

---

**Supplementary Table J2.** Number of journals referring to guidance in other external sources (not reporting guidelines). DOIs or URLs are in brackets when available.

---

External statistical guidance	Journals ( <i>n</i> )
Cummings & Rivara 2003 (10.1001/archpedi.157.4.321)	3
Cumming et al. 2007 (10.1083/jcb.200611141)	2
Olsen 2003 (10.1128/iai.71.12.6689-6692.2003)	2
Olsen 2014 (10.1128/iai.00811-13)	2
Richardson & Overbaugh 2005 (10.1128/jvi.79.2.669-676.2005)	2
Altman et al. 1983 (10.1136/bmj.286.6376.1489)	1

...

# Examples of guidance – sufficient details?

## **Bayesian statistics**

“For Bayesian analysis, [report] information on the choice of priors and Markov chain Monte Carlo settings.”

(Scientific Data)

## **Categorisation of continuous data**

“Categorizing of continuous data (e.g. into quartiles, quintiles) is discouraged. It leads to a loss of information, usually needs more complicated methods than for continuous data and introduces demarcations which are valid only for this particular study.”

(European Heart Journal)

## **Handling outliers**

“How were outliers defined and handled? Were they defined before the beginning of the study? Have you reported outliers that were excluded?...Data pre-processing steps such as transformations, re-coding, re-scaling, normalization, truncation, and handling of below detectable level readings and outliers should be fully described; any removal or modification of data values must be fully acknowledged and justified.”

(Science Translational Medicine)

## **Handling missing data**

“Report losses to observation, such as dropouts from a clinical trial or those lost to follow-up or unavailable in an observational study. Consider multiple imputation methods to impute missing data and include an assessment of whether data were missing at random. Approaches based on “last observation carried forward” should not be used.”

(JAMA Internal Medicine)

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

**Researchers**

## First in a Series of Papers for the Biometric Bulletin

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

**STRATOS**  
INITIATIVE

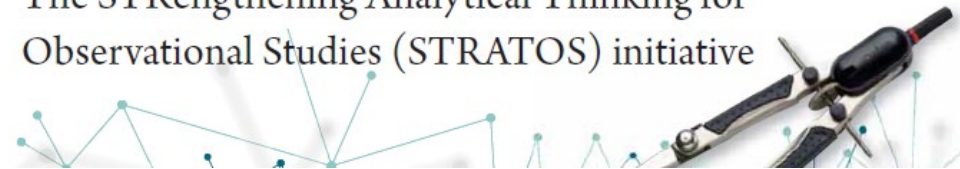
Willi Sauerbrei<sup>1</sup>, Marianne Huebner<sup>2</sup>, Gary S. Collins<sup>3</sup>, Katherine Lee<sup>4</sup>, Laurence Freedman<sup>5</sup>, Mitchell Gail<sup>6</sup>, Els Goetghebeur<sup>7</sup>, Joerg Rahnenfuehrer<sup>8</sup> and Michal Abrahamowicz<sup>9</sup> on behalf of the STRATOS initiative.

➔ 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<sup>1</sup>, Gary S. Collins<sup>2</sup>,  
Marianne Huebner<sup>3</sup>, Stephen D. Walter<sup>4</sup>,  
Suzanne M. Cadarette<sup>5</sup>, and  
Michal Abrahamowicz<sup>6</sup> 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

**since 3/2017: Series in Biometric Bulletin with 23 short overviews published, to proceed until 4/2024**

**2021 Memorandum of Understanding with ISCB**

**2019 Partner in the Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints (SISAQOL) project lead by EORTC (>40 stakeholders, including pharma and regulators)**

**As of 2023: >100 members (from 20 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	Victor Kipnis (US), Pam 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	Lisa McShane (US), Joerg Rahnenfuehrer (GER), Riccardo de Bin (NOR)

Chairs from 11 countries and 4 continents

# STRATOS Cross-cutting Panels

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

# Cooperations

STRATOS was influenced by reporting guidelines, for more than a decade coordinated by the Enhancing the QUALity and Transparency Of health Research (**EQUATOR**) network and is an intellectual child of **ISCB** (Sauerbrei, Abrahamowicz, le Cessie, 2016).

