

The STRengthening Analytical Thinking for Observational Studies (STRATOS) initiative – introduction and brief overview

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<http://stratos-initiative.org/>

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STRATOS
I N I T I A T I V E



Aims of the STRATOS virtual conference

- 3 days: 2 Nov, 9 Nov, 14 Dec
- Day 1: To provide an overview of current and future TG activities to
 - Long-term members
 - Newbies
 - Interested guests
- Day 2: To report on and stimulate new cross-TG activities
 - Panels
 - Existing STRATOS projects
 - New cross-TG activities
- Day 3: To follow-up on new STRATOS activities

NEED for GUIDANCE

- Profusion of new, complex statistical techniques and algorithms
- Unclear which methods are useful in practice, and under what conditions?
- Insufficient awareness and understanding, among practitioners, of both well-established and, especially, new approaches and methods
- For some complex analytical challenges, there is no consensus, 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**

STRATOS Initiative: STRengthening Analytical Thinking for Observational Studies

- The overarching long-term goal:

To improve design and statistical analyses of observational studies in practice

by 'closing the gap' between (i) recent relevant developments in statistical methodology versus (ii) methods applied in real-life observational studies

- Specific aims:

- Develop **evidence-supported guidance** for statistical issues of practical importance (*through discussions among experts with different views, and simulations to systematically assess and compare alternative methods*)
- Provide **guidance at several levels** of statistical knowledge
- Start with **state-of-the-art** guidance for issues where there is consensus and necessary evidence
- **Identify and explore complex analytical challenges requiring more primary research and/or combining expertise** in different areas of statistical research

Different levels of statistical knowledge

Level 1: Low statistical knowledge

- Most analyses are done by analysts at this level

Level 2: Experienced statistician

- Methodology perhaps slightly below state of the art, but doable by every experienced analyst

Level 3: Expert in a specific area

- To improve statistical models and to adapt them to complex real problems, researchers develop new and more complex approaches. Advantages and usefulness in practice need to be assessed

Guidance for analysis is needed for many stakeholders
(analysts with different levels of knowledge, reviewers,
teachers, journalists,)

Researchers

First in a Series of Papers for the Biometric Bulletin

**STRATOS initiative – Guidance for designing and
analyzing observational studies**

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Willi Sauerbrei¹, Marianne Huebner², Gary S. Collins³, Katherine Lee⁴, Laurence Freedman⁵, Mitchell Gail⁶, Els Goetghebeur⁷, Joerg Rahnenfuehrer⁸ and Michal Abrahamowicz⁹ 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 Sauerbrei¹, Gary S. Collins²,
Marianne Huebner³, Stephen D. Walter⁴,
Suzanne M. Cadarette⁵, and
Michal Abrahamowicz⁶ on behalf of the
STRATOS initiative**

Volume 26 Number 3 | Medical Writing September 2017 | 17

Journal of the European Medical Writers Association (EMWA)

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

..... STRATOS – History and Milestones

- **Invited STRATOS Sessions and Mini-Symposia:**
 - Int Soc Clin Biost (ISCB): 2014, 2015, 2016, 2018, 2019, 2020, 2021,2022
 - Int Biometric Conf (IBC): 2016, 2020, 2022 + Regional IBS meetings: 2017, 2018, 2021, 2022
 - Royal Statistical Soc (RSS): 2018, 2020, 2021
 - Other international conferences: HEC 2016, CEN 2018, GMDS 2017, Soc Epi Res (SER) 2021, DAGStat 2022
- **Series in Biometric Bulletin (since 3/2017), 16 articles published, to proceed until 4/2024**
- **2021 Memorandum of Understanding with ISCB**
- **Partner in the SISAQOL project lead by EORTC (>40 stakeholders, including pharma and regulators)**
- **As of 2021: >100 members (from 19 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), Carsten Oliver Schmidt (GER)
4	Measurement error and misclassification	Laurence Freedman (ISR), Victor Kipnis (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), Per Kragh Andersen (DEN), Terry Therneau (US)
9	High-dimensional data	Lisa McShane (US), Joerg Rahnenfuehrer (GER), Riccardo de Bin (NOR)

Chairs from 12 countries and 3 continents

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)
		Co-Chairs:	Mitchell Gail (US), Petra Macaskill (AUS)
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:	Rolf Groenwold (NL), Maarten van Smeden (NL)
CP	Contact Organisations	Chairs:	Willi Sauerbrei (GER)
VP	Visualisation	Chairs:	Mark Baillie (SWITZ/CH)

