *RA Watch*, our contributors (who are generally in favour of data sharing since they are involved in research) tackled many of the challenges, potential advantages, and pitfalls of data sharing from different angles. Their contributions can help shape the ongoing dialogue on this controversial topic. Happy reading!

Marc Froissart, Director of the Clinical Research Centre (CRC) Lausanne

DEEP DIVE

DATA PRIVACY AND DATA SHARING WITHIN THE REGULATORY FRAMEWORK GOVERNING HUMAN, HEALTH-RELATED RESEARCH IN SWITZERLAND

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doi: 10.54920/SCTO.2022.RAWatch.7.4

Since entering into force in 2014, the Human Research Act (**HRA**) and its ordinances have provided the regulatory framework in Switzerland for accessing health-related personal data and biological material for the purposes of research related to human diseases and to the structure and functioning of the human body. This legislation aims to protect participants' privacy. At the same time, the scientific community wants to generate knowledge. Aside from the HRA, data privacy in Switzerland is more widely covered by the Federal Act on Data Protection (**FADP**) and in some cases by the EU's General Data Protection Regulation (**GDPR**). When preparing and conducting a clinical study, researchers have to comply with a number of requirements and guidelines in order to respect the rights of patients (i.e. data privacy) and fulfil their duties to the scientific community (i.e. data sharing). This article discusses how these statutory requirements apply to specific clinical study documents, processes, and tools.

The topics of data privacy and data sharing in the context of clinical research can be addressed from many angles. The overall scientific rationale for data sharing, international recommendations, the perimeters of research data sharing, the legal basis in Switzerland, technical aspects of data processing and documentation, governance, and policies for data sharing were recently addressed in a collective initiative led by the Swiss Clinical Trial Organisation's (**SCTO's**) Clinical Trial Unit Network. The resulting guidance document on sharing data from clinical research projects is available on the SCTO Platforms' website.[1] This article focuses on the regulatory framework governing data privacy and data sharing in clinical research and how it pertains to specific elements of clinical studies.

Although the Human Research Act (**HRA**) addresses the topic of accessing health-related personal data, it does not directly address the topic of sharing research data (i.e. data collected for the purpose of conducting research or data generated by research activities) – with the exception of Article 56, which makes the registration of clinical trials mandatory in order to ensure a first step towards transparency to the public on past and ongoing clinical research. It should be kept in mind that the HRA was finalised in 2011, when sharing research data was not as high of a priority as it is nowadays. And at that time, open data – an issue increasingly raised by evidence-based medicine initiatives such as the Cochrane collaboration and journal editors (e.g. the International Committee of Medical Journal Editors (**ICMJE**)) – was not yet transposed within the clinical research regulatory frame. Nevertheless, many principles contained in the HRA have to be taken into account when addressing diverse aspects of research data sharing and when analysing the impact regulation has on practices highlighted in this article.

USING HEALTH-RELATED DATA FOR RESEARCH: CODED VERSUS ANONYMISED DATA

In Switzerland, the Human Research Act defines data as follows:

- *Health-related personal data* means information concerning the health or disease of a specific or identifiable person, including genetic data (Art. 3, let. f).
- *Genetic data* means information on a person's genes, obtained by genetic testing (Art. 3, let. g).
- *Coded health-related personal data* means health-related data linked to a specific person via a code (Art. 3, let. h).
- *Anonymised health-related data* means health-related data which cannot (without disproportionate effort) be traced to a specific person (Art. 3, let. i).

Before being analysed, data sets of all clinical studies (interventional and observational) contain **coded health-related data**. A code links the identifying data to the study data, and the key is kept in a matching table that must be stored in a protected environment in order to ensure data privacy.

According to Switzerland's Human Research Ordinance (**HRO**), the **anonymisation** of health-related personal data requires all items which, when combined, would enable the data subject to be identified without disproportionate effort to be **irreversibly masked or deleted**. In particular, this means that an individual's name, address, date of birth, and unique identification numbers must be masked or deleted (Art. 25, paras. 1 and 2). It is important to note that the ability to guarantee the anonymisation of biological material and genetic data is increasingly being questioned due to technological advances. **If consent to participating in a clinical study is revoked**, according to Article 9, paragraph 1 of Switzerland's Clinical Trials Ordinance (**ClinO**) and Article 10 of the HRO, the biological material and health-related personal data of the person concerned must be anonymised after data evaluation has been completed. However, the anonymisation of that person's biological material and personal data may be dispensed with if: a) the person concerned expressly renounces this right when revoking consent or b) it is established at the beginning of the clinical trial that anonymisation is not possible and the person concerned, having been adequately informed of this fact, consented to participate in the trial (ClinO, Art. 9, para. 2).

For researchers, anonymisation leads to a loss in value of data because it is no longer possible to compare anonymised data with other data or future data related to the same source persons. In the context of clinical trials, anonymisation makes it impossible to perform audits and controls on medical data that can only be performed on the source data. Furthermore, anonymisation prevents participants from withdrawing their consent if they change their minds.[2,3] And finally, anonymisation can also impact participants by, for example, preventing long-term safety follow-up if there are concerns about delayed adverse events.

INFORMED CONSENT FORM

Before any participant's health-related data and biological materials can be used for research, the participant must give his or her consent, usually in writing. Exceptions to written informed consent are outlined in Article 9 of the HRO. An informed consent form (**ICF**) is the document containing all information for patients on the following topics:

- how the participant's personal and health data will be protected (including for genetic data) and whether the data may reveal the participant's identity
- the person(s) who may use the participant's health-related data and samples
- the access that a limited number of people may have to the participant's data because it is necessary for their functions in the study
- the coded (or uncoded) form of data to be transmitted to other research teams within the framework of the project or to be available for data sharing
- information on the retention of health-related data and samples
- how to access a synthesis of the global results, research results, and/or findings of the study
- conditions for participants in the event that their data or samples are commercialised.

swissethics has proposed a variety of informed consent templates regarding the further use of coded or uncoded health-related personal data or materials, which are available on its website. Two of these templates (for general consent and for informed consent according to HRA/HRO Art 28.) are for research projects subject to Chapter 3 of the HRO and contain informed consent forms for coded health-related personal data or biological materials that are collected as per clinical routine or where additional procedures are performed. According to Article 28 of the HRO, when health-related personal data or biological materials are used in an uncoded form, additional information is to be provided in the informed consent form.

In clinical studies subject to the ClinO or the Ordinance on Trials with Medical Devices (**ClinO-MD**), participants who have given their consent in a specific clinical study do not automatically authorise the further use of their health-related data or biological materials outside that study. To allow such further use of research data, participants have to sign an additional informed consent form. This template is embedded in the template for study information for participants in clinical trials according to HRA, ClinO, and ClinO-MD (available in French, German, and Italian).

In the absence of informed consent, further use may be made of health-related personal data or biological materials for research purposes in the exceptional cases outlined in Article 34 of the HRA. An exemption from the requirement of informed consent may be requested from the competent ethics committee, which is granted if the justification meets the ethics committee's expectations.

It is important to note that, in contrast to coded or anonymised health-related data, truly at source anonymous health-related data are outside the scope of the HRA, and informed consent is not needed for them to be used for research purposes.

STUDY PROTOCOL

A study protocol is an essential reference document that describes the practical methods of how a clinical study is conducted and, in particular, how its clinical data are managed. The choice of data collected must be proportional to the purposes of the research: data must be adequate to be able to confront the research hypotheses, and there can be no random collection of all kinds of irrelevant data. Moreover, the use of data from a protocol must be justified and limited to the objectives listed in the protocol.

According to Article 15 of the HRA, the study protocol has to precisely define measures for protecting confidentiality before, during, and after the clinical trial when processing individual health-related data about potential and enrolled participants. The protocol should also describe the means whereby personal information is collected, kept secure, and maintained.[4, 5] In general, this involves the following:

- assigning a unique participant identification number that replaces a participant's identifying information; the creation of the study participant code should be clearly described in the protocol (ClinO, Art. 18; HRO, Art. 5)
- securely storing the coded data, the identifiable information, and the linking code in separate, independent locations (e.g. in paper format in a locked cabinet or within password-protected digital files and storage media) (ClinO, Art. 18; HRO, Art. 5)[6]
- limiting access to the minimum number of individuals necessary for quality control, auditing, and analysis; the protocol should stipulate that for data verification purposes, authorised personnel (e.g. the clinical monitor), regulatory authorities, or the ethics committee may require direct access to nominative source data or documents that are relevant to the study, such as parts of the medical records (ClinO, Art. 18).[7, 8]

Moreover, the access and transmission of a clinical data set to authorised individuals should be outlined in the protocol, including measures to guarantee data privacy (e.g. via virtual private network internet transmission). Participants' anonymity must be ensured when data are presented at scientific meetings in coded form or published in scientific journals.

CASE REPORT FORM

Case report forms (**CRFs**) are an integral component of clinical trials and are addressed in regulations and guidelines (e.g. ClinO, Art. 5 and Art. 18; HRO, Art. 5; and ICH GCP E6(R2), Section 1.1). Each clinical trial participant has a CRF file. Research site staff (investigators and study coordinators) note measures and findings, as defined in the study protocol, and transfer the data to the study sponsor and/or statistician for analysis. If the data in the individual CRFs are not correct, the overall results of the trial may be compromised.

Two types of CRFs are used in clinical research: a traditional paper CRF and an electronic CRF (**eCRF**). Electronic CRFs are generally preferred over paper-based CRFs due to improved data quality and integrity, relatively better discrepancy management, and a faster database lock. Electronic CRFs also facilitate remote monitoring and real-time access to data. It is, however, essential to ensure that the equipment used for data entry (e.g. computers, mobile phones, and tablets) is password-protected and can be accessed only by the appointed personnel. Secure equipment and restricted access, together with the exclusion of personal identifiable information (such as a participant's name, date of birth, social security number, address, phone number, or email address), are recommended to guarantee confidentiality and protect the privacy of research participants. The ultimate goal of a well-designed CRF is to provide researchers with a tool that allows them to collect all the relevant information the study needs to answer the research question, that will facilitate later data sharing, and that protects participants' information and anonymity. **Table 1** summarises the main points to consider when designing a CRF.

Table 1: Essential criteria for a case report form

Essential criteria for a case report form
• Reflects the protocol
• Ensures data quality and integrity
• Ensures the protection of personal data and ethical principles
• Provides a complete audit trail system (traceability of interventions)
• Guarantees secure access to the eCRF system
• Complies with local, regional, and international regulatory requirements

DATA MANAGEMENT PLAN

A data management plan (**DMP**) is a living document that explains the life cycle of all data used in a clinical study. It presents how data are generated and/or collected, how data are documented, where data are stored, how data are shared, and how data are preserved and protected. Two types of DMPs are used in clinical research: one for submitting a grant application and one for conducting a clinical study. When applying for funding, the DMP is a declaration of intent that shows the applicant has anticipated all aspects of data management, from generating and/or harvesting data to sharing and/or archiving data. Most universities provide guidelines and support for completing the four sections of the DMP that the Swiss National Science Foundation (**SNSF**) requires with grant applications. Even though this DMP is mandatory, its content is not yet evaluated at the time of the grant application.