*The STRATOS Initiative - Motivation, Mission, Structure and Main Aims*

From Willi Sauerbrei, Michal Abrahamowicz and Saskia Le Cessie, for the STRATOS initiative

ISCB News #62

International Biometric Society (**IBS**)



# Biometric Bulletin – STRATOS initiative has a series with short articles since 3/2017

## First in a Series of Papers for the Biometric Bulletin

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

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

Biometric Bulletin 2017(3)

Each author represents one TG

Sept 2017:

Dec 2017 – March 2020:

June 2020 – Dec 2020:

Since March 2021:

introduction of the initiative

9 TG articles

Panels Simulation, Visualisation and Glossary  
updated articles for several TGs, 5y update of  
STRATOS, Data quality, Summary of level 1  
material, Open Science

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

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

Biometric Bulletin 2022(3)

Authors: members of ExCom and chairs of  
the Publication Panel

Agreement with the Editor: article series until Dec. 2024

# Program

- Talks of TGs 1, 2, 3, 9, Simulation Panel
- For other TGs - short summaries

## ***Initial data analysis is a necessary step in the research workflow***

Huebner M, Schmidt CO, Lusa L for TG3

## ***Level 1 guidance on conducting and reporting sensitivity analyses for missing data***

Lee K, Mainzer R, Carpenter J for TG1

## ***Statistical analysis of high-dimensional biomedical data: A gentle introduction to analytical goals, common approaches and challenges***

Rahnenfuehrer J, Ambrogi F, De Bin R, McShane L for TG9

## ***Ongoing research towards state-of-the-art in variable and functional form selection for statistical models***

Heinze G, Perperoglou A, Sauerbrei W for TG2

## ***Data-Driven Simulations to Assess the Impact of Data Imperfections in Real-World Time-to-Event Analyses***

Abrahamowicz M, Beauchamp M-E, Boulesteix A-L, Morris TP, Sauerbrei W, Kaufman JS for the STRATOS Simulation Panel

## ***Methodological research needs to improve – getting involved to increase future contributions of the STRATOS initiative***

Sauerbrei W, Abrahamowicz M, Le Cessie S, Huebner M, Keogh R, Carpenter J for the STRATOS initiative

# TG4 – Measurement error and misclassification

## Epidemiologic analyses with error-prone exposures: **review of current practice** and recommendations

Shaw PA, Deffner V, Keogh R, Tooze JA, Dodd KW, Küchenhoff H, Kipnis V, Freedman LS on behalf of Measurement Error and Misclassification Topic Group (TG4) of the STRATOS Initiative (2018)  
*Annals of epidemiology 28 (11): 821–828.*

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

Ruth H. Keogh<sup>1</sup> | Pamela A. Shaw<sup>2</sup> | Paul Gustafson<sup>3</sup> | Raymond J. Carroll<sup>4,5</sup> | Veronika Deffner<sup>6</sup> | Kevin W. Dodd<sup>7</sup> | Helmut Küchenhoff<sup>8</sup> | Janet A. Tooze<sup>9</sup> | Michael P. Wallace<sup>10</sup> | Victor Kipnis<sup>11</sup> | Laurence S. Freedman<sup>12,13</sup>

Statistics in Medicine 2020

## Analysis in an imperfect world

Michael Wallace

Significance 2020

## STRATOS **guidance** document on measurement error and misclassification of variables in observational epidemiology: Part 2—More complex methods of adjustment and **advanced topics**


