



## 1. Objective

The objective of this Standard Operating Procedure (SOP) is to describe the steps to be followed when using data from the Tinnitus Research Initiative (TRI) Database for statistical analyses in order to answer research questions.

## 2. Background

The TRI Database is an international effort to collect raw data from clinical studies and to allow statistical analysis on an aggregate level. Studies are eligible to be included into the TRI Database if patients undergo specific treatments and are assessed in the course of this treatment by means of predefined standardized clinical, diagnostic, and outcome measures ([see Landgrebe et al. 2010 for details](#)) [1].

The primary objectives of the TRI Database are (1) collecting a standardized set of data on patient characteristics, treatments, and outcomes of tinnitus patients consulting specialized tinnitus clinics all over the world (in May 2011: 13 centers in 8 countries), (2) delineating different subtypes of tinnitus based on systematically collected data and (3) identifying predictors for individual treatment response based on clinical profiles [1].

## 3. Processes

### 3.1. Entering data into the TRI database

Data are entered into the TRI Database at the Tinnitus Research Center in Regensburg according to the [Data Handling Plan](#) (TRI-DHP) [2], either manually or by means of a scan. Participating centers have signed a contract that specifies the transmission of raw data to the Tinnitus Research Center Regensburg and the participants' rights to make use of their own data and the entire TRI database.

## **Data import from the TRI Database into a statistical software package**

### Whole data set

For statistical analyses, data need to be imported from the TRI database into a file that can be handled by a statistical software package (SAS, SPSS, Stata). The amount of data in the TRI Database is steadily growing. Therefore, in order to ensure that statisticians share a common data file, the TRI Database will be imported twice a year (1st of May and 1st of November). The corresponding dataset will be the basis for all analyses in this period.

### Center specific data set

If a participating center wishes to analyze its own data, importing this specific data set is permissible at any time.

## **3.2. Generation of research questions**

Research questions can be generated by everybody involved in the database project (e.g., leading clinicians or researchers of contributing centers and statisticians).

Research questions need to be of scientific interest and formulated in such a way that they can be addressed by variables stored in the TRI database.

Research questions are expected to fall into one of the following five categories:

1. Efficacy analyses of specific treatments
2. Conceptual questions, e.g., psychometric performance of outcome instruments or interrelations among assessment instruments
3. Interrelations between clinical or demographic characteristics
4. Examination of prognostic factors for treatment success
5. Ad hoc research questions, i.e., issues that arise from new findings or conceptualizations in tinnitus research

### **3.3. Development of a brief Statistical Analysis Plan (SAP)**

Statistical analyses will be done by the statistician in charge who is affiliated either with the Center for Clinical Studies Regensburg, with the Tinnitus Research Center Regensburg, or with any of the participating study centers.

Before the statistician in charge starts working on the analyses he or she should write up a brief Statistical Analysis Plan (SAP) according to the following outline:

1. Research question
2. Description of the dataset used for the analysis
  - Date when dataset was generated
  - Number of patients
3. Variables used in this analysis
4. Statistical methods
5. Planned start and end of analysis
6. Literature (if necessary)

The SAP should be concise (about 2 to 5 pages), yet give sufficient information to make the results reproducible by any statistician not involved in the project.

A SAP template for further information can be found [here](#) (TRI-SAP) [3].

### **3.4. Submission of the SAP to the Steering Committee**

The SAP should be sent to the Steering Committee for approval. The Steering Committee will decide whether further review by the Advisory Board or by a Scientific Expert Board is required. The Steering Committee will provide a summary of the comments raised in the review process.

### **3.5. Finalizing the SAP**

Based on the Steering Committee's review, the statistician in charge will finalize the SAP.

### **3.6. Changes to finalized SAP**

#### **Minor changes**

All adjustments to analyse techniques made during the analysis that does not affect contents requires the online placement of a minor amendment including the respective changes. Such a minor amendment does not have to be approved by the Steering Committee.

#### **Major changes**

All adjustments to analyse techniques or evaluation strategies made during the analysis that sets new standards with regard to the contents requires the online placement of a major amendment including the respective changes. Such a major amendment has to be approved by the Steering Committee.

### **3.7. Documentation on the TRI Website**

After the finalization, the SAP will be published on the TRI Website. The date of publication will be documented.

### **3.8. Analyses**

The analyses described in the SAP should be done by the statistician in charge by means of a validated and approved software (e.g., SAS, SPSS, Stata).

### 3.9. Results and Publications

The results should be reviewed and commented by all people involved in the particular project and the Steering Committee. The Steering Committee may also invite the Advisory Board and an Expert Scientific Committee for comments. Results should be published at national and international conferences and scientific journals in the field. Publications whose data analysis was done according to the here specified SOP should include the following phrase in the methods section:

“The data analysis was based on data of the Tinnitus Research Initiative Database. Data management was conducted according to the Data Handling Plan (TRI-DHP *insert appropriate version number and date*). Data analysis was conducted according to the Standard Operating Procedure (TRI-SA *insert appropriate version number and date*), thereby following a study-specific Statistical Analysis Plan (SAP) that was written according to the SAP template (TRI-SAP *insert appropriate version number and date*). All documents are to be found under <http://database.tinnitusresearch.org/>.”

### 3.10. Quality assurance

The request to comply with this SOP should not be seen as a bureaucratic hurdle but as a means for assuring the highest quality of the statistical analyses and the highest validity of the obtained results.

Goals of the proposed procedures include

- avoiding the analysis of useless research questions
- avoiding the analysis of questions that (unknowingly) have already been analyzed before
- creating transparency with regard to research methods and statistical analyses
- avoiding the neglect of null results (“not significant”)
- addressing the statistical problem of multiplicity

## References

- [1] Landgrebe M, Zeman F, Koller M, Eberl Y, Mohr M, Reiter J, Staudinger S, Hajak G, Langguth B. The Tinnitus Research Initiative (TRI) database: A new approach for delineation of tinnitus subtypes and generation of predictors for treatment outcome.  
BMC Medical Informatics and Decision Making 2010, 10:42  
<http://www.biomedcentral.com/1472-6947/10/42>
- [2] Eberl Y, Zeman F. Data Handling Plan for Tinnitus Research Initiative (TRI-DHP) (English and German Version).  
<http://database.tinnitusresearch.org/en/publications/documents/tri-dhp.pdf>
- [3] Schecklmann M. Template for Statistical Analysis Plan for Tinnitus Research Initiative (TRI-SAP).  
<http://database.tinnitusresearch.org/en/publications/documents/tri-sap.doc>

## Workflow

Action	When	Who
Data collection and entry	at any time	TRI center
Import of data set for analyses	complete dataset: 1st May/1st Nov	Center for Clinical Studies
Generation of research questions	at any time	every clinician and statistician
SAP	at any time, based upon research question	statistician in charge
Analyses	after SAP	statistician in charge
Publications	after having obtained the results	clinicians and statistician