STRATOS foci for the next three years

Sauerbrei W[1], Carpenter J, Abrahamowicz M, van Geloven N, Gustafson P, Huebner M, Keogh R, Shaw P, Goetghebeur E

for the STRATOS initiative

[1]Institute for Medical Biometry and Statistics, Medical Center University of Freiburg, Germany

http://stratos-initiative.org/

ISCB 2024

Program

STRATOS foci for the next three years –
Willi Sauerbrei for Stratos

Talks of TGs: 1, 2, 3, 4, 6, 7 and 8

Building blocks of Efficient Initial Data Analysis and Data Quality Assessments – Best practice examples –
Carsten Oliver Schmidt for TG3

An Overview and Recent Developments in the Analysis of Multistate Processes –
Malka Gorfine for TG8

Assessing performance when developing or validating clinical risk prediction models in the era of machine learning –
Ben van Calster for TG6
BREAK

Adjusting for covariate measurement error on functional form estimation: design and early results from a blinded, collaborative STRATOS project –
Aris Perperoglou for TG2/TG4 collaborative project

Causal inference moving forward – embracing joint (dis)appearances –
Els Goetghebeur for TG7

Current and future initiatives in missing data –
Katherine Lee for TG1

General Discussion

STRATOS initiative: STRengthening Analytical Thinking for Observational Studies

Main goal

To **improve the current practice** in design and statistical analyses of observational studies in practice by **closing the gap** between available statistical methodology and methods applied in real-life though **guidance for researchers** with different levels of statistical expertise.

NEED for GUIDANCE

– Profusion of new, complex statistical techniques and algorithms

– Unclear which methods are useful in practice, and under what conditions

– Databases are more complex, RWD with many complications appear jointly and software is (often) not easily available

– There is **insufficient awareness and understanding** among practitioners, of both well-established and, especially, new approaches and methods

The need for collaboration and further research

– For some complex analytical challenges, there is no agreement, even among experts, as to the best approach

– Very **limited guidance** on key issues that are **vital in practice** discourages analysts from utilizing possibly more appropriate methods in their real-life applications, thus, **reducing the scientific yield of empirical research**

UNIVERSITÄTS
KLINIKUM FREIBURG

Guidance and educational material is needed for many stakeholders (analysts with different levels of knowledge and experience, reviewers, readers, teachers, journalists, ……)

Researchers

First in a Series of Papers for the Biometric Bulletin

STRATOS initiative – Guidance for designing and analyzing observational studies

Willi Sauerbrei[1], Marianne Huebner[2], Gary S. Collins[3], Katherine Lee[4], Laurence Freedman[5], Mitchell Gail[6], Els Goetghebeur[7], Joerg Rahnenfuehrer[8] and Michal Abrahamowicz[9] on behalf of the STRATOS initiative.

➡ Short papers from all TGs and some panels

Consumers

Guidance for designing and analysing observational studies:

The STRengthening Analytical Thinking for Observational Studies (STRATOS) initiative

Willi Sauerbrei[1], Gary S. Collins[2],
Marianne Huebner[3], Stephen D. Walter[4],
Suzanne M. Cadarette[5], and
Michal Abrahamowicz[6] on behalf of the
STRATOS initiative

Volume 26 Number 3 | Medical Writing September 2017 | 17

Journal of the European Medical Writers Association (EMWA)

Different levels of statistical knowledge

Level 1: Low statistical knowledge
• Many studies are analysed by researchers with this level
Level 2: Experienced statistician
• Uses methodology which is ok, however often not according to state of the art
Level 3: Expert in a specific area
• Performs research to improve statistical models and adapts them to complex real problems.

STRATOS – History and Milestones

- **2011: Epi Subcom** at **I**nt **S**oc **C**lin **B**iostatistics (ISCB) in Ottawa

- **2013: First mini-symposium** at **ISCB** in Munich, **initiative launched**

- **2014: 1st STRATOS paper,** *Statistics in Medicine* 2014

- **2016 & 2019: 2 General meetings**, Banff Int Res Station (BIRS), Canada

- **Series in Biometric Bulletin (since 3/2017):** 27 articles published

- **2019:** Partner in the **Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints (SISAQOL) project**, lead by EORTC (41 stakeholders, including pharma, regulators, patients)

- **2021: Memorandum of Understanding** with **ISCB**

- **2024: 3rd General meeting**, Lorentz Center, Leiden (NL)

As of 2024: >100 members (from 21 countries on 5 continents)

STRATOS Topic Groups (TGs)

Topic Group		Chairs
1	Missing data	James Carpenter (UK), Kate Lee (AUS)
2	Selection of variables and functional forms in multivariable analysis	Georg Heinze (AUT), Aris Perperoglou (UK), Willi Sauerbrei (GER)
3	Initial data analysis	Marianne Huebner (US), Lara Lusa (SL), Carsten Oliver Schmidt (GER)
4	Measurement error and misclassification	Victor Kipnis (US), Pam Shaw (US)
5	Study design	Suzanne Cadarette (CAN), Mitchell Gail (US)
6	Evaluating diagnostic tests and prediction models	Ewout Steyerberg (NL), Ben van Calster (BEL)
7	Causal inference	Els Goetghebeur (BEL), Ingeborg Waernbaum (SWE)
8	Survival analysis	Michal Abrahamowicz (CAN), Malka Gorfine (IS), Terry Therneau (US)
9	High-dimensional data	Lisa McShane (US), Joerg Rahnenfuehrer (GER), Riccardo de Bin (NOR)