The second type of DMP, a clinical DMP, is a formal document that provides all information on how data has been obtained, processed, organised, stored, protected, and shared during a clinical study and after it (archiving). A clinical DMP:

- exhaustively defines and describes all study (meta)data and, if needed, data sets
- identifies all tasks to be conducted with data (including tests and the validation of tools and/or procedures, e.g. eCRF validation)
- identifies all roles and responsibilities in detail (including names, resources, and competencies)
- lists risks linked to long-term data management
- presents how data safety, storage, and/or archiving are handled and how confidentiality and ethical principles are protected (e.g. standards and methodology used in the study as well as quality assurance processes used for data collection and/or generation in order to ensure data protection; the latter may include a confidentiality agreement, permission to access/share data, information to participants about data sharing, and/or facilities for storage)
- indicates how (meta)data are accessed and shared, including information on a license for publishing and sharing data or the existence of a steering committee for sharing data; it should be noted that some constraints exist that prevent data sharing (e.g. legal, confidentiality, and intellectual property rights constraints).

The clinical DMP is updated on a regular basis, with versioning and signatures, and is approved by the sponsor and/or project leader.

DATA TRANSFER AGREEMENT

Once data are collected, cleaned, and analysed, they can be shared. Data transfer agreements (**DTAs**), also referred to as data transfer and use agreements (**DTUAs**), are inter-institutional or intra-institutional contractual documents that regulate the overarching architecture for the collaborative use and exchange of data. In regard to biomedical research, this mostly relates to personal and health-related data. A DTA/DTUA assigns the participating parties within a research project their roles as data provider, data recipient, and data controller. It typically defines a set of rules that regulate data processing, which includes the collection, transmission, storage, security, access, reuse (further use), archiving, and destruction of data. Additionally, but not exclusively, a DTA/DTUA regulates confidentiality, intellectual property rights, and publication rights. Therefore, the terms and conditions outlined in a DTA/DTUA depend on the predefined specifications of the corresponding research project as well as on the responsibilities of the participating parties.[9] DTAs/DTUAs are legal contracts and, as such, must comply with data protection laws and regulations.

In Switzerland, the processing of personal and health-related data is subject to the Federal Act on Data Protection (**FADP**), which is expected to be updated in 2023. The relevant regulations are defined in Switzerland's Human Research Act, the Clinical Trials Ordinance, and the Human Research Ordinance as well as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (**ICH**) Guideline for Good Clinical Practice (E6) and all cantonal data protection legislation. In the European Economic Area (**EEA**), the processing of data is subject to the General Data Protection Regulation (**GDPR**). The US Health Insurance Portability and Accountability Act (**HIPAA**) provides a list of 18 items considered to be identifiers.[10] Transferring sensitive data within Switzerland and/or abroad is only permitted if the research project's participants have been informed and have given their consent. In general, data may not be transferred outside the EEA unless it is transferred to a country or territory that provides an adequate level of protection for personal data. However, exceptions can be made if participants have been informed and have given their consent. DTAs/DTUAs have become an integral part of the legal and regulatory framework of multicentre research projects and require approval from institutional review boards (**IRBs**), namely the competent ethics committee.

PUBLICATION

In most circumstances, clinical researchers aim to present their clinical trial results in a peer-reviewed paper that is published in a reputable academic journal. However, publishing and disseminating research results is not only desirable from a "prestige" perspective; it is often required and governed by laws and regulations.

With the aim of enhancing the public transparency of clinical trial data, regulatory agencies have implemented certain disclosure rules. These concern all data, including positive, inconclusive, and negative clinical trial results. In Switzerland, the registration of clinical trials and public access to registries is regulated by the HRA and ClinO. Studies with medical devices (ClinO-MD) are regulated accordingly until the corresponding legal regulations come into force. For an authorised clinical trial, sponsors must register clinical trial data in a primary registry equivalent to the World Health Organization's International Clinical Trials Registry Platform (**ICTRP**), such as the ClinicalTrials.gov registry of the US National Library of Medicine or the European Union Drug Regulating Authorities Clinical Trials Database (**EudraCT**) registry powered by the European Medicines Agency (**EMA**). Additionally, data from clinical trials authorised in Switzerland have to be entered in the Swiss National Clinical Trials Portal (**SNCTP**) federal registry. Retrospective and prospective studies without interventions (studies regulated by the HRO) do not have to be registered. However, since registration is often a requirement for publication in international journals, it is recommended for all studies. Since the ICMJE issued its widely distributed statement in 2017 calling for sharing data from clinical trials,[11] most registries have implemented additional fields to be completed with information about the data sharing policy for the registered study.

European Union (**EU**) initiatives and legislation, such as the EMA's guidance on its Policy 0070, the EU's new Clinical Trials Regulation (**CTR**) and the EU's Medical Device Regulation (**MDR**), have gradually increased public access to clinical trial data over the last few years. Recently, the EMA established a Clinical Trials Information System (**CTIS**) as a single electronic entry point for clinical trials information in the EU and the EEA. CTIS offers study participants, healthcare professionals, and the general public the possibility to search for clinical trial information. Swiss clinical trial sponsors are also eligible to register their trials in CTIS if they have sites located within the EU/EEA. For medical devices, the European Database on Medical Devices (**EUDAMED**) will be created, which will provide similar insight into study data.

However, offering access to data and information demands the consideration of confidentiality and data protection regulations, such as the EU's General Data Protection Regulation and Switzerland's revised Federal Act on Data Protection. Therefore, it is imperative to understand the interrelated challenges and compliance issues around data sharing and data protection regulations when navigating through the regulatory landscape of clinical trial data publication.

RESPONSIBILITIES FOR DATA HANDLING

Respecting data privacy and organising data sharing are responsibilities shared between different functional roles in clinical research: the sponsor or project leader and his or her team, the investigator and his or her team, and clinical study monitors as well as external partners receiving partial or complete data sets from the clinical study. Although the sponsor or project leader is clearly in charge of a study's main activities (creating the database, implementing monitoring, signing DTA/DTUA, etc.), the investigator and his or her team as well as external partners also play an active role in protecting data privacy and must also comply with laws and regulations when sharing data. **Table 2** gives an overview of roles and responsibilities for data privacy and data sharing.

As researchers navigate through the complex world of clinical study data, they must know and respect many legal requirements and guidelines in their research practice – regardless of their role within a clinical study. Implementing a trial or an observational study requires time, energy, and information. Prior to beginning a study, it is advisable to check the HRA and its ordinances and the ICH's Guideline GCP E6(R2) and to consult the local legal department in order to be well prepared for the data privacy and data sharing aspects of the study.

Table 2: Roles and responsibilities for data privacy and data sharing

Responsible person(s)	Protect data privacy	Enable data sharing
Sponsor and team	• **Protocol**: Include measures for data protection (e.g. data coding, decoding policy, limited and authorised access to data, and secure data storage) • **ICF**: Provide clear information concerning data coding, access to study results, data privacy, and the policy for consent withdrawal • **DMP**: Include information about the data life cycle – from data collection to data processing, quality control, preservation, and storage – and standard operating procedures (**SOPs**) • Minimise data collection variables when designing the database and eCRF • Perform quality assurance (e.g. SOPs and monitoring) • Register the study • Publish anonymised study results	• Register the study (for publication and public access) • Establish a registry for data storage and undefined future projects • **DTA/DTUA**: Establish a controlled process for data access and exchange and for the collaborative use of data • Define the data sharing policy (according to **FAIR** guidelines: findable, accessible, interoperable, and reusable) • Make anonymised data accessible on a valid data repository
Investigator and site team	• Inform participants • Respect the data privacy policy during data collection and data entry into the database or on a paper CRF (according to the protocol) • Ensure secure storage and archiving of source data • Ensure that personal data are redacted before transmission	• Use a secure data transmission system
Study monitor	• Respect the data privacy policy during data quality control of CRFs and source documents	
External researchers requesting data		• **DTA/DTUA**: Respect the process of data transmission and use • Use a secure data transmission system

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VIEWS AND OPINIONS

CANTONAL ETHICS COMMITTEE ZURICH

FURTHER USE OF DATA IN RESEARCH: CURRENT TRENDS, LEGAL BACKGROUND, AND TYPICAL PROBLEMS

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* The views expressed in this article represent the personal views of the authors and are not binding for the Cantonal Ethics Committee Zurich.

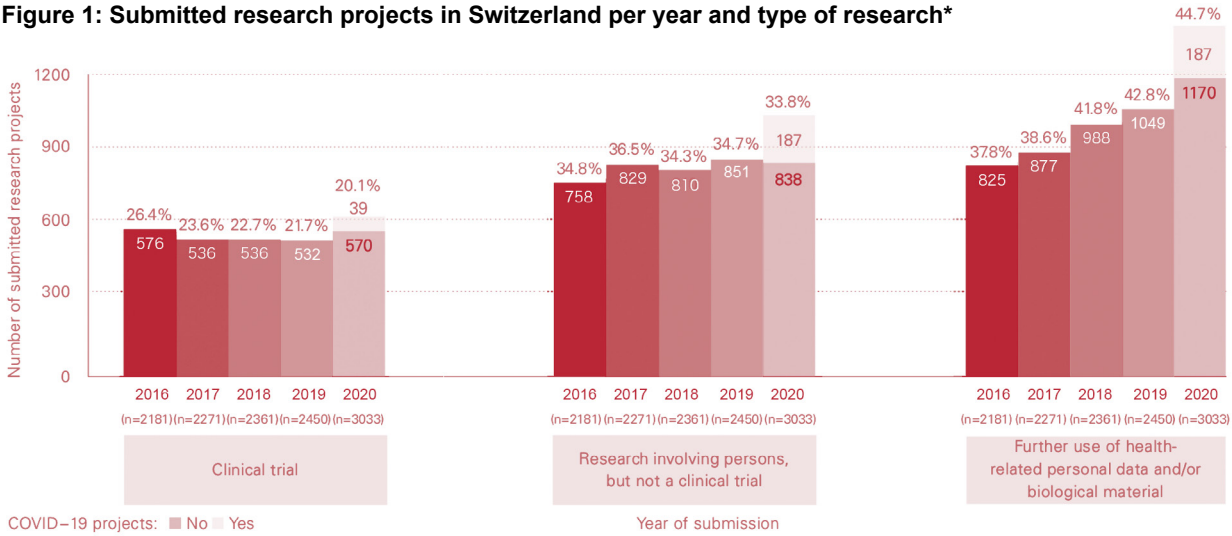
doi: 10.54920/SCTO.2022.RAWatch.7.12

Over the past few years, Switzerland has seen a marked increase in the further use of routine clinical data, research data, and biological materials for research purposes. This article aims to shed some light on a few typical problems the Cantonal Ethics Committee Zurich encounters in the area of the further use of biological material and patient data for research with or without consent. Other difficult questions may arise in emergency situations, in the evaluation of sample size and pre-screening patients for clinical studies, and in situations when a patient revokes consent.

CURRENT TRENDS IN THE FURTHER USE OF MATERIAL AND DATA FOR RESEARCH

The further use of biological material, routine clinical data, or research data in Switzerland has significantly increased over the last several years, as shown by the following statistics from the Federal Office of Public Health's (FOPH's) annual report Human Research in Switzerland 2020[1] (**Figure 1**) and the internal statistics from the Cantonal Ethics Committee Zurich (**Figure 2**). This development also implies that increasingly more people who are not engaged in patient treatment are working with patient data.

