Procedure for multi-center research proposals based on data in the Swiss Stroke Registry

Version, Date: **17.01.2023**
Author: Leo Bonati, reviewed by Mira Katan
Reviewed by: SSR Steering Committee, DKF Basel

General rules and principles

1. The rules outlined herein apply to the retrospective analysis of data in the Swiss Stroke Registry (SSR) ***involving more than one participating Stroke Center / Unit*****.** The analysis of single-center data lies within the responsibility of the local Stroke Center / Unit.
2. Research proposals must be submitted to the Steering Committee for content approval, in the form of a summary analysis plan (see template below).
3. Research on SSR data requires approval by the locally competent ethics committee of the responsible investigator leading the research project (**Lead Investigator**). The Lead Investigator is responsible for obtaining this approval. (Please note that this also applies to mono-centric research projects).
4. **Coded (reversibly anonymized) SSR data** for research can only be used from Stroke Centers and Stroke Units where a system is in place ensuring that patients are informed on the use of their data for research purposes and about their right to refuse the use of their data. The SSR data center at the Department of Clinical Research (DKF) Basel maintains a list of Stroke Centers and Stroke Units where this is the case. If a patient refuses the use of his/her data for research, a tick box must be checked in the SSR Admission and Treatment form saying "Patient/relative refuses the use of data for research purposes". In this case, the data of the patient will **not be used for any research projects** but will still be used for the purpose of quality assurance, including the annual reports for the Stroke Centers / Units and the HSM reports prepared by the DKF Basel.
5. Alternatively, research projects can be done using **irreversibly anonymized data**. In this case, no information of patients on the use of their data is required. The ethics committee may decide that a project with irreversibly anonymized data does not require authorization. Irreversibly anonymizing procedure and feasibility should be always discussed with DKF Basel, which hosts the database in advance. Be aware that all projects which need additional information from the Stroke Centers / Units not entered into the SSR do not fall into this category.
6. The Lead Investigator is responsible for the funding of project-specific costs such as analyses plans, data-exports etc.

Template for summary analysis plan

- Title of the research proposal
- Name and contact details of the Lead Investigator responsible for the analysis
- Name of the locally competent ethics committee
- Other investigators involved in the analysis and their specific tasks (if already known)
- Background
- Aim including primary and secondary research questions
- Methods including:
    - Analysis population (inclusion and exclusion criteria)

- Participating Stroke Centers / Units (as planned)
- Primary and secondary outcome measures
- Statistical analysis plan for primary and secondary research questions
- Will the analysis data set be coded (reversibly anonymized) or irreversibly anonymized (see definitions above)
- Required SSR variables (as separate Excel file):
  - Please carefully study the current variable list in Excel format downloadable at the secuTrial® SSR welcome page; you will see which variables are available in which format and whether variables are mandatory or optional. It is recommended to use only mandatory variables for analyses involving several Stroke Centers / Units. Using optional variables will require more time to fill in missing data at the participating sites.
  - Please cut out the variables (lines) that you don't need, leaving in all the columns.

- Timeline with proposed milestones (e.g. full analysis plan circulated, data collected, data cleaned and locked, data analyzed, first manuscript draft)
- Funding (any existing funding or funding source the research proposal will be submitted to, including time of expected response).

Procedural steps for proposals

1. Initial counseling by DKF Basel (*optional*)

1.1. Of note, the DKF Basel offers **free initial** counseling on project ideas for Investigators who wish the statistical analysis of their project to be performed at DKF Basel. Please contact the DKF Basel via the contact form of the Department of Clinical Research of the University Of Basel using the following link, and indicate that you are interested in a counseling for an SSR sub-study: https://kontaktformular.dkfbasel.ch/#en. The DKF Basel will assign a member to the project who will respond to the Investigator.

1.2. Initial counselling is optional. In such a case, the statistical analysis itself will be invoiced additionally (see item 6).

1.3. Initial counselling includes a rough estimation of total project costs.

2. Submission and approval of analysis plan

2.1. The **Lead Investigator** submits the summary analysis plan (Word or PDF file) and the project-specific variable list (Excel file) to the SSR Steering Committee Info | Neurovasc <info@neurovasc.ch>(c/o Mira Katan, mira.katan@usb.ch).

2.2. The **SSR Steering Committee** evaluates the research proposal in terms of scientific merit, clinical potential impact, 4 times per year (SSR-Steering committee meeting) and finally informs the Lead Investigator within one week after these quarterly meetings about the decision.

