A brief overview of the STRATOS initiative

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Acknowledgements

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Outline

Motivation for STRATOS

Organizational Structure and membership

History and milestones

Past, current, future work

What is STRATOS?

The **Strengthening Analytical Thinking in Observational Studies** (STRATOS) Initiative is a large collaboration of experts whose aim is

"…to provide accessible and accurate guidance in the design and analysis of observational studies. The guidance is intended for applied statisticians and other data analysts with varying levels of statistical education, experience and interests."

Sauerbrei et al *Statistics in Medicine,* 2014

www.stratos-initative.org

Launch of the STRATOS initiative 2013

Mini-Symposium on the last day of the ISCB2013 meeting in Munich

Situation in 2013:
- Reporting guidelines were still in the 'early days'
  - EQUATOR started in 2006, TRIPOD published in 2015
- Lancet series 'Reduce waste, increase value' not published (in 2014)
- Medical research needs to change – HOW?
- Open Access papers – rare and often rather negative reputation
- Center for Open Science started in 2013
- FAIR (**F**indability, **A**ccessibility, **I**nteroperability, and **R**euse) principles in 2016
- Meta Research still in its early days
- Funding for a guidance initiative was (and still is) a problem
- Funders and journals prioritize novelty over incremental replication research

Why do we need such an initiative?

"In return for the altruism and trust that make clinical research possible, the research enterprise has an obligation to conduct research ethically and to report it honestly." [i.e. transparently and completely]
   [International Committee of Medical Journal Editors, 2004]

- **Medical research is very important – it affects people's lives**

- There are weaknesses in many analyses appearing in the literature
- Many analyses are conducted by people with limited statistical knowledge
- Rapid developments of statistical methodology requires guidance and education
- Analytical issues for observational studies are very similar in all areas of science

Guidance and education required

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

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Current situation

- Statistical methodology has seen substantial development

- Computing resources 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 four decades ago

- Machine learning approaches are often interesting alternatives to more traditional statistical approaches

- Wealth of new statistical software packages allow a rapid implementation and verification of new statistical ideas

Unfortunately, many sensible improvements and technological innovations are ignored in practical statistical analyses

Reasons that improved strategies are ignored

- Many methodology papers emphasize **theoretical over practical aspects**
  - **Simulation studies** of finite sample properties and comparisons with other methods **are typically very limited**
- 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
- **Poor dissemination** of new methods to statistical practitioners and other non-experts (e.g. clinician and epidemiologist scientists)

Improving the current state

At least **two tasks** are essential

1. **Experts** in specific methodological areas have to work towards **developing guidance**

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 **actively 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**

Main goal of STRATOS

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.**

The focus is on health sciences research, but the content is also relevant for applications of statistics in other empirical sciences.

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**

Level 1: Low statistical knowledge
• Limited to no formal training in statistics, many studies analyzed by researchers at this level
Level 2: Experienced statistician
• Has understanding of appropriate methodology, but often not using state of the art
Level 3: Expert in a specific area
• Performs research to improve statistical methods and adapt them to complex real problems

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**	Paul Gustafson (CAN), Pamela Shaw (US)
5	**Study design**	Mitchell Gail (US), Suzanne Cadarette (CAN)
6	**Evaluating diagnostic tests and prediction models**	Ewout Steyerberg (NL), Ben van Calster (NL)
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**	Federico Ambrogi (IT), Riccardo de Bin (NOR), Lisa McShane (US)

Chairs from 13 countries and 4 continents

STRATOS Cross-cutting Panels

Panel		Chairs
MP	**Membership**	James Carpenter (UK), Willi Sauerbrei (GER)
PP	**Publications**	Pamela Shaw (US), Lisa McShane (US), Mark Baillie (CH)
GP	**Glossary**	Martin Boeker (GER), Marianne Huebner (US)
WP	**Website**	Joerg Rahnenfuehrer (GER), Willi Sauerbrei (GER)
SP	**Simulation Studies**	Michal Abrahamowicz (CAN), Anne-Laure Boulesteix (GER)
TED	**Towards Excellent Data**	Georg Heinze (AUT), Carsten Oliver Schmidt (GER)
TP	**Knowledge Translation**	Maarten van Smeden (NL)
CP	**Contact Organisations**	Willi Sauerbrei (GER)
VP	**Visualisation**	Mark Baillie (CH)
OS	**Open Science**	Daniela Dunkler (AUT), Sabine Hoffmann (GER)

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: 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.