Figure 1: Submitted research projects in Switzerland per year and type of research*

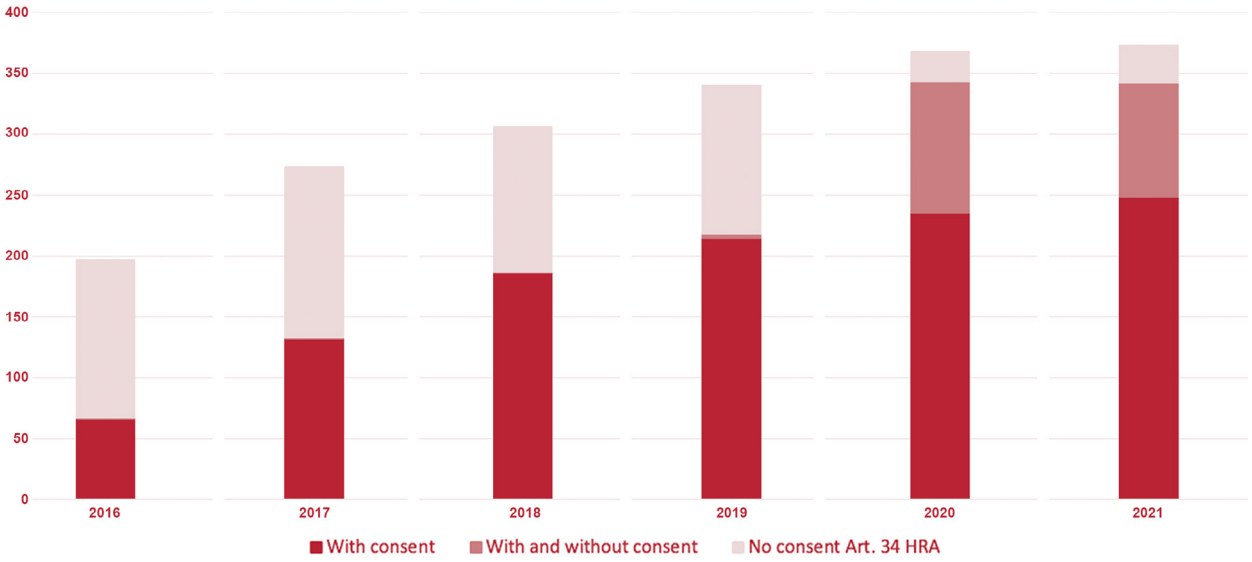


Data not shown in the above figure: Research involving deceased persons (2017: 29, 2018:27, 2019:17, 2020:41) and Reasearch involving embryos and fetuses from induced abortions or stillbirths (2017: 0, 2018: 0, 2019: 1, 2020:1)

Source: Adapted from the FOPH report Human Research in Switzerland 2020[1] (Fig. 12).

* Percentages on the top of the bars refer to the proportion of studies of a given type compared to all studies submitted in a given year.

Figure 2: Further use projects approved by the Cantonal Ethics Committee Zurich*

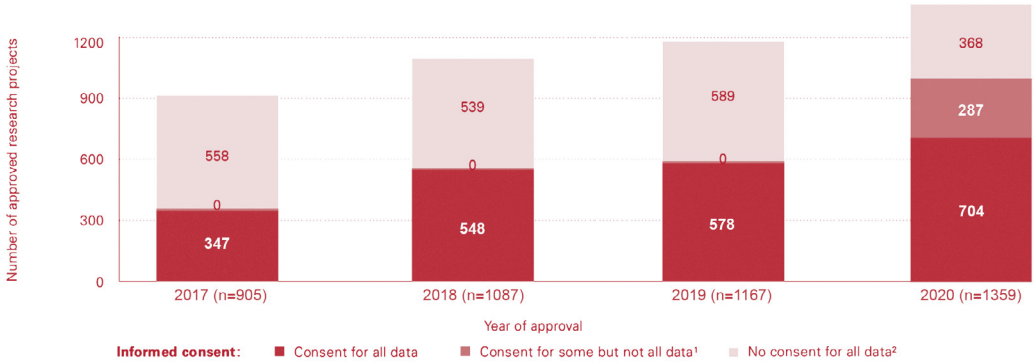


Source: Internal statistics of the EC Zurich.

* Before 2020, a distinction was rarely made between projects with and without consent or projects without consent for all the data or samples.

In parallel with this increase in further use projects, the use of general consent has greatly increased. Consequently, the proportion of project applications to ethics committees (ECs) without consent according to Article 34 of the Human Research Act (HRA) has decreased relatively in relation to the total number of further use studies (see **Figure 3**). In other words, the more recent the data records are that are the subject of an EC application, the more likely it is that there is project-specific consent, general consent for the further use of clinical data, or specific study consent covering research data reuse.

Figure 3: Approved further use projects in Switzerland



Source: Adapted from the FOPH report Human Research in Switzerland 2020[1] (Fig. 21).

[1] In the years 2017, 2018, and 2019, it was not possible to determine this category.

[2] For the years 2017, 2018, and 2019, research projects for which consent was available for some but not all data (partially Art. 34 HRA) have been included in this category.

SCOPE AND LEGAL BACKGROUND

Not only are existing biological materials and patient data extremely valuable for research, but the extent to which they are used is tremendous. And research based on patient data continues to increase. These circumstances and the sensitivity of data protection have prompted the Swiss legislature to set up special rules regarding the protection of the right to self-determination in the further use of material and data.[2]

The further use of biological material, genetic data, and non-genetic health-related personal data was legally regulated for the first time in Switzerland with the HRA and its corresponding Human Research Ordinance (HRO), which came into force on 1 January 2014. Consent and the substitution of consent for the further use of data and biological material are based on Articles 32–34 of the HRA and Articles 24–40 of the HRO.

As the relevant ordinance/regulation, the HRO broadly defines the concept of further use as any handling of biological material that has already been removed or data that have already been collected (Art. 24). This includes, in particular, the procurement, merging, or collection of biological material or health-related personal data (Art. 24, let. a), the registration or cataloguing of biological material or health-related personal data (let. b), the storage or inclusion in biobanks or databases (let. c), or making accessible, providing, or transmitting biological material or health-related personal data (let. d).

The introduction of regulations on the reuse of biological material, genetic data, and non-genetic health-related personal data is also in line with the internationally recognised soft law regulations of the Declaration of Helsinki. According to Articles 32 and 33 of the HRA, the reuse of non-anonymised human materials, genetic data, or non-genetic health-related data requires researchers to obtain informed consent. There is an exception to this rule of informed consent for non-genetic health-related coded data for which it suffices if the affected persons have been informed in advance and have not dissented.

Involving humans in research should be restricted to projects that are not feasible without doing so. Such a postulate for a conservative approach to exposing participants to research is the basis for the principle of subsidiarity, which is an essential part of human research law (HRA, Art. 11). The further use of data is then of particular importance, since some research projects with humans might be replaced by the further use of data. *Further use* in this sense means the second and possibly subsequent research-related use of biological material, genetic data, and non-genetic health-related personal data. It is immanent that the material or data have already been taken or collected for another purpose, for example for diagnostic purposes or as part of another research project.

FURTHER USE AND CONSENT: TYPICAL PROBLEMS ENCOUNTERED BY ETHICS COMMITTEES

1. Absence of informed consent

Article 34 of the HRA lists the exceptional situations in which consent is absent yet consent and/or providing information to the individual concerned regarding the right to dissent to the further use of biological material or health-related personal data may be substituted by the ethics committees for research purposes. These exceptions are allowed only if certain preconditions are fulfilled cumulatively: 1) it has to be impossible or disproportionally difficult to obtain consent or to provide the required information on the right to dissent, or this would impose an undue burden on the person concerned; 2) no documented refusal is available; and 3) the interests of research outweigh the interests of the person concerned in deciding on the further use of his or her biological material and data. Therefore, whenever possible, informed consent should be obtained. However, if a consent was not obtained, there is no clear timeframe beyond which the application of Article 34 would generally be excluded. Thus, different research ethics committees in Switzerland tend to handle this issue in different ways. Templates for general consent forms were created in 2017 by the Swiss Academy of Medical Sciences (**SAMS**) together with swissethics. In response to ensuing discussions, a new template was created in 2018 under the leadership of unimedsuisse and with the cooperation of the five university hospitals. This template for general consent can be found on swissethics' website.

As of 2016, the EC Zurich generally requires that applications for further use projects include (general) consent from patients whose data are to be used. Institutions that were able to implement general consent shortly after the HRA came into force are now at an advantage. For data that have been collected more recently, there have to be very good reasons for why consent cannot be obtained. If reasons exist, the EC Zurich carefully assesses whether or not the scientific significance outweighs the intrusion into the privacy of individual patients. Reasons that might be accepted by the EC Zurich are that patients passed away prior to the application or that the circumstances of treatment did not allow time to properly inform the patient, as can be the case in emergency situations. If feasible, consent usually has to be subsequently obtained.

2. Data collection in emergency situations

Patients often enter an intensive care or emergency unit under exceptional circumstances. Obtaining informed consent in these situations is often not possible. Thus, in most cases the only option is to obtain consent from relatives (i.e. representatives). Due to the special circumstances, this may only be specific consent. The usual form currently being used in hospitals for general consent seems inappropriate in this situation. It is not in line with Articles 30 and 31 of the HRA. General consent applies to all data instead of just the data needed for a certain situation. However, the exclusion of intensive care or emergency patient data from research would not seem reasonable and would not be justifiable ethically. Suitable solutions therefore have to be found. A consent form specifically for intensive care patients has turned out to be the best way to make research with these data possible in an ethically and legally satisfying manner. Relatives are able to consent to the use of data related only to the current situation. As soon as patients are able to give their re-consent, it should, of course, always be sought.

3. Evaluating sample size or screening participants

Usually, the number of potential patients to be included in a study has to be known in order to obtain approval from the EC. Otherwise, it is possible that not enough patients can be recruited for a study. Under certain circumstances, estimating the number of suitable patients can only be done successfully by viewing patients' records. The same problem occurs when pre-screening is necessary for selecting participants, who may be asked to give their consent to research. When pre-screening is needed, researchers have to be aware of the implications of the duty of confidentiality. This duty of confidentiality forbids disclosure (i.e. any behaviour that results in an outsider receiving knowledge of secret information). So any disclosure of patient data assumes that the physician's duty of confidentiality will be violated. Thus, viewing patient data is certainly in line with criminal law (Swiss Criminal Code, Art. 320 et seq.) if it is done by the treating physician and as long as the viewing/screening itself does not go beyond a point that could be considered research (HRA, Art. 3, let. a; Art. 62 et seq.). If pre-screening is done by doctors from the same department as the treating physicians, one can still argue that they are allowed to view the data because the confidentiality obligation does not necessarily apply to doctors from the same department and because data were created during the patients' treatment in that department. In practice, it becomes trickier when, for instance, masters students are foreseen to do such pre-screening. This is an aspect that should clearly be regulated in the context of the pending revision of the regulations that concretise the HRA (HRO, ClinO, and ClinO-MD).