Biometric Bulletin

- TGs have given short overviews in a series of papers published in the Biometric Bulletin
 - Sept 2017: introduction of the initiative
 - Dec 2017 – March 2020: 9 TG articles
 - June 2020 – Dec 2020: Panels Simulation, Visualisation and Glossary
 - Since March 2021: updated articles for TGs 4, 2 & 3 (in December TG1)
- Agreement with the Editor: article series until Dec. 2024

Papers

Received: 30 March 2020 | Revised: 4 September 2020 | Accepted: 4 September 2020
DOI: 10.1002/sim.8757

TUTORIAL IN BIOSTATISTICS

Statistics
in Medicine WILEY

Analysis of time-to-event for observational studies: Guidance to the use of intensity models

Per Kragh Andersen¹ | Maja Pohar Perme² | Hans C. van Houwelingen³ | Richard J. Cook⁴ | Pierre Joly⁵ | Torben Martinussen¹ | Jeremy M. G. Taylor⁶ | Michal Abrahamowicz⁷ | Terry M. Therneau⁸

TUTORIAL IN BIOSTATISTICS

Statistics
in Medicine WILEY

STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology: Part 1—Basic theory and simple methods of adjustment

Ruth H. Keogh¹ | Pamela A. Shaw² | Paul Gustafson³ | Raymond J. Carroll^{4,5} | Veronika Deffner⁶ | Kevin W. Dodd⁷ | Helmut Küchenhoff⁸ | Janet A. Tooze⁹ | Michael P. Wallace¹⁰ | Victor Kipnis¹¹ | Laurence S. Freedman^{12,13}



Journal of Clinical Epidemiology 134 (2021) 79–88

Journal of
Clinical
Epidemiology

ORIGINAL ARTICLE

Framework for the treatment and reporting of missing data in observational studies: The Treatment And Reporting of Missing data in Observational Studies framework

Katherine J. Lee^{a,b,*}, Kate M. Tilling^c, Rosie P. Cornish^c, Roderick J.A. Little^d, Melanie L. Bell^c, Els Goetghebeur^f, Joseph W. Hogan^g, James R. Carpenter^h, on behalf of the STRATOS initiative

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Accepted 13 January 2021; Published online 2 February 2021

Sauerbrei *et al. Diagnostic and Prognostic Research* (2020) 4:3
<https://doi.org/10.1186/s41512-020-00074-3>

Diagnostic and
Prognostic Research

COMMENTARY

Open Access

State of the art in selection of variables and functional forms in multivariable analysis—outstanding issues



Willi Sauerbrei^{1*}, Aris Perperoglou², Matthias Schmid³, Michal Abrahamowicz⁴, Heiko Becher⁵, Harald Binder¹, Daniela Dunkler⁶, Frank E. Harrell Jr⁷, Patrick Royston⁸, Georg Heinze⁶ and for TG2 of the STRATOS initiative

Publication Panel

STRATOS Papers

At least two authors, agreement from chairs and the publication panel

REGISTERED REPORT PROTOCOL

Systematic review of education and practical guidance on regression modeling for medical researchers who lack a strong statistical background: Study protocol

Paul Bach^{1,2,3}, Christine Wallisch^{1,2,4}, Nadja Klein³, Lorena Hafermann^{1,2}, Willi Sauerbrei⁵, Ewout W. Steyerberg⁶, Georg Heinze⁴, Geraldine Rauch^{1,2*}, for topic group 2 of the STRATOS initiative[¶]

1 Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Biometry and Clinical Epidemiology, Charité - Universitätsmedizin Berlin, Berlin, Germany, **2** Berlin Institute of Health (BIH), Berlin, Germany, **3** School of Business and Economics, Applied Statistics, Humboldt-Universität zu Berlin, Berlin, Germany, **4** Section for Clinical Biometrics, Center for Medical Statistics, Informatics and Intelligent Systems, Medical University of Vienna, Vienna, Austria, **5** Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center—University of Freiburg, Freiburg, Germany, **6** Department of Biomedical Data Sciences, Leiden University Medical Center, Leiden, The Netherlands

[¶] Membership of the STRATOS initiative is provided in the Acknowledgments.

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STRATOS Publication Panel

Guidance on STRATOS publication policies: Version 9.0

December 16, 2019

This document outlines the proposed structure and activities of the STRATOS Publication Panel (PP). It should be noted that this document outlines *guidance* for publications in STRATOS, and it is *not* intended as a set of rigid regulations. Rather, we adopt the ICMJE guidelines for authorship to make it suitable for STRATOS publications (e.g. <http://journals.plos.org/plosmedicine/s/authorship#loc-group-authorship>)

The STRATOS Visualisation Panel (VP) offered to provide guidance for visualisations in STRATOS papers. For details see the addendum from the STRATOS Visualisation Panel.