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

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STRATOS – History and Milestones

2011 Epi Subcom at 42th Int Soc Clin Biostatistics (ISCB) in Ottawa
2013: Initiative launched at 44th ISCB in Munich
2014: 1st STRATOS paper [1]: *Statistics in Medicine* 2014; 33(30):5413-5432.

Sauerbrei W, Abrahamowicz M, Altman D, le Saskia, Carpenter J. *STRengthening Analytical Thinking for Observational Studies: The STRATOS initiative.*

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

2024: Lorenz Workshop, Leiden, the Netherlands

Pamela Shaw – JSM 2025

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… STRATOS – History and Milestones

Invited STRATOS Sessions and Mini-Symposia:

Int Soc Clin Biost (ISCB): 2014, 2015, 2016, 2018 - 2025
Int Biometric Conf (IBC): 2016, 2020, 2022, 2024 + Regional IBS meetings:
2017, 2018, 2021 - 2025
Royal Statistical Soc (RSS): 2018, 2020, 2021
Other international conferences: HEC 2016, CEN 2018, GMDS 2017, Soc Epi
Res (SER) 2021, DAGStat 2022, CEN 2023, DAGSTAT 2025, JSM 2025

since 3/2017: Series in Biometric Bulletin with 31 short overviews published

2021 Memorandum of Understanding with ISCB

As of 2025: about 120 members from 20 countries on 5 continents

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STRATOS publications: Reviews aimed to improve current practice

- Sauerbrei W, Perperoglou A, Schmid M, Abrahamowicz M, Becher H, Binder H, Dunkler D, Harrell Jr. FE, Royston P, Heinze G for TG2 of the STRATOS initiative (2020). State of the art in selection of variables and functional forms in multivariable analysis - outstanding issues. Diagnostic and Prognostic Research, 4:3, 1-18.

- Perperoglou A, Sauerbrei W, Abrahamowicz M, Schmid M on behalf of TG2 of the STRATOS initiative (2019): A review of spline function procedures in R. BMC Medical Research Methodology (19:46).

- Lusa L, Proust-Lima C, Schmidt CO, Lee KJ, le Cessie S, Baillie M, Lawrence F, Huebner M, on behalf of TG3 of the STRATOS Initiative (2024): Initial data analysis for longitudinal studies to build a solid foundation for reproducible analysis. PLoS ONE 19(5): e0295726. Gail MH, Altman DG, Cadarette SM, Collins G, Evans SJ, Sekula P, Williamson E, Woodward M (2019): Design choices for observational studies of the effect of exposure on disease incidence. BMJ open, 9:e031031 short summary

- McLernon DJ, Giardiello D, Van Calster B, Wynants L, van Geloven N, van Smeden M, Therneau T, Steyerberg EW, topic groups 6 and 8 of the STRATOS Initiative (2023): Assessing performance and clinical usefulness in prediction models with survival outcomes: practical guidance for Cox proportional hazards models. Annals of Internal Medicine. 176(1), pp.105-114

- Rahnenführer J, De Bin R, Benner A, Ambrogi F, Lusa L, Boulesteix AL, Migliavacca E, Binder H, Michiels S, Sauerbrei W, McShane L, for topic group "High-dimensional data" (TG9) of the STRATOS initiative (2023): Statistical analysis of high-dimensional biomedical data: a gentle introduction to analytical goals, common approaches and challenges. BMC Medicine. 2023 May 15;21(1):182.

STRATOS publications: Comprehensive Guidance and Tutorials

A sample of our guidance papers:

- Lee KJ, Tilling K, Cornish RP, Little RJ, Bell ML, Goetghebeur E, Hogan JW, Carpenter JR for the STRATOS initiative (2021): Framework for the Treatment And Reporting of Missing data in Observational Studies: The TARMOS framework. Journal of Clinical Epidemiology. 2021 Jun 1;134:79-88.

- Keogh RH, Shaw PA, Gustafson P, Carroll RJ, Deffner V, Dodd KW, Küchenhoff H, Tooze JA, Wallace M, Kipnis V, Freedman L (2020): STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 1 - Basic theory and simple methods of adjustment. Statistics in Medicine. Statistics in Medicine, 39(16), pp.2197-2231.

- Shaw PA, Gustafson P, Carroll RJ, Deffner V, Dodd KW, Keogh RH, Kipnis V, Tooze JA, Wallace M, Küchenhoff H, Freedman L (2020): STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 2 - More complex methods of adjustment and advanced topics. Statistics in Medicine. 2020 20;39(16):2197-231.