For the time being, it can be argued that patients who have given general consent for their data to be part of research have also agreed to screening as part of a research activity. However, what should be done if there is no documented consent? This could especially be the case in projects in which the substitution of consent on the basis of Article 34 of the HRA is needed. The application of such a project to an EC must specify for how many patients the responsible EC is to grant a substitution of missing consent. Ideally, the number would be clarified via an automated, anonymous query of patient data. In practice, this often does not work out to the desired extent. Often fewer suitable patients are found in an automated query than would actually be available. Therefore, emerging feasibility tools that retrieve aggregated data only from automated, anonymous queries on institutional data warehouses may become increasingly important in planning research projects, especially with the expected increase in data interoperability. Another option is that the treating physician clarifies how many patients are involved. In case of doubt, only an estimate can be given in the ethics application, which may have to be corrected later in the approved protocol. Last but not least, until the FOPH provides clarification in the form of suitably revised regulation, case-by-case decisions may be made in a legal grey area.

4. Revocation of consent

The law stipulates that patients can revoke their consent to the use of their data and biological samples for research projects. Project managers are responsible for ensuring that in the event of revocation, the revocation is also registered at other institutions to whom they pass on data or samples and for ensuring that those locations no longer use the affected data and samples. It is therefore of tremendous importance that project managers keep track of all other institutions with whom they share data and biological samples. As a rule, data and samples that have already been used for research projects can continue to be used for ongoing projects (as described in an interpretation guide to ClinO (Art. 9)).[3] However, the data and samples can no longer be used for new projects. If data and samples are being passed on, it is absolutely necessary to draw up a transfer agreement so that in the event of revocation, it can be guaranteed that the data and samples affected will no longer be used at the other location. Such an agreement should also ensure that data and samples are not being used for any purpose other than the intended one.

CONCLUSION

Accessing sensitive data for the purpose of science while at the same time protecting data privacy represents a challenge. The issue of consent as it relates to the further use of biological material and patient data for research purposes is not always clear cut. Grey areas remain that may trigger different interpretations, fuel discussions within ethics committees, and result in different ways of handling the issue in practice. This article reflects the authors' experiences at the Cantonal Ethics Committee Zurich. Different ethics committees do not necessarily handle these typical, problematic issues in the same way. The pending revision of regulations (HRA, HRO, and ClinO) may resolve some of the issues mentioned in this article.

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VIEWS AND OPINIONS

AN EXPERT IN PUBLIC LAW

DATA PROTECTION IN CLINICAL TRIALS: KEY ISSUES FROM A LEGAL PERSPECTIVE

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doi: 10.54920/SCTO.2022.RAWatch.7.18

Human research is one of the most regulated academic domains. A main focus of regulations is the protection of trial participants' physical integrity and personal data. In Switzerland, the federal Human Research Act (HRA) and its related ordinances are primarily relevant. These research regulations contain provisions on how research data are to be managed in order to protect participants' data privacy. When cantonal universities conduct clinical trials, they must also comply with their cantonal data protection laws. Standards set by the EU and international organisations also have a major impact on human research. Despite the increased protection of personal data, there is some room for improvement. This article reviews the legal basis for data privacy in Switzerland as it relates to research participants' data and takes a closer look at a few key issues from the perspective of study participants.

NATIONAL AND INTERNATIONAL DATA PRIVACY LEGISLATION AND GUIDELINES

Several national and international regulations contain provisions aimed at protecting study participants' data and privacy. Switzerland's Human Research Act (**HRA**) is a key piece of federal legislation and contains general principles such as the right to informed consent and special safeguards for vulnerable individuals in research. The related ordinances on clinical trials (Clinical Trials Ordinance (**ClinO**)) and on human research (Human Research Ordinance (**HRO**) set out the detailed framework of research regulation in Switzerland and address the specifics of data privacy.

This is where the international regulations come into play. The Swiss ordinances are largely based on the guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (**ICH**). The ongoing revision of the ICH Guideline for Good Clinical Practice E6(R3) places a high priority on digitisation in research and data safety. The Swiss ordinances should be adapted accordingly in the future. Because medical research does not stop at national borders, EU regulation is also relevant to researchers and research participants in Switzerland, although it is not directly applicable to Switzerland. Especially worthy of mention is the EU's Clinical Trials Regulation (**CTR**), which entered into application on 31 January 2022. And towering over all the regulations is the EU's bureaucratic behemoth, the General Data Protection Regulation (**GDPR**), whose most visible impact is that internet users may now freely choose cookies when visiting websites. The GDPR, however, does not directly protect patients from sharing their personal experience too freely on the internet.

IMPROVED PROTECTION AT THE PRICE OF COMPLEXITY?

Although many research participants may not be familiar with the provisions in these regulations and guidelines, having this legal framework is essential for protecting their data and their privacy. Undoubtedly, this mass of new regulations improves the legal position of trial participants. Standards for informed consent, the safe handling of genetic data, or privacy by design in trials are set to benefit participants. However, there are concerns that a multiplicity of standards does not ensure data security beyond that which a principal investigator (**PI**) can provide by drawing up a professionally designed study plan and responsibly monitoring the execution of a trial. What is certain, though, is that the regulatory requirements for researchers have become much more complex. In 2019, *Regulatory Affairs Watch 1* took a deep dive into the GDPR, pointing out certain inconsistencies within research law. Legal desks at industry and university trial centres must tackle these mandatory requirements. In the end, the right balance needs to be struck between having legislation and standards in place that effectively protect research participants without adding unnecessary complexity to the research process.

DATA CONTROLLER AND STUDY PARTICIPANT

An important aspect of data protection is the recurring question regarding data ownership. Participants in a trial usually consider themselves the owners of their personal data. However, legal ownership according to the Swiss Civil Code is possible only with physical objects (e.g. biological samples or a paper medical record) and not data (Art. 641 et seq.). Alternatively, intellectual property could be considered. Data can be subject to exclusive rights if it involves an invention or the result of a creative process (Copyright Act, Art. 2). A participant's physical address or therapy plan, however, are not considered results of a creative process and are therefore not his or her intellectual property.

Data protection laws therefore refer to the ownership of a database on the one hand and the protection of individual rights on the other. Switzerland's current Federal Act on Data Protection (**FADP**) defines the controller of a data file as private persons or federal bodies that decide on the purpose and content of a data file (Art. 3, let. i). In human research, the person responsible for study data is the sponsor or the sponsor-investigator/principal investigator. They take strategic decisions regarding the safe handling and the purpose of use of data in a clinical trial, which therefore makes them the owners, or rather *controllers*, of the database as a whole. The participant, on the other hand, is the *data subject* (i.e. the data donor and the beneficiary of the rules of data protection).

INFORMED CONSENT AS A KEY ELEMENT OF DATA PROTECTION

Due to the particularities of data protection laws, disclosure of data in a clinical trial by participants means, above all, that they consent to the processing of their personal data. Therefore, informed or general consent and the right to withdraw it are of great importance. Generally speaking, a study participant transfers control over his or her data to the PI while retaining sovereignty over his or her personal data. This extends to a participant's right to withdraw consent and have his or her data deleted, which is not easy to achieve in practice but is one of the core requirements of the GDPR and Switzerland's revised FADP, which will be enacted in 2023. The right to deletion also conflicts with the data storage obligations under research law. A solution to this conflict could possibly be the anonymisation of the data in question because anonymised data are no longer personal data.

PARTICIPANTS' BIOLOGICAL SAMPLES AND GENETIC INFORMATION

Swiss research law contains special provisions on the handling of research participants' biological material and genetic data (HRO, Art. 28). Depending on the degree of coding or anonymisation, different requirements exist for general consent for further use in research. The requirements range from written consent to the mere right to object to the use of anonymised data. At the same time, genetic data are generally exposed to reidentification, so technical safeguards must be established.

RESEARCH WITH CHILDREN AND ADOLESCENTS AND RESEARCH ON RARE DISEASES

Children and adolescents are vulnerable persons, which is why the HRA contains a chapter that sets stricter provisions for their protection (Chapter 3, Section 1). First, no research should be conducted with children and adolescents if the findings can also be obtained with adults. Second, the principle of the best possible involvement in the consent process applies. Children are defined as persons up to the age of 14 years (HRA, Art. 3). In addition to age, a relevant criterion is capacity of judgment, which has to be assessed individually by the researcher. Children who have the capacity to judge must give their own written consent to a clinical trial in addition to the consent of their legal representatives (HRA, Art. 22). There is no provision for the renewal of consent when an adolescent reaches the age of majority; however, the right to withdraw previous consent still applies.

Another point to consider is that research with children is often research on rare diseases. As the word *rare* implies, the data available for this research is usually sparse and requires international cooperation and cross-border data disclosure (i.e. the guarantee that Swiss minimum standards are met abroad). Swiss data protection rules require specific guarantees for cross-border data sharing (FADP, Art. 6). Within the framework of the Swiss Personalized Health Network (**SPHN**) funding program, a multicentre project is dedicated to improving the data situation and strengthening cooperation among paediatric clinics

HIGH WILLINGNESS TO PARTICIPATE IN RESEARCH STUDIES

Why are patients willing to disclose sensitive data and participate in trials at all? According to a recent survey of 10,000 patients in the US,[1] there is a high willingness of patients to participate in studies, despite the public debate about privacy and the risk of abuse. Participants not only expect a personal benefit but also see a larger societal benefit to participating in a scientific project. Participation was shown to be highest for people with rare diseases and for better educated individuals. It is not possible to say conclusively whether the results of the US survey can be transferred to the conditions in Europe and Switzerland; however, the findings can inform researchers' efforts to improve participation. For example, by including patient representatives early on in the planning stage of a trial and by providing a clear, even personal and verbal, explanation of a trial that is easy to understand, more individuals with less education might be persuaded to participate in a trial.

PATIENTS APPRECIATE FEEDBACK

In a recent, albeit non-representative, unpublished survey in a Swiss registry study, it emerged that study participants highly value regular feedback from the PI. There is a trend toward periodic digital exchange in which communication with participants does not end with the mere signing of the informed consent form. Especially in longitudinal studies such as cohorts, communication in newsletters is a suitable means of staying in contact with participants. Communication also improves retention within a study. However, effective communication requires an appropriate study design in which, in the best case, patients can share their ideas in advance. The Swiss Clinical Trial Organisation (**SCTO**) is currently building a platform of relevant patient boards that will foster a more patient-centred approach in Swiss clinical trials.

CONCLUSION

There is no lack of legal standards when it comes to protecting the personal data of study participants. This is due to the rapidly evolving regulation of data protection and human research in Switzerland. Researchers in Swiss institutions also need to keep an eye on international developments, such as the GDPR and CTR. Although the regulations aim to benefit patients and participants, it is the task of principal investigators to effectively meet the standards by setting up professional and compliant study designs. Despite a public debate about the risks of data abuse, there is a high willingness to participate in trials. And those who participate in trials appreciate updates. Investigators should take advantage of this willingness and involve patients early on in the study design as a standard of practice.