Chairs from 12 countries and 3 continents

UNIVERSITÄTS KLINIKUM FREIBURG

STRATOS Cross-cutting Panels

Panel		Chairs and Co-Chairs	
MP	Membership	Chairs:	James Carpenter (UK), Willi Sauerbrei (GER)
PP	Publications	Chairs:	Bianca De Stavola (UK), Pam Shaw (US), Mitchell Gail (US), Mark Baillie (CH)
GP	Glossary	Chairs:	Martin Boeker (GER), Marianne Huebner (US)
WP	Website	Chairs:	Joerg Rahnenfuehrer (GER), Willi Sauerbrei (GER)
RP	Literature Review	Chairs:	Gary Collins (UK), Carl Moons (NL)
BP	Bibliography	Chairs:	to be determined
SP	Simulation Studies	Chairs:	Michal Abrahamowicz (CAN), Anne-Laure Boulesteix (GER)
DP	Data Sets	Chairs:	Saskia Le Cessie (NL), Maarten van Smeden (NL)
TP	Knowledge Translation	Chair:	Maarten van Smeden (NL)
CP	Contact Organisations	Chair:	Willi Sauerbrei (GER)
VP	Visualisation	Chairs:	Mark Baillie (CH)
OS	Open Science	Chair:	Sabine Hoffmann (GER)

An overview of activities is summarized in the Biometrical Bulletin, since 2017

(STRATOS): Six foci for the next three years

James Carpenter (1), Michal Abrahamowicz (2), Nan van Geloven (3), Paul Gustafson (4), Marianne Huebner (5), Ruth Keogh (1), Willi Sauerbrei (6), Pamela Shaw (7), Els Goetghebeur (8)

(STRATOS): Introducing the Open Science Panel

Sabine Hoffmann1, Kim Luijken2, Willi Sauerbrei3, Pamela Shaw4, Anne-Laure Boulesteix5

(STRATOS): On the importance of Data Quality Assessments and Initial Data Analysis

C. O. Schmidt[1], G Heinze[2], L Lusa[3], M Huebner[4]

(STRATOS): Overview of methodological issues when analyzing high-dimensional biomedical data

De Bin R., McShane L., Rahnenführer J. on behalf of STRATOS TG9 (2023)

(STRATOS): Guidance for analysts with limited statistical knowledge

Georg Heinze1, Anne-Laure Boulesteix2, Daniela Dunkler1, Mitchell H. Gail3, Katherine J. Lee4, Ben van Calster5, Michael Wallace6, Willi Sauerbrei7

a very brief update on the achievements of the STRATOS initiative in the last 5 years

Willi Sauerbrei[1], Michal Abrahamowicz[2], Mark Baillie[3], Bianca De Stavola[4], Mitchell Gail[5], Marianne Huebner[6], Ruth Keogh[7] and Pamela A. Shaw[8] for the STRATOS initiative

(STRATOS): Progress in the Topic Group on Evaluating Diagnostic Tests and Prediction Models (TG6)

Ewout W Steyerberg[1], Ben Van Calster[1,2], on behalf of STRATOS TG6

STRATOS foci for the next three years

1. Simulation studies
2. Open science
3. Initial Data Analysis (IDA)
4. Machine learning (ML) enhanced statistical methods
5. Estimands in observational data analysis
6. More guidance for researchers with limited statistical knowledge and experience

1. Simulation studies

- Simulation studies are key tools for validating and comparing statistical methods, and hence critical to the development of evidence-based statistical guidance
- STRATOS will maintain a focus on simulation studies and prioritize improving their methodology over the coming years

Topics
- **Neutral comparison studies**. See special collection Biometrical Journal. BioBull article in June
- Structured approach for planning and reporting simulation studies, which involves defining aims, data-generating mechanisms, estimands, methods, and performance measures ("**ADEMP framework**").
- **Phases of methodological development**
- **Generation of synthetic data**

2. Open Science

– The importance of open science is evident, but it is an extremely broad topic, and still in its infancy
– For some challenges we will work on accessible guidance for making research more transparent, reproducible and hence credible

Topics
– Role of synthetic data
– Federated data analysis
– Curated data sets to share

– More to be added

3. Initial Data Analysis (IDA)

– The 'Initial data analysis' TG3 **aims to improve awareness of IDA** as a **critical component of the research process**, and develop **guidance** on conducting IDA in a systematic, reproducible manner
– Some issues will be discussed in the talk by CO Schmidt

4. Machine learning (ML) enhanced statistical methods

– ML and statistical methodologies have their specific strengths and weaknesses

– Each could benefit from the insights offered by the other
How to do that best and when is not obvious.

– We plan to identify the ML enhanced statistical methods that are most important for different TG's, and systematically assess their properties in realistic settings

UNIVERSITÄTS
KLINIKUM FREIBURG

5. Estimands in observational data analysis

- Estimand: what is being estimated and for whom
- Guidance emerges from different angles:
  - Trial context: ICH-E9 addendum (ICH, 2019)
  - Causal inference notation in potential outcomes/counterfactuals
  - Target trial emulation framework

- We aim to unify the different views on estimands and explore the added value in the different topic groups of STRATOS.

- Parallel mini-symposium: '**Beyond conventional RCTs: Exploring design options and modeling in drug development'.** Contribution from STRATOS in the Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints (**SISAQOL**) project

UNIVERSITÄTS
KLINIKUM FREIBURG

6. More guidance for researchers with limited statistical knowledge and experience

- From the beginning, the STRATOS initiative highlighted that many methodological developments are not implemented in practice
- Lack of guidance on practical issues is presumed to be an important hurdle
- Researchers with only basic statistical knowledge and limited experience in using statistical methodology need much more help

Getting involved

Four membership categories
– Regular members
– Experienced adjunct members
– Early career adjunct members
– Clinical affiliates

https://stratos-initiative.org/de -> Contact
– Short contact form
– Two page CV

UNIVERSITÄTS
KLINIKUM FREIBURG