

Guidance for key issues of design and analysis of observational studies

General overview of the aims and strategies of the international initiative

Willi Sauerbrei (Freiburg, Germany)
for the steering group of the initiative

Why do we need such an initiative?

- Weaknesses of many analyses
- Many analyses are conducted by people with limited statistical knowledge
- Analysis of observational studies – issues are very similar in all areas of science
- Rapid developments of statistical methodology requires guidance and education

Guidance and education required

- Statistical models are always a simplification of real life processes. To improve these models, researchers develop new and more complicated approaches
- Different and partly conflicting approaches are proposed
- Expert knowledge is required to use methods
- Statistical software has to be available

Current situation

- Statistical methodology has seen some substantial development
- Computer facilities can be viewed as the cornerstone
- Possible to assess properties and compare complex model building strategies using simulation studies
- Resampling and Bayesian methods allow investigations that were impossible two decades ago
- Machine learning approaches may be interesting alternatives to more traditional approaches
- Wealth of new statistical software packages allow a rapid implementation and verification of new statistical ideas

Unfortunately, many sensible improvements are ignored in practical statistical analyses

Reasons that improved strategies are ignored

- Overwhelming concern with **theoretical aspects**
- Very **limited guidance** on key issues that are **vital in practice**, discourages analysts from utilizing more sophisticated and possibly more appropriate methods in their analyses

Improvement

At least **two tasks** are essential

1. **Experts** in specific methodological areas have to work towards **developing guidance documents**
2. An ever-increasing need for **continuing education** at all stages of the career

For busy applied researchers it is often **difficult to follow methodological progress** even in their principal application area

- Reasons are diverse
- Consequence is that analyses may be deficient
- **Knowledge** gained through research on statistical methodology needs to be **transferred** to the broader community
- Many **analysts** would be **grateful for** an overview on the current **state of the art** and for **practical expert guidance**

Aims of the initiative

- **Provide guidance documents** for highly relevant issues
- As the statistical **knowledge** of the analyst **varies** substantially, guidance has to keep this background in mind. **Guidance** documents have to be provided **at several levels**
- For the **start** we will concentrate on **state-of-the-art** documents for experienced statisticians (**level 2**)
- Help to identify questions **requiring more primary research**

The overarching long-term aim is to improve key parts of statistical analyses of observational studies in practice

Different levels of statistical knowledge

Level 1: Low statistical knowledge

- Most analyses are done by analysts at that level
- **Point out weaknesses** of approaches often **used despite of problems** (e.g. categorizing continuous variables in the analysis; complete case analysis if a case has missing values in one or more variables)
- Propose **methods** which may not be optimal or state of the art, but which are easy to use and which are **still acceptable** from a methodological point of view
- **Software** should be generally available

Different levels of statistical knowledge

Level 2: Experienced statistician

- Methodology perhaps slightly below **state of the art**, but doable by every experienced analyst
- **Advantages and disadvantages** of competing approaches, point to the importance and implications of underlying assumptions
- Sufficient guidance about **software** plays a key role that the approaches are also used in practice

Different levels of statistical knowledge

Level 3: Expert in a specific area

- To improve statistical models and to adapt them to complex real problems, researchers **develop** new and **more complicated approaches**
- Advantages and usefulness in practice are unclear
- Often, advantages are presented in a small number of examples and in specific situations but a **more systematic comparison to the state of the art is needed**
- **Software** requires **specific knowledge** and may not be generally available
- **Overview of recent research** with statements about possible advantages and disadvantages is needed
- Could help to **identify** important **weaknesses** of **level 2** proposals
- Help to identify **areas** needing **more** methodological **research**
- Trigger the development of **software** for more general use

Short term aims

- For a small number of **highly relevant topics** we will try to assess the current **state of practice** and identify current documents which try provide some guidance
- Try to find '**agreement**' **what to recommend** within each of the three levels mentioned
- Documents have to be **understood** and at least broadly **accepted**
- **Positive examples** from the current literature will help to reach the latter goal

Long term aims

- **Improvement of statistical analyses**, acceptance of guidance documents by analysts could be a cornerstone
- The percentage of analysts who reflect only the '**level 1**' knowledge should **decrease substantially**
- Guidance **documents** have to be **regularly improved**. Based on evidence some approaches should be ready to be moved from level 3 into a level 2 recommendation
- **Software** is generally available and usable at a broader level
- Number of **topics** is large and there is often a **relation between them** or one is influenced by the other.
For example, variable selection and missing data: First it is important to **derive guidance for both of them separately**. For practical reasons it is highly relevant to **consider the implications of** missing data **on** guidance for variable selection.

Program

Design and analysis of observational studies in medical research

Willi Sauerbrei	General overview of the aims and strategies of the international initiative
Doug Altman	Why we need guidance documents for the design and analysis of observational studies
James Carpenter	Guidance initiative: a route map, and the journeying of the missing data topic group (TG 1) Discussion 1
Coffee break	
Saskia Le Cessie	TG 3: Descriptive and initial data analysis
Michal Abrahamowicz	TG 2: Selection of variables and functional form; flexible approaches improve estimation and inference
Els Goetghebeur	TG 7: Causal Inference – at work
Petra Macaskill	TG 6: Evaluating diagnostic tests and prediction models
Helmut Küchenhoff	TG 4: Measurement error
Doug Altman	TG 5: Design Discussion 2

Steering Group

Members:

- Michal Abrahamowicz (Mc Gill, Montreal, Canada)
- Doug Altman (Oxford, UK)
- James Carpenter (London, UK)
- Ray Carroll (College Station, US)
- Stephen Evans (London, UK)
- Mitch Gail (NCI, Bethesda, US)
- Els Goetghebeur (Gent, Belgium)
- Göran Kauermann (Munich, Germany)
- Saskia Le Cessie (Leiden, The Netherlands)
- Petra Macaskill (Sydney, Australia)
- Jörg Rahnenführer (Dortmund, Germany)
- Willi Sauerbrei (Freiburg, Germany)
- Sebastian Schneeweiss (Harvard, Boston, US)
- Ewout Steyerberg (Rotterdam, The Netherlands)
- Andrew Vickers (Sloan Kettering, New York, US)

Aim of this symposium

Informing you!
Getting you involved!

- Interest further colleagues to work on guidance documents
For both the seven topics presented and on some new topics, to be proposed to the Steering Group
- Afternoon session of the members of the initiative
Interested colleagues are very welcome!

For Further information

Willi Sauerbrei

(IMBI, University Medical Center Freiburg, Germany,
wfs@imbi.uni-freiburg.de)