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VIEWS AND OPINIONS

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HEALTH DATA ECOSYSTEMS: SHARING HEALTH DATA TO FACILITATE MEDICAL PROGRESS

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doi: 10.54920/SCTO.2022.RAWatch.7.22

Sharing health data in a meaningful way that preserves privacy is the foundation of a well-functioning digital health data ecosystem. A digital ecosystem implies that stakeholders are embedded in the necessary conditions to collect, store, share, and use health data electronically. Health data ecosystems can provide many benefits to society, including effective personalised medicine for patients, greater innovation in research, and improved policymaking. As an integral part of these health data ecosystems, the pharmaceutical industry already contributes substantially to them by investing in and sharing health data in order to facilitate medical progress. While many countries have recognised the value of health data ecosystems, Switzerland lags massively behind when it comes to secondary health data usage. To change this, Switzerland needs to develop a coherent strategy to create a health data ecosystem involving all relevant stakeholders.

SHARING DATA RESPONSIBLY WITHIN HEALTH DATA ECOSYSTEMS FOR GREATER SOCIETAL IMPACT

The pharmaceutical industry is committed to responsibly sharing data in health data ecosystems to foster collaboration and innovation that can have a sustainable impact on society. Aggregated health data from population-level sources – including electronic health records, wearable technologies, health insurance claims, health registries (or burden of disease registries), clinical trials, drug consumption analyses, and other research – can not only significantly boost innovation and medical progress but can also lead to better policymaking and more efficient, sustainable healthcare systems.

Drawing from over 100 years of experience with responsibly handling sensitive data in clinical trials, the pharmaceutical industry upholds robust data protection standards for all stakeholders involved, including patients, academics, and public institutions. The pharmaceutical industry supports both financial and non-financial incentives for structuring and sharing data, such as reciprocity, equal exchange of value, and intellectual property-based mechanisms for a functioning ecosystem. It fosters the principle of providing qualified scientific researchers access to anonymised participant-level data and full clinical study reports (**CSRs**) from clinical trials to conduct legitimate scientific research.

PHARMACEUTICAL INDUSTRY'S COMMITMENT TO DATA SHARING INITIATIVES

One example of the pharmaceutical's commitment to responsible data sharing is its participation in the global effort of the US National Academy of Medicine (**NAM**) (formerly the Institute of Medicine) to develop principles for responsibly sharing clinical trial data. Another initiative is HARMONY, a private-public partnership that receives funding from industry and the EU's Horizon programme. The HARMONY project aims to leverage health data to deliver information that will help to improve patient care, in particular in the field of rare blood cancers, where data is scarce. Specifically, the project gathers, integrates, and analyses anonymous patient data from a number of high-quality sources. This helps specialists in the field to define clinical endpoints and outcomes for these diseases that are recognised by all key stakeholders. Another Innovative Medicines Initiative 2 (**IMI2**) project is Big Data for Better Outcomes (**BD4BO**), which focuses on maximising the potential of big data in order to improve health outcomes and European healthcare systems. A fourth initiative, backed by funds from the public and foundations, is UK Biobank, a large-scale biomedical database and research resource containing in-depth genetic and health information from half a million UK participants. The database is globally accessible to approved researchers, both from academia and private industry, who undertake research into the most common and life-threatening diseases. The platform is based on reciprocity. The UK Biobank encourages researchers to share their findings by publishing in open access scientific journals. Once results are published, researchers are required to return their results to the UK Biobank so they can be shared with other scientists, who can then test the findings or use them to advance their own work.

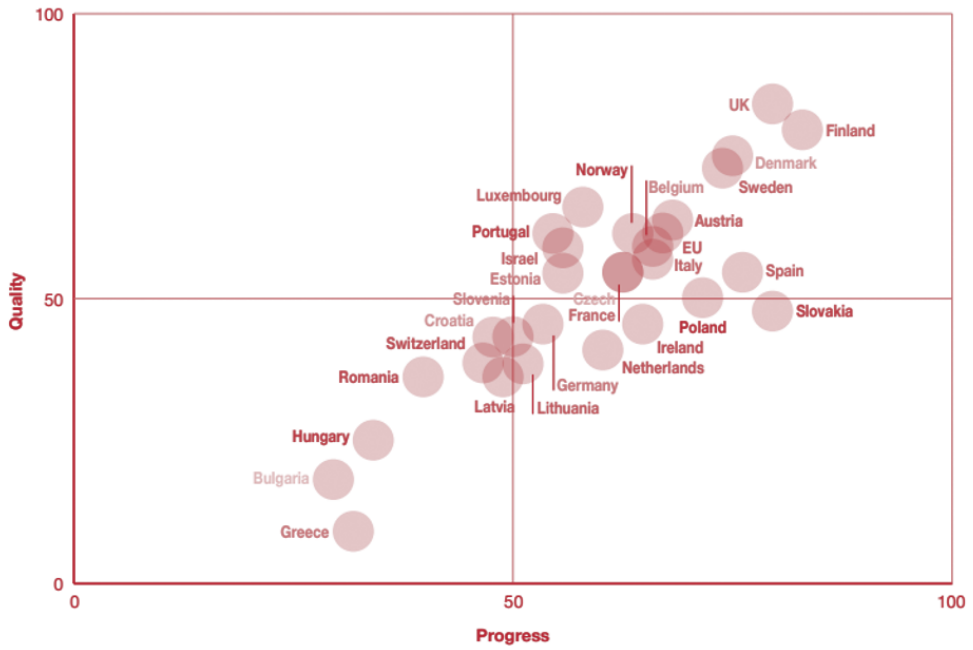
BENEFITS OF HEALTH DATA ECOSYSTEMS

Health data ecosystems hold many benefits, also in regard to clinical trials. Not only do they allow those running clinical trials to better find and match potential candidates who have the appropriate profile, but health data ecosystems can also help simplify many processes used in clinical trials. For example, the emerging concept of decentralised clinical trials, where patients do not have to enter a hospital to participate in a study, depend on patients' ability to collect their health data electronically and safely submit it to the organisation collecting the clinical data. Another example of the use of health data ecosystems is the possibility to build synthetic control arms. With access to longitudinal health data from different sources, researchers can emulate *in silico* eligible populations and randomised trials, including the generation of control groups from real-word evidence and hybrid-design trials.[1] This is particularly important for areas with small samples, for example in rare diseases. Synthetic control arms can also help alleviate the inherent ethical dilemmas of placebo treatments.

SWITZERLAND'S UNTAPPED POTENTIAL

The benefits of a robust, national health data ecosystem, however, currently remain untapped in Switzerland. The country lags massively behind in terms of taking advantage of the potential of digitalisation in its healthcare system. There are no regulatory incentives for structuring and sharing health data, structured health data are scarce, and, if existent, they are often locked up in silos, which is why there is little to no primary and secondary usage. This is reflected in Switzerland's very low ranking in a European index measuring secondary use of health data that was created by the non-profit, multipartner Open Data Institute (**ODI**) based in the UK (see **Figure 1**).[2]

Figure 1: Secondary use of health data in Europe: Country policy rankings



Source: Adapted from ODI report (2021), Figure 1[2]

Switzerland's research-based pharmaceutical industry has been making efforts to unlock the potential of a digital transformation in the Swiss healthcare system. This is shown by a study conducted by the BAK Economics consultancy firm.[3] The analysts found that digital elements are becoming increasingly prevalent in patents in the pharmaceutical sector. However, these patents are being filed in the US and Asia, and Switzerland is losing ground. This comes to the detriment of patients, who will lose their privileged access to innovative medicines and therapies.

But Switzerland is far from being a lost cause. Within Switzerland lies the potential of high-quality health data due to its excellent institutions, well-educated professionals in healthcare, and its competitive and innovative industry. To unleash this potential, Switzerland needs to develop a coherent strategy to create a health data ecosystem while involving all relevant stakeholders in the process. To facilitate this process, Interpharma has published a booklet (available in French and German) in which industry experts outline different factors to be included in a strategy for a successful digital health data ecosystem and provide a roadmap demonstrating what such a strategy could look like.

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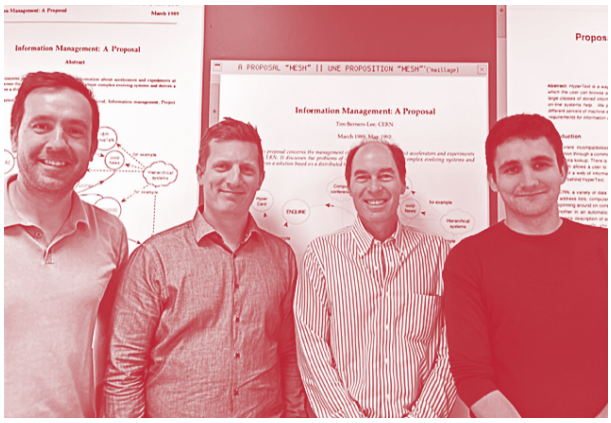

ZENODO DATA REPOSITORY: PROVIDING PRACTICAL SOLUTIONS FOR DATA STORAGE AND DATA SHARING

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doi: 10.54920/SCTO.2022.RAWatch.7.25

Properly managing, preserving, and sharing data can be a daunting task, especially for busy researchers who are constantly confronted with new tasks and requirements from funders and their institutions. Zenodo is a general-purpose data repository that enables researchers, scientists, project managers, and institutions to share, preserve, and showcase multidisciplinary research results (data, software, publications, and other research objects) that are outside the scope of existing institutional or subject-based repositories. Based in the trustworthy CERN data centre, Zenodo is a service provided by researchers to researchers contributing to open science by capturing research objects and making them **FAIR** (findable, accessible, interoperable, and reusable). This article addresses some of the challenges of data storage and data sharing, such as finding the right place to store data, citing data properly, and using hybrid data sharing solutions. It also demonstrates how using a data repository like Zenodo can help researchers address these challenges.

ZENODO IN A NUTSHELL

The idea of the Zenodo data repository was conceived when the European Commission (**EC**) decided that, in order to support its nascent open data policy, it needed a catch-all repository to ensure that every EC funded research output could have a home. In the vanguard of the open access and open data movements in Europe, the EC commissioned the OpenAIRE project to build this repository. As an OpenAIRE partner and pioneer in open source, open access, and open data, the European Organization for Nuclear Research (**CERN**) had the capabilities to create the repository, and Zenodo was launched in May 2013. Zenodo is currently being used by more than 200,000 researchers and 7,000 communities from around the world.

FINDING THE RIGHT PLACE FOR DATA

Researchers often ask where they should deposit/archive data and why their own hard drive or server is not suitable. Unfortunately, places under the control of an individual researcher are probably the worst choices for archiving data because the task of ensuring they stay operational and accessible often rapidly falls off priority lists as research is completed. Archiving and preserving data are tasks for professionals that require considerable knowledge and both the appropriate technical and organisational infrastructure. This is important not only to guarantee the safekeeping of research data but also to ensure that research data that was previously not citable and discoverable becomes so.

The most suitable place for depositing/archiving data is a repository that can best serve the data and its user community. Often, the best solution ends up being a domain-specific repository that has the necessary domain expertise to make the data as useful as possible for its user community and that also has appropriate funding and organisational structures. Data, however, exist in many shapes and forms, and many intermediary or non-standard research outputs do not neatly fit in a domain-specific repository. That is why Zenodo exists. As a generic repository, Zenodo can step in when there is no appropriate domain or institutional data repository. And because it accepts research data in any shape and form, it ensures there is always a safe place for the long tail of science. In addition, as a generic repository, Zenodo can often better transcend domains by making data findable and accessible outside the normal boundaries of a researcher's own domain.