- Goetghebeur E, le Cessie S, De Stavola B, Moodie E, Waernbaum I on behalf of the topic group Causal Inference (TG7) of the STRATOS initiative (2020): Formulating causal questions and principled statistical answers. Statistics in Medicine. 30;39(30):4922-48.

- Andersen PK, Perme MP, van Houwelingen HC, Cook RJ, Joly P, Martinussen T, Taylor JMG, Abrahamowicz M, Therneau TM for the STRATOS TG8 topic group (2021): Analysis of time-to-event for observational studies: Guidance to the use of intensity models. Statistics in Medicine. 15;40(1):185-211.

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STRATOS publications: Biometric Bulletin articles

STRATOS initiative has a series with short articles since 3/2017

- Introductory article for STRATOS (Sauerbrei et al 2017, Biometric Bulletin; 34(3):18-20.)

- Articles introducing each of the TG and panels, with special topics and recurring updates of activities

- A sample of the 30 articles that have appeared in this series

  - De Bin R, McShane L, Rahnenführer J (2023): STRengthening Analytical Thinking for Observational Studies (STRATOS): Overview of methodological issues when analyzing high-dimensional biomedical data. Biometric Bulletin; 40(3):11-12.

  - Boulesteix A-L, Baillie M, Edelmann D, Held L, Morris T, Sauerbrei W (2024): STRengthening Analytical Thinking for Observational Studies (STRATOS): Neutral comparison simulation studies as the cornerstone to compare statistical methods. Biometric Bulletin; 41(2):14-15.

  - Bakewell N, Bartlett J, Van Lancker K , Goetghebeur E, Shaw P, Thomassen D, Boutmy E, Cadarette SM, le Cessie S, van Geloven N (2024): STRengthening Analytical Thinking for Observational Studies (STRATOS): Estimands – Summary from the "STRATOS Accelerated Guidance for Real World Data Analysis" Workshop. Biometric Bulletin, 41(4): 12-14.

  - le Cessie S, Goetghebeur E, Amdal CD, Musoro JZ, Pe M, Reynders D, Roychoudhury S, Thomassen D, Sauerbrei W (2024): STRengthening Analytical Thinking for Observational Studies (STRATOS): Cooperation in the Setting International Standards in Analyzing Patient Reported Outcomes and Quality of Life Endpoints (SISAQOL-IMI) project. Biometric Bulletin; 41(3): 13-14.

STRATOS – current work and priorities for future

- To date, many STRATOS papers in peer reviewed journals
  - Reviews of current practice
  - Guidance on pitfalls to avoid
  - Comprehensive tutorials – broad and specialized topic
  - Developing software and methods extensions where necessary
- Each topic group has built a website that offers resources, tutorial papers, shiny apps, videos, and other educational resources
- Paper to summarize first 10-years of STRATOS in progress
- Continuing need to expand Level 1 and Level 2 guidance to keep up with and navigate the constantly changing and expanding statistical literature
- Current directions involve inter-topic collaborations: e.g. missing data and measurement error
- Level 3 guidance starting to emerge

The STRATOS initiative
STRengthening Analytical Thinking for Observational Studies

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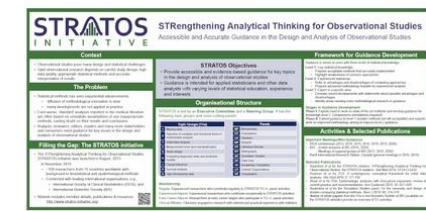
STRATOS initiative

The validity and practical utility of observational medical research depends critically on good study design, excellent data quality, appropriate statistical methods and accurate interpretation of results. Statistical methodology has seen substantial development in recent times. Unfortunately, many of these methodological developments are ignored in practice. Consequently, design and analysis of observational studies often exhibit serious weaknesses. The lack of guidance on vital practical issues discourages many applied researchers from using more sophisticated and possibly more appropriate methods when analyzing observational studies. Furthermore, many analyses are conducted by researchers with a relatively weak statistical background and limited experience in using statistical methodology and software. Consequently, even 'standard' analyses reported in the medical literature are often flawed, casting doubt on their results and conclusions. *An efficient way to help researchers to keep up with recent methodological developments is to develop guidance documents that are spread to the research community at large.*

These observations led to the initiation of the STRATOS (STRengthening Analytical Thinking for Observational Studies) initiative, a large collaboration of experts in many different areas of biostatistical research. *The objective of STRATOS is to provide accessible and accurate guidance in the design and analysis of observational studies. The guidance is intended for applied statisticians and other data analysts with varying levels of statistical education, experience and interests* (click to enlarge).

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News

STRATOS Newsletter (May 2018)

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Finding STRATOS

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