Van Calster et al. *BMC Medicine* (2019) 17:230
<https://doi.org/10.1186/s12916-019-1466-7>

BMC Medicine

OPINION

Open Access

Calibration: the Achilles heel of predictive analytics

Ben Van Calster^{1,2,6*}, David J. McLernon^{3,6}, Maarten van Smeden^{2,4,6}, Laure Wynants^{1,5}, Ewout W. Steyerberg^{2,6}
On behalf of Topic Group 'Evaluating diagnostic tests and prediction models' of the STRATOS initiative⁶



Simulation panel


Comparison of statistical methods: How?

Simulation studies play a key role

LETTER TO THE EDITOR

Biometrical Journal →

On the necessity and design of studies comparing statistical methods

Anne-Laure Boulesteix¹ 

Harald Binder²

Michal Abrahamowicz³

Willi Sauerbrei²

for the Simulation Panel of the STRATOS Initiative

For the future: **ADEMP structure** (Morris et al., 2019) and **neutral comparison studies** will play a key role

Educational work

TG 2

PLOS ONE | <https://doi.org/10.1371/journal.pone.0241427> December 21, 2020

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Introduction to statistical simulations in health research

Anne-Laure Boulesteix ,¹ Rolf HH Groenwold,^{2,3} Michal Abrahamowicz,⁴ Harald Binder,⁵ Matthias Briel,^{6,7} Roman Hornung,¹ Tim P Morris ,⁸ Jörg Rahnenführer,⁹ Willi Sauerbrei,⁵ for the STRATOS Simulation Panel

SIGNIFICANCE | February 2020

Analysis in an imperfect world

TG 4

When we observe the world, we sometimes make mistakes. **Michael Wallace**, on behalf of the measurement error topic group of the STRATOS Initiative, explains the potentially severe consequences of this often overlooked issue, and how statistics can help bring us back – or at least a little closer – to the truth

Stratos - 2 November 2021

Websites of Topic Groups

Educational Work - TG4

Teaching about measurement error

Tutorials and tools for learning about handling measurement error in the statistical analysis

Toolkit for measurement error correction



- Toolkit for measurement error correction using repeated measurements
- Classical, systematic, heteroscedastic and differential measurement error
- Correction methods: regression calibration, moment reconstruction, multiple imputation
- Error in continuous exposures and categorized continuous exposures

MEM-Explorer



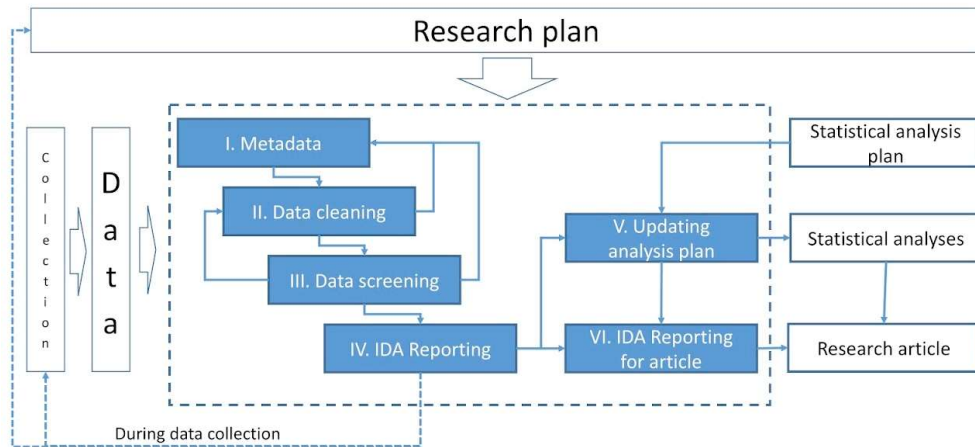
- User-friendly Shiny app for interactive exploration of the impacts of measurement error and misclassification
- Linear regression models
- Classical, linear and Berkson error in categorical and continuous covariates
- Based on the STRATOS guidance document on measurement error and misclassification of variables in observational epidemiology

Other tools

- Shiny app: "Impact of measurement error in a predictor" developed by Christian Gray, London School of Hygiene and Tropical Medicine ([Link](#))
- Shiny app: "Classical measurement error in linear, logit and Poisson regression" developed by Stefanie Muff, Norwegian University of Science and Technology ([Link](#))

Websites of Topic Groups

TG3



IDA consists of six elements

TG7

Causal Inference Literature

Below we link to books and papers in different fields of causal inference.