CITING DATA PROPERLY

Once an appropriate data repository has been identified, a follow-up question that often arises is: How should data be cited? There is no straightforward answer to this. It often depends on the data itself as well as the community and publishing standards of a specific domain. The most important – and quite often the most overlooked – aspect of citing data, though, is to ensure that a persistent identifier is included when citing data (e.g. a digital object identifier (**DOI**)). A persistent identifier not only ensures that the data used is uniquely identified and provides access to the data itself, but discovery systems also require a persistent identifier to be able to properly attribute citations. Currently, DOIs are the persistent identifiers that can be most easily integrated into existing scholarly communication infrastructures and that are understood inside and outside a specific domain.

KEEPING DATA AS OPEN AS POSSIBLE AND AS RESTRICTED AS NEEDED

Sharing clinical trial data has strict regulatory requirements. Even when consent for data sharing and further use has been obtained and data have been anonymised as required by law, data can be difficult to share due to the risk of future cross-correlation. This is why Zenodo supports restricted and controlled access records. In addition, sometimes researchers hoard data locally, hoping to exploit their data set for future projects. Unfortunately, when the data are eventually deposited into a repository, descriptions may have been forgotten, processing steps overlooked, and most likely people with key knowledge have moved on to other positions. That is why Zenodo allows for the depositing of closed access records, which makes it possible for researchers to deposit and describe their data when the information is still fresh in their minds and later flip the switch to open access. Zenodo also provides features that allow data to be selectively shared as needed, for instance by requiring a justification and the researcher's approval (scientific collaboration, licenses, intellectual property protection, etc.).

SHARING RESEARCH DATA: GIVE IT A GO!

Overall, sharing research data can be a complex and daunting task. Finding the right place to store data, citing data correctly, and making data openly available can be especially difficult for clinical trial data. Therefore, Zenodo's best advice is to always start thinking early on about FAIR data before it is too late. And try exploring Zenodo's features, since it is quite likely that solutions for some of your needs have already been found and implemented by others!

NEWS FROM

MODEL-BASED META-ANALYSIS IN DRUG AND DEVICE DEVELOPMENT AND THE ADDED VALUE OF DATA SHARING

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doi: 10.54920/SCTO.2022.RAWatch.7.28

Meta-analysis, the highest level of evidence, is a statistical analysis that includes a mathematical combination of the results from different studies. Meta-analysis can be a subset of systematic review or the pooling of results from individual patient data (**IPD**). The number of published systematic reviews and meta-analyses has grown exponentially in recent years: a search in PubMed showed that around 1,600 systematic review and meta-analysis publications were indexed in 2000 compared to over 35,000 in 2020. And this upward trend is projected to continue. With the new regulatory landscape making the development and maintenance of clinical evaluation reports (**CERs**) a priority for drug and device manufacturers, methodologically sound meta-analysis will be key to guiding strategic drug and device development decisions.

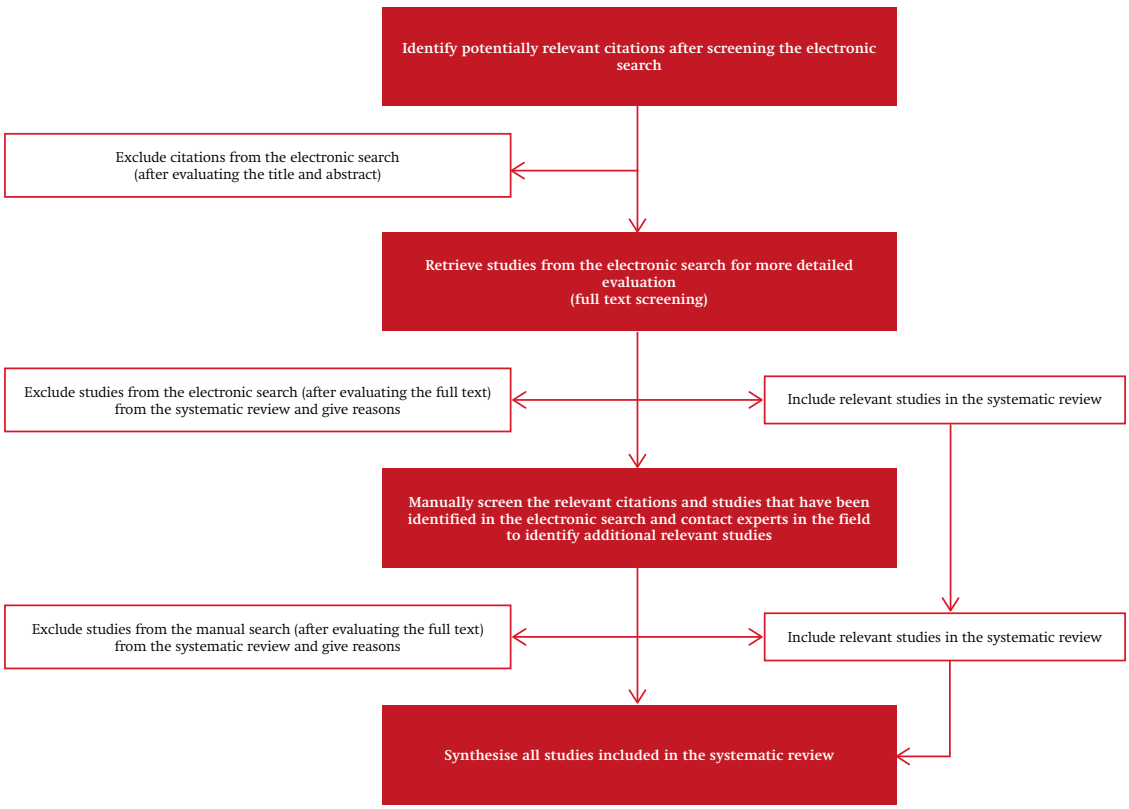
META-ANALYSIS – WHAT FOR?

Swiss stakeholders and international funders generally agree that new clinical trials should be justified by a systematic review of the evidence that includes meta-analysis assessment. This highlights the importance of systematic reviews and meta-analysis in the future.[1] This standpoint is in line with the changes in the regulatory landscape in Europe and beyond, which require methodologically sound systematic reviews and meta-analysis for drug and medical devices approval (the results of which should be included in a clinical evaluation report) that should be updated on a regular basis (e.g. every two to three years). Model-based meta-analysis is an emerging methodology that quantifies the evidence on efficacy, tolerability, and safety in an unbiased manner in order to support better decision-making in clinical development and drug and device development. Meta-analysis is a systematic review of evidence that includes a mathematical combination of results from different studies. Combining and pooling results from different animal and human studies, which are selected based on a comprehensive search of the literature with well-defined inclusion and exclusion criteria, can lead to an unbiased and more comprehensive evaluation of the evidence. It also increases precision due to a larger sample size. Furthermore, the synthesis of study results across different studies can resolve research questions left unanswered by individual studies and explore factors that can explain conflicting results.

WHAT INFORMATION IS ESSENTIAL FOR PERFORMING META-ANALYSIS?

To perform a meta-analysis, it is important to start with a team that has different types of expertise, including clinical and methodological knowledge of study design and meta-analysis. Next, a focused research question with a defined exposure and/or intervention, study population, and outcome should be formulated. Well-defined inclusion and exclusion criteria are important in order to help select the final studies that will contribute to the analysis. This, together with a systematic search of different bibliographic databases, assures a thorough and unbiased investigation of the literature in the research topic of interest (see the selection procedure in **Figure 1**).[2]

Figure 1: Selection procedure for studies for a systematic review and meta-analysis



Source: Adapted from Muka et al. (2020)[2]

Once studies have been selected that fulfil the eligibility criteria and should be included in the final analysis, data from individual studies need to be extracted in order to pool and analyse the results (see example in **Table 1**). The information extracted should be based on an *a priori* decision and will depend on the research questions and the subgroup analysis that will be conducted as well as potential factors being explored as sources of heterogeneity (differences in results across studies). In general, it is important to extract information related to the author's name, publication year, study title, study design, location, study name, duration (follow-up time), number of participants, percentage of female participants, number of events, age mean and standard deviation of participants, obesity, ethnicity, definition and/or assessment of the exposure and outcome, levels of adjustments, analysis type, estimates and their 95% confidence intervals or standard error for each adjustment level, funding (private vs. public), and the risk of bias and/or quality assessment. The extraction must be brief with clear abbreviations, consistent definitions, and the same units. It is advisable to have at least two independent researchers extract the data in order to minimise errors and potential biases. In addition, training and orientation should be provided prior to the extraction. To pool the results, information on summary statistics from each individual study needs to be extracted, including the measure of association estimate (e.g. mean difference, odds ratio, relative risk, or hazard ratio), the 95% confidence interval, and/or the standard error.

Table 1: Example of data extracted for a meta-analysis

Author, year of publication	Country	Study design	Number of participants	Number of cases	Relative risk	Lower confidence interval	Upper confidence interval
Ding, 2016	USA	cohort	30,202	1,807	0.92	0.85	0.99
Ko, 2015	South Korea	nested case-control	633	317	1.14	0.75	1.71
Muller, 2012	China	cohort	610	300	0.76	0.58	1
Zamora-Ros, 2013	Europe	cohort	16,835	778	0.92	0.81	1.05
Nettelton, 2006	USA	cohort	35,816	3,375	0.97	0.86	1.1
Nanri, 2006	Japan	nested case-control	130,789	221	0.91	0.71	1.17
Villegas, 2008	China	cohort	64,191	896	0.67	0.62	0.72
Song, 2005	USA	cohort	38,018	1,614	0.92	0.78	1.09

Source: Adapted from Muka et al. (2020)[2]

CONDITIONS FOR USING DATA

Because the meta-analysis of literature uses data from published articles, there are no specific conditions for using the data. Extraction can be done with electronic forms or a database management software such as Microsoft Access or REDCap. Using one of the many data systems available (e.g. EPPI-Reviewer, Systematic Review Data Repository (SRDR), DistillerSR (Evidence Partners), or Doctor Evidence) can be a more sophisticated alternative since they can be integrated with the title and abstract, allow for full-text screening, and export data directly into analysis software. However, it requires an investment to set up these commercial systems and train data extractors. It is recommended to share the data collected as part of systematic reviews and meta-analyses. Sharing extracted data has several potential benefits: it can minimise redundant work, improve the quality and efficiency of future reviews and meta-analyses, and support additional analyses.[3]

DATA SHARING: INDIVIDUAL PATIENT DATA META-ANALYSIS

Sharing research data at the individual patient level is a tremendous opportunity to perform more impactful meta-analysis with greater generalisability and increase the quality of evidence. Performing meta-analysis on individual patient data (**IPD**) relies on access to shared raw data from studies included in the meta-analysis. This allows for the reanalysis of data sets and the combination of the information from different studies, which are typically clinical trials. When accessible, such an approach has many advantages, which makes IPD meta-analysis the gold standard for systematic reviews.[4]

Generally, the first step to accessing IPD is convincing the sponsor-investigators from all of the different studies (including those studies that may have not been published) to share IPD on a scientific collaboration basis. Their active participation is also a way to get much more knowledge from the leading investigator on board. Additionally, access to individual patient data may override the limitation of poorly reported studies that otherwise would not be included in an aggregated data meta-analysis, thus reintroducing the data of numerous patients that would have been excluded. Using IPD also allows researchers to work on data quality, impute missing data, redefine and homogenise exposure measures and the criteria of judgment (duration of follow-up, composite outcomes, etc.), better assess the effect size of an intervention, gain a lot of analysis power that allows multivariate and time-to-event analysis, and introduce sensitivity analysis within their meta-analysis. Of course, all data transfer and sharing should be covered by data sharing agreements and should fully respect data confidentiality and protection standards.