3. Initial data check by DKF Basel

3.1. If approved by the **SSR Steering Committee**, The **Lead Investigator** sends the agreed analysis plan (including the list of planned participating Stroke Centers / Units) to DKF **Basel** via the contact form (please indicate that the request is related to the SSR): https://kontaktformular.dkfbasel.ch/#en

3.2. The study variables should be provided as a separate Excel file (see template for summary analysis plan above), or as a comma-separated text file, using the variables names as defined in current variable list downloadable at the SecuTrial® SSR welcome page (example): “event_type”, “age”, “onset_time”

3.3. In- and exclusion criteria must be clearly defined and specifically refer to the relevant variable names.

3.4. **DKF Basel** (data center) performs an initial check of the completeness of project-specific variables at planned Stroke Centers / Units and reports to Lead Investigator (written report in electronic format). *This service will be included in the project costs (see item 6) only if the project is implemented*; if on the other hand the Lead Investigator decides to abandon the project for reasons of feasibility, the initial data check will not be invoiced. This also applies if the local ethics committee does not approve the research project. The DKF reserves the right to charge for expenses exceeding 6 hours of working time.

3.5. The initial data check includes a rough estimation of total project costs, if not already provided under step 1.3.

4. Amendment and finalization of the analysis plan.

4.1. The **Lead Investigator** re-assesses the feasibility of the proposed analysis plan based on the report by DKF Basel, and if necessary revises the analysis plan by limiting the number of project-specific variables and/or planned Stroke Centers / Units.

4.2. The **Lead Investigator** sends a copy of the final analysis plan to the SSR Steering Committee as well as DKF Basel.

5. Obtaining agreement to use data from Stroke Centers / Units

5.1. **DKF Basel** sends the contact list (including email addresses) of the planned Stroke Centers / Units (i.e., local Heads and/or other designated contact persons) to the Lead Investigator.

5.2. The **Lead Investigator** sends a cover letter and the final analysis plan to the panned Stroke Centers / Units inviting them to participate in the research project and asking for approval to use the Units / Centers data.

5.3. **Invited Stroke Centers / Units** respond directly to Lead Investigator.

5.4. **Lead Investigator** informs DKF on which Stroke Units and Stroke Centers agreed to participate in project.

6. Estimation of project-specific costs and agreement

6.1. **DKF Basel** estimates costs for project-specific tasks and sends offer to Lead Investigator. Tasks include:

- Creating project-specific reports (database management) in case Stroke Centers / Units need to complete missing data
- Extraction of analysis data set (data center).
- *Optional*; *if requested by Lead Investigator:* Data analysis, tables and figures, etc.

6.2. **Lead Investigator** confirms offer.

7. Obtaining ethics approval

7.1. The **Lead Investigator** submits the research proposal including the final variable list to the local ethics committee.

7.2. The **Lead Investigator** sends a copy of the approval letter from the ethics committee to the responsible member of **DKF Basel**

8. Completion of missing data (if required)

8.1. **DKF Basel** (data management) creates a project-specific report for participating Stroke Centers and Stroke Units to fill in any missing project-specific variables.

8.2. **Collaborators at the participating Stroke Centers / Units** fill in the missing data.

9. Extraction of analysis data set

9.1. **For coded (reversibly anonymized) data: DKF Basel** (data center) extracts the coded ("verschlüsselt") analysis data set and sends it to the Lead Investigator. Data do not contain personal information and are only identified by the SSR-specific patient ID.

9.2. For irreversibly anonymized data: DKF Basel (data center) extracts the irreversibly anonymized analysis data set and sends it to the Lead Investigator: Data neither contain personal information nor the SSR-specific patient ID.

9.3. The **Lead Investigator** analyses the data, writes the manuscript and circulates it among all authors for critical revision and important intellectual content.

General authorship principles

Authors

1. **The Lead Investigator determines** lead, senior and corresponding authorship, as well as co-authorship(s) of supervised researchers from the Lead Institution, according to their contribution to the manuscript.
2. The following persons qualify as co-authors, **provided they fulfil the ICMJE authorship criteria listed under point 4** and confirm their willingness to do the additional work to the Lead Investigator:
    a. Members of the SSR Steering Committee
    b. Colleagues from the participating Stroke Centers and Stroke Units contributing data to the particular analysis, based on data quantity and quality
3. Authors from all disciplines involved in the research project (based on point 4) should be included (e.g., Neurology, Neuroradiology, Neurosurgery, etc.)
4. **The ICMJE recommends** that authorship be based on the following 4 criteria:
    1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
    2) Drafting the work or revising it critically for important intellectual content; AND
    3) Final approval of the version to be published; AND
    4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Investigators

1. The author list on the title page is followed by "*on behalf of the Swiss Stroke Registry Investigators*", referring to the appendix of the manuscript where these Investigators are listed.
2. Participating Stroke Centers and Stroke Units will name all individuals who have contributed in a significant and documentable manner to the current project to be included in this list of

Investigators, irrespective of whether they are also regular co-authors of the manuscript or not.

3. Individuals must provide their written signed approval to be listed as Investigators. For this purpose, the Lead Investigator will distribute a "List of Investigators" in the format below to the participating Stroke Centers and Stroke Units to be reviewed updated if necessary. The signature form has the following format:

"List of Investigators – Swiss Stroke Registry

The following Investigators participated in the Swiss Stroke Registry and contributed in a significant and documentable manner. They hereby confirm that their names can be listed in any manuscript (i.e. appendix, acknowledgement) arising from this registry. "

Stroke Center / Stroke Unit:

Name	Date	Signature