Causal inference tutorial by Topic Group 7

[Formulating causal questions and principled statistical answers](#)

Books

Hernán MA, Robins JM (2020). [Causal Inference: What If](#). Boca Raton: Chapman & Hall/CRC, feb20.pdf. Boca Raton: Chapman & Hall/CRC, forthcoming.

Imbens, G.W. and Rubin, D.B., 2015. [Causal inference in statistics, social, and biomedical sciences](#). Cambridge University Press.

Pearl, J., 2009. [Causality](#). Cambridge University Press.

Pearl, J., Glymour, M. and Jewell, N.P., 2016. [Causal inference in statistics: a primer](#). John Wiley & Sons.

Courses

TG 4

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Here you will find information and contents for upcoming and completed courses.

- [Causal Inference Course in Paris November 2020](#)
- [Causal Inference Course in Prague November 2020](#)
- [Causal Inference Course in Paris November 2019](#)
- Causal Inference Course in Paris November 2018
- [Annual meeting: Statistical Society of Canada June 3rd 2018](#)
- Causal Inference Course in Paris January 2018
- [ISCB Pre-conference course 2017 9/7](#)

TG 3+2

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Only fools rush in! – initial data analysis is required for developing and validating prediction models

Marianne Huebner¹, Georg Heinze², Mark Baillie³

¹Michigan State University, East Lansing, MI, USA; STRATOS-TG3
²Medical University of Vienna, Vienna, Austria; STRATOS-TG2
³Novartis Pharma AG, Basel, Switzerland; STRATOS-VP

Marianne Huebner, Georg Heinze and Mark Baillie
Regression without regrets

MEDICAL UNIVERSITY OF VIENNA MICHIGAN STATE UNIVERSITY NOVARTIS

Summary

- Data and data science becomes more and more important
- Answering questions empirically through data analyses often requires the use of complex methodology. It is important to develop suitable approaches; needs to be done by experts (Level 3)
- Experienced statisticians (Level 2) need to be supported by suitable guidance. There are (too) many approaches (some are useless) available and suitable comparisons are missing
- Better simulation studies are required to assess properties, compare approaches and derive evidence based guidance for practice.
- Suitable educational material is the key to improve analyses at a broad level
- For practically relevant topics we need greater emphasis on development of Level 1 and 2 guidance

Day 1: Topic group updates and plans

- **Session 1:** Chaired by Michal Abrahamowicz
- 2.00-2.20: Introduction by Willi (welcome, recent developments of STRATOS, overview of the meetings)
- 2.20-2.50: Presentation TG 5 Study Design (20 min + 10 min discussion)
- 2.50-3.20: Presentation TG3 Initial data analysis (20 min + 10 min discussion)
- 3.20-3.50: Presentation TG2 Selection of variables and functional forms for multivariable analysis (20 min + 10 min discussion)
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- *3.50-4.10: Break*
-
- **Session 2:** Chaired by Georg Heinze
- 4.10-4.40: Presentation TG8 Survival analysis (20 min + 10 min discussion)
- 4.40-5.10: Presentation TG7 Causal inference (20 min + 10 min discussion)
- 5.10-5.40: Presentation TG4 Measurement error (20 min + 10 min discussion)
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- *5.40-6.00: Break*
-
- **Session 3:** Chaired by Ruth Keogh
- 6.00-6.30: Presentation TG6 Evaluating diagnostic tests and prediction models (20 min + 10 min discussion)
- 6.30-7.00: Presentation TG9 High-dimensional data (20 min + 10 min discussion)
- 7.00-7.30: Presentation TG1 Missing data (20 min + 10 min discussion)

Day 2 (November 9, 2-7.30 pm UK time)

- 2.00-3.30: Presentations from panels (Simulation, Visualisation, Glossary, Knowledge Translation, Data sets, who else?)
- 3.30-4.00: *Break*
- 4.00-5.30: Presentations from STRATOS-wide projects
 - 1. p – values
 - SISAQOL
 - Paper in statistical and ML techniques
 - Series of videos and shiny apps
 - Parts of all projects were presented at various STRATOS sessions and some information is available on the website (see below)
- 5.30-6.00: *Break*
- 6.00-7.30: Discussion of cooperative projects in breakout sessions (ongoing and new projects; please let us know if you want to organize/join a breakout session)

Day 3 (December 14, TBC)

- Cooperative projects initiated on November 9 can be followed-up individually until December 14.
- On December 14 an update should be given on these projects. The program for Dec 14 will be determined accordingly.