A two-step approach is normally used for IPD meta-analysis: first, each study data set is reanalysed according to a homogenised statistical analysis plan; second, a standard random- or fixed-effects meta-analysis is performed based on an *a priori* decision. When performing time-to-event analysis or subgroups and interactions analysis, a one-step multi-level modelling approach is preferred that takes into account both study-level and patient-level covariates.

If IPD is not accessible for all studies, some analysis techniques may allow a combination of IPD and aggregated data in the meta-analysis. Thus, the advantages of IPD meta-analysis clearly outweigh meta-analysis with only aggregated data. This clearly demonstrates the enormous benefits of sharing research data at the individual participant level – as long as one ensures that processes are in place that uphold the most stringent confidentiality and data protection standards.[5]

RELEVANCE OF META-ANALYSIS

Meta-analysis provides the highest levels of evidence and is used to generate guidelines, policies, and evidence-based practices in health care. Meta-analysis can help quantify the average effect of certain interventions (e.g. a drug or device), identify potential side effects, and compare the efficacy of different interventions. In general, medical and public health questions are studied more than once and are thus addressed by different research groups and conducted in different populations and locations. By combining data from different studies and heterogeneous populations, meta-analysis can provide insights into the generalisability of the findings, and it can identify subgroups of a population that can benefit the most from an intervention. By identifying these knowledge gaps, primary research such as clinical trials may be designed and conducted to fill such gaps. Thus, meta-analysis can inform and improve the design of future clinical trials and help guide drug and device development decisions.

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NEWS FROM

SCTO

STEAM

META-RESEARCH: USING SHARED DATA TO PROVIDE PRACTICAL SOLUTIONS FOR CURRENT RESEARCH CHALLENGES

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doi: 10.54920/SCTO.2022.RAWatch.7.32

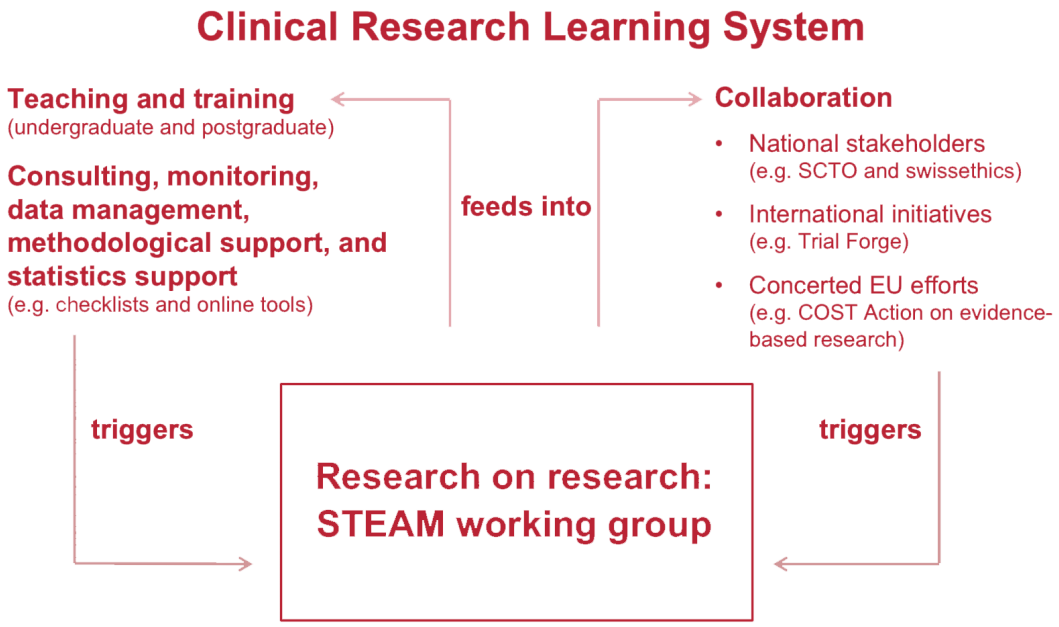
Research on research (**RoR**), or meta-research, is the study of research itself. In 2019, a group of meta-researchers and members of the SCTO's Clinical Trial Unit Network interested in meta-research founded the Swiss clinical Trials Empirical Assessment & Methods (**STEAM**) working group to promote RoR in Switzerland. Specifically, STEAM aims to continually improve the quality, transparency, and value of Swiss clinical research through RoR. The first part of this article takes a brief look at why RoR is needed and describes its potential role in the Swiss clinical research arena. The second part of the article discusses the topic of data sharing in clinical research from a meta-research perspective.

RESEARCH ON RESEARCH: FINDING REAL SOLUTIONS TO REAL RESEARCH PROBLEMS

Clinical studies face many methodological and practical challenges that sometimes limit the validity of study results or lead to premature study discontinuation or even non-publication. It would be helpful for researchers to have reliable information about the advantages and disadvantages of specific research methods and processes available; however, such evidence is scarce. Research on research (**RoR**), or meta-research, aims to investigate the research process or research methods themselves in order to create this evidence and provide guidance. It should produce actionable findings and outputs (e.g. tools, recommendations, or new statistical methods) that can be used by actors and stakeholders in the clinical research ecosystem. Close collaboration between evidence producers (e.g. meta-researchers) and evidence users (e.g. CTU staff or clinical researchers) is necessary in order to ensure that pressing problems in research practice are addressed and results are delivered in the most convenient formats. This idea of collaboration between meta-researchers and CTU staff across Switzerland led to the foundation of the STEAM (Swiss clinical Trials Empirical Assessment & Methods) working group in 2019, a bottom-up initiative of meta-researchers working with the Swiss Clinical Trial Organisation (**SCTO**) and its Clinical Trial Unit (**CTU**) Network to tackle methodological and practical aspects of clinical studies. The White Paper: Clinical Research, published by the Swiss Academy of Medical Sciences in 2021, mentioned STEAM and the promotion of RoR as part of a roadmap to further strengthen clinical research in Switzerland.[1]

In principle, STEAM members take up issues and problems identified by clinical research stakeholders or encountered in actual clinical studies. They then generate the corresponding research questions and devise methodology for RoR projects that address these issues. The results and outputs from STEAM's RoR projects (e.g. checklists, tools, publications, and guidelines) are fed back into research practice through teaching and training as well as consulting and collaboration. This creates a clinical research learning system for the continuous improvement of the quality, transparency, and value of clinical research (see **Figure 1**). In addition, STEAM members actively reach out to national stakeholders (e.g. swissethics and the Swiss National Science Foundation), they contribute to international initiatives (e.g. Trial Forge), and they participate in European and international RoR efforts (e.g. the European Cooperation in Science and Technology (COST) Action on evidence-based research). The STEAM working group currently meets twice per year to discuss current projects, recommendations, tools, publications, and priorities and to initiate new RoR projects among members. It welcomes new researchers with an interest in RoR.

Figure 1: Clinical research learning system



RESEARCH DATA SHARING: THE KEY TO META-RESEARCH

Access to research data is key to RoR. The further use of collected data can improve current knowledge and help update recommendations. Data sharing in clinical research has many advantages and faces various challenges that are discussed in other articles of this issue of *RA Watch*. The following viewpoint focuses exclusively on research data sharing from the RoR perspective.

First, it is important to point out that individual participant data (**IPD**) from a clinical trial can be useful for investigating trial processes such as participant recruitment or retention. For example, in a current study we are using IPD on the enrolment dates of almost 300 randomised trials to empirically investigate recruitment patterns and to develop and evaluate user-friendly recruitment prediction tools.[2] Second, apart from IPD, there are metadata in the form of trial protocols, case report forms, or data analysis plans that may be shared to enable meta-researchers to empirically investigate risks for bias (e.g. selective outcome reporting), problems of study conduct (e.g. insufficient recruitment), or non-publication.[3,4,5] Other metadata that would be valuable for RoR are resource use and cost data for various tasks in clinical studies.[6] An increased availability of shared cost data would help meta-researchers, for instance, to evaluate new study designs such as registry-based randomised trials[7] or clinical researchers and funding agencies to make more accurate budget estimations and budget approval decisions. A third important aspect of sharing metadata is related to the confidentiality concerns of various stakeholders. Traditionally, concerns about confidentiality have been raised mainly by data producers and ethics committees. However, as patient representatives have become increasingly engaged in clinical research in recent years – a positive development thanks to patient and public involvement (**PPI**) initiatives – they, too, have started expressing concerns about the risks of privacy breaches. Yet despite these concerns, patients are generally very much in favour of data sharing.[8,9] Such concerns were addressed in STEAM's past RoR projects through direct mandates from stakeholders (e.g. ethics committees) in combination with signed confidentiality agreements.[10] Finally, sharing IPD itself – as one process in the clinical research enterprise – is a timely topic for RoR. Unanswered questions about data sharing are, for instance, the following: Which methods of de-identification of participant data are most appropriate in the Swiss context? What is a suitable metadata scheme for data sets from clinical studies to ensure findability in data repositories? What is the best way to monitor and assess the impact of IPD reused from clinical trials?

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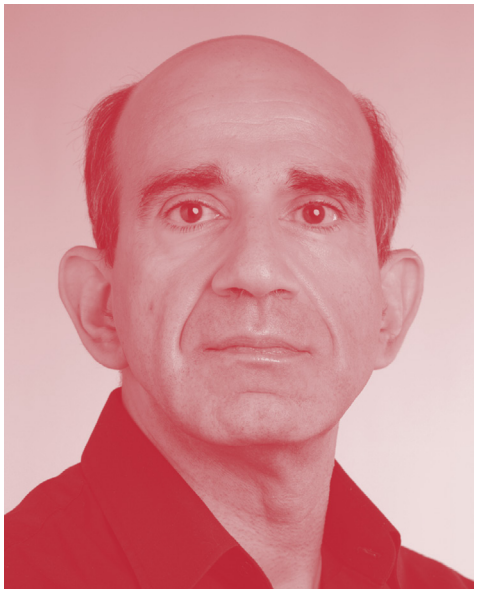
CASE STUDY

colaus psycolaus



HOW THE COLAUS|PSYCOLAUS STUDY SHARES DATA WHILE ENSURING PRIVACY

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doi: 10.54920/SCTO.2022.RAWatch.7.35

While data sharing is important in an international research setting, ensuring the privacy of participants is just as important. For several years, the CoLaus|PsyCoLaus study has been sharing data with national and international research teams while ensuring that no breach of privacy regarding the participants occurs. A series of procedures have been put in place, including checking the research protocol, data encryption, and legally binding agreements. The original data are also distributed between sites and informatics systems, thus making re-identification of the participants difficult. These procedures allow a high level of security, and the participants are guaranteed that no data leakage will occur.

The CoLaus|PsyCoLaus study is an ongoing, prospective, population-based, cohort study investigating the relationships between cardiovascular and psychiatric diseases. Participants sign consent forms prior to the study, which are stored indefinitely in a secure location. Information collected for the study includes socio-economic, family and personal history of disease, medicines, lifestyle, clinical, biological, metabolomic, and genetic data. Over 1,000 variables and 7 terabytes of raw and processed data have been collected so far. One major issue is ensuring that this data is safely stored and shared without enabling the identification of the participants. To achieve this double objective, several procedures have been implemented.

1. DATA DISTRIBUTION

CoLaus|PsyCoLaus data is split into three geographically and informatically different sites (phenotypic, psychiatric, and genetic) that are under the responsibility of three different data managers who do not have direct access to each other's databases. Access to the databases is limited to the principal investigators, and passwords to enter the system are replaced regularly. Automatic backups are conducted regularly.

2. SELECTIVE COLLABORATION

Each research group that would like to use data from the CoLaus|PsyCoLaus team has to fill out a research protocol, which is evaluated by the study's scientific committee. There are several restrictions regarding data sharing. For instance, full genome data cannot be shared (but a limited number of genotypes can) and the number of variables requested must be justified. If the scientific committee finds a data request to be excessive, it can either reject the project or limit the number of variables provided. If a research group requesting data is located in a country whose legislation regarding data privacy is less stringent than Switzerland's, no data is provided. Similarly, data that could identify an individual (i.e. birthdate or geolocation) is either deleted (birthdate) or blurred (geolocation) before being sent.

3. LEGALLY BINDING DATA TRANSFER AGREEMENTS

If a research protocol is accepted by the scientific committee and the research group is outside the Lausanne University Hospital (**CHUV**) or the University of Lausanne (**UNIL**), a data transfer agreement (**DTA**) has to be signed by both parties. The legal office at CHUV has created a generic DTA template, which can be modified to suit both parties. The DTA states, among other things, that no individual participant data will be shared by the requesting research group, including in the publication of the results (see below). Each approved research protocol is given a number, and the protocols are stored in a dedicated folder within a server with limited access. The protocol title, contact information of the principal investigator, date of acceptance, duration of the research, and the study status (abandoned, research ongoing, publication, etc.) is entered in a registry that contains all research protocols approved by the CoLaus|PsyCoLaus scientific committee (over 300 as of March 2022). This registry makes it possible to contact research groups for an update on the status of their research.

4. RECORDED DATA EXTRACTION

After signing the DTA, data can be extracted. A statistical script code is written that indicates all the source databases used and all the variables extracted (or generated specifically for the research protocol). This code and the corresponding data are kept indefinitely in a specific folder for future checking. If a database is updated, all previous versions are kept.

5. ENCRYPTED DATA TRANSFER

If no secure email system is available, the data to be sent to an external research group is zipped and encrypted. The encrypted data is sent via email, and the password is sent via another channel, most frequently via SMS to the principal investigator. In some cases, instead of individual participant data, metadata is provided, such as frequencies, averages, and number of participants fulfilling a given condition.

6. DATA SHARING POLICY FOR PUBLICATIONS

There is an increasing number of journals that request the analysis database to be shared as a condition for publication. After consulting the cantonal ethics committee, it was concluded that such types of sharing would be a violation of the Swiss legislation that aims to protect the personal rights of participants. Hence, journals that explicitly request individual participant data are excluded from the publication strategy. A generic statement indicating that no individual participant data can be shared has been written and is copied and pasted in all papers submitted for publication. In any case, journal guidelines are subordinate to legislation, and it is the researcher, not the journal, who is legally responsible if a breach of privacy occurs.

CONCLUSION

When sharing research data, it is necessary to find a subtle balance between openness and participants' rights to privacy. It is imperative to implement procedures that ensure such a balance.

REGULATORY NEWS, EVENTS, AND PUBLICATIONS

SWITZERLAND

Federal Council

NEWS

● **MAY 2022**

Federal Council wants to allow research to make better use of health data

The Federal Council would like to improve the framework conditions for the transfer and further use of health data. To this end, it instructed the Federal Department of Home Affairs (**FDHA**) to create conditions for setting up a data system for research in the health sector at its meeting on 4 May 2022. Data protection must remain guaranteed.

Source: FOPH website (Media releases) DE, FR, IT

Federal Office of Public Health (FOPH)

NEWS

● **MAY 2022**

Completion of revision of Swiss medical device law

On 4 May 2022, the Federal Council adopted the new Ordinance on In Vitro Diagnostic Medical Devices (**IvDO**) and an amendment to the Ordinance on Clinical Trials with Medical Devices (**ClinO-MD**). Both entered into force on 26 May 2022. This completes the revision of Swiss medical device law.

Source: FOPH website (Medicine & research)

Swiss Clinical Trial Organisation (SCTO)

EVENT

● **15 JUNE 2022 | LUGANO**

SCTO Symposium 2022: Data science and artificial intelligence in clinical research

Data science, artificial intelligence, and machine learning are buzzwords we come across nearly everywhere when looking at innovative technologies in medicine. The SCTO's symposium, held this year at the Università della Svizzera italiana in Lugano, addressed the use of these technologies specifically for clinical research to find out where we are today and where we should be heading.

Source: SCTO website (Event calendar)

PUBLICATIONS

● **2022**

New tools and resources on the SCTO Platforms' website

The Swiss Clinical Trial Organisation's Platforms have developed and continually update a wide range of practical, user-friendly tools and resources for clinical research professionals. They are all freely available on the SCTO Platforms' Tools & Resources website, including the following recent releases:

- Risk-Based Monitoring Score Calculator: A user-friendly web app that helps sponsors and sponsor-investigators determine the recommended monitoring strategy for their clinical study
- Monitoring Close-Out-Visit Report Template: Includes a step-by-step checklist for close-out visits and completes a series of monitoring templates created by the Monitoring Platform.

Source: SCTO Platforms website (Tools)

Swissmedic

PUBLICATION

- **MAY 2022**

Technical requirements for clinical trial applications for medicinal products

Swissmedic has summarised and clearly presented the technical requirements for the submission of applications for clinical trials for medicinal products. It has also published a Q&A document with the most frequently asked questions about clinical trial applications.

Source: Swissmedic website (Services & lists)

EVENT

- **20 SEPTEMBER 2022 | BERN**

Swissmedic information event: Regulatory & Beyond

Swissmedic will hold an event showing how it already uses innovative approaches to prepare for the future in therapeutic products regulation, what steps it has taken in digitalisation, and what steps are still ahead. There will also be sessions on authorisation and life cycle management.

Source: Swissmedic website (Events)

EUROPE

European Commission (EC)

NEWS

- **MAY 2022**

EC launches new European Health Data Space (EHDS)
The European Commission has launched the European Health Data Space (**EHDS**), one of the central building blocks of a strong European Health Union. The EHDS will help the EU to achieve a quantum leap forward in the way healthcare is provided to people across Europe by empowering individuals to control and utilise their health data in their home country or in other Member States. It fosters a genuine single market for digital health services and products. And the EHDS offers a consistent, trustworthy, and efficient framework for using health data for research, innovation, policy-making, and regulatory activities while ensuring full compliance with the EU's high data protection standards.
Source: European Commission website (Press corner)

PUBLICATIONS

- **Speich B et al. (2022 Apr 27)** Nonregistration, discontinuation, and nonpublication of randomized trials: A repeated metaresearch analysis. PLOS Medicine.
doi: 10.1371/journal.pmed.1003980

- **Mitchell EJ et al. (2022)** Clinical trial management: A profession in crisis? Trials 23:357.
doi: 10.1186/s13063-022-06315-8

ABBREVIATIONS

BD4BO: Big Data for Better Outcomes
CER: clinical evaluation report
CERN: Organisation Européenne pour la Recherche Nucléaire (European Organization for Nuclear Research)
CHUV: Centre Hospitalier Universitaire Vaudois (Lausanne University Hospital)
CJEU: Court of Justice of the European Union
ClinO: Clinical Trials Ordinance
ClinO-MD: Ordinance on Clinical Trials with Medical Devices
COST: European Cooperation in Science and Technology
CRC: Clinical Research Centre (Lausanne and Geneva)
CRF: case report form
CSR: clinical study report
CTIS: Clinical Trials Information System
CTR: Clinical Trials Regulation (EU)
CTU: clinical trial unit
DKF: Departement Klinische Forschung (Department of Clinical Research at the USB)
DMP: data management plan
DOI: digital object identifier
DTA: data transer agreement
DTUA: data transfer and use agreement
EC: European Commission
EC: ethics committee
eCRF: electronic case report form
EEA: European Economic Area
EHDS: European Health Data Space
EMA: European Medicines Agency
EU: European Union
EUDAMED: European Database on Medical Devices
EudraCT: European Union Drug Regulating Authorities Clinical Trials Database
FADP: Federal Act on Data Protection
FAIR: findable, accessible, interoperable, and reusable
FDHA: Federal Department of Home Affairs
FDPIC: Federal Data Protection and Information Commissioner
FOPH: Federal Office of Public Health
GCP: good clinical practice
GDPR: General Data Protection Regulation (EU)
HIPAA: Health Insurance Portability and Accountability Act (US)
HRA: Human Research Act
HRO: Human Research Ordinance
HUG: Hôpitaux Universitaires de Genève (Geneva University Hospitals)
ICF: informed consent form
ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICH GCP: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guideline for Good Clinical Practice
ICMJE: International Committee of Medical Journal Editors
ICTRP: International Clinical Trials Registry Platform
IMI2: Innovative Medicines Initiative 2
IPD: individual patient data; individual participant data
IRB: institutional review board
ISPM: Institute of Social and Preventative Medicine
IvDO: Ordinance on In Vitro Diagnostic Medical Devices
MDR: Medical Device Regulation (EU)
NAM: National Academy of Medicine (US)
NHS: National Health Service (UK)
ODI: Open Data Institute
PI: principal investigator
PPI: patient and public involvement
RA Platform: Regulatory Affairs Platform (SCTO)
RoR: research on research
SAMS: Swiss Academy of Medical Sciences
SCTO: Swiss Clinical Trial Organisation
SNCTP: Swiss National Clinical Trials Portal
SNSF: Swiss National Science Foundation
SOP: standard operating procedure
SPHN: Swiss Personalized Health Network
STEAM: Swiss clinical Trials Empirical Assessment & Methods
swissethics: Swiss Association of Research Ethics Committees
Swissmedic: Swiss Agency for Therapeutic Products
UNIL: Université de Lausanne (University of Lausanne)
USB: Universitätsspital Basel (University Hospital Basel)

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We would also like to thank all members of the Regulatory Affairs Platform.

Sources of information

- We gather news on regulatory topics linked to human research.
- We regularly read newsletters and visit the websites of relevant sources, including regulatory authorities in Switzerland, Europe, and the USA; ICH and WHO; major Swiss academic organisations and health associations; and professional associations.
- Additionally, we review major clinical research journals.

Contact information

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ISSN (online): 2813-2548
ISSN (print): 2813-2556
DOI (Issue 7): 10.54920/SCTO.2022.RAWatch.7

Regulatory Affairs Platform

The Regulatory Affairs Platform one of the Swiss Clinical Trial Organisation's (**SCTO's**) eight topic-based platforms that promote excellence in clinical research in Switzerland. Find out more about the Regulatory Affairs Platform and read past issues of *Regulatory Affairs Watch* on the SCTO Platforms' Tools & Resources website.