Pamela A. Shaw<sup>1</sup> | Paul Gustafson<sup>2</sup> | Raymond J. Carroll<sup>3,4</sup> | Veronika Deffner<sup>5</sup> | Kevin W. Dodd<sup>6</sup> | Ruth H. Keogh<sup>7</sup> | Victor Kipnis<sup>6</sup> | Janet A. Tooze<sup>8</sup> | Michael P. Wallace<sup>9</sup> | Helmut Küchenhoff<sup>5</sup> | Laurence S. Freedman<sup>10,11</sup>

Statistics in Medicine 2020

# TG5 – Study design

## Design choices for observational studies of the effect of exposure on disease incidence

---

Mitchell H Gail ,<sup>1</sup> Douglas G Altman,<sup>2</sup> Suzanne M Cadarette,<sup>3</sup> Gary Collins,<sup>4</sup>  
Stephen JW Evans,<sup>5</sup> Peggy Sekula ,<sup>6</sup> Elizabeth Williamson,<sup>7</sup> Mark Woodward<sup>8</sup>

BMJ open 2019

### Biometric Bulletin

Introducing the Study Design Topic Group (TG5)

Mitchell H. Gail and Suzanne Cadarette, 2/2019

# TG6 – Evaluating diagnostic tests and prediction models

Flawed **external validation** study of the ADNEX model to diagnose ovarian cancer

B Van Calster,<sup>a,b,\*1</sup> EW Steyerberg,<sup>b,1</sup> T Bourne,<sup>a,c,d</sup> D Timmerman,<sup>a,c</sup> GS Collins,<sup>e,1</sup> and on behalf of TG6 of the STRATOS initiative

Gynecological Oncology Reports 2016

**Calibration:** the Achilles heel of predictive analytics

Ben Van Calster<sup>1,2,6\*</sup>, David J. McLernon<sup>3,6</sup>, Maarten van Smeden<sup>2,4,6</sup>, Laure Wynants<sup>1,5</sup>, Ewout W. Steyerberg<sup>2,6</sup>  
On behalf of Topic Group 'Evaluating diagnostic tests and prediction models' of the STRATOS initiative<sup>6</sup>

BMC Medicine 2019

## Biometric Bulletin

Introducing the Topic Group on Evaluating Diagnostic Tests and Prediction Models (TG6)

Ben Van Calster, Ewout Steyerberg, 1/2020

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

Ewout W Steyerberg, Ben Van Calster, 2/2022

Three myths about **risk thresholds** for prediction models

Laure Wynants<sup>1,2\*</sup>, Maarten van Smeden<sup>3,4</sup>, David J. McLernon<sup>5</sup>, Dirk Timmerman<sup>1,6</sup>, Ewout W. Steyerberg<sup>4</sup>, Ben Van Calster<sup>1,4</sup> and on behalf of the Topic Group 'Evaluating diagnostic tests and prediction models' of the STRATOS initiative

BMC Medicine 2019

**Validation of prediction models in the presence of competing risks:** a guide through modern methods

Nan van Geloven,<sup>1</sup> Daniele Giardiello,<sup>1,2</sup> Edouard F Bonneville,<sup>1</sup> Lucy Teece,<sup>3</sup> Chava L Ramspek,<sup>4</sup> Maarten van Smeden,<sup>5</sup> Kym I E Snell,<sup>3</sup> Ben van Calster,<sup>1,6</sup> Maja Pohar-Perme,<sup>7</sup> Richard D Riley,<sup>3</sup> Hein Putter,<sup>1</sup> Ewout Steyerberg,<sup>1,8</sup> on behalf of the STRATOS initiative

BMJ 2022

Assessing Performance and Clinical **Usefulness** in Prediction Models With Survival Outcomes: Practical Guidance for **Cox** Proportional Hazards Models


David J. McLernon, PhD; Daniele Giardiello, MSc; Ben Van Calster, PhD; Laure Wynants, PhD; Nan van Geloven, PhD; Maarten van Smeden, PhD; Terry Therneau, PhD; and Ewout W. Steyerberg, PhD; for topic groups 6 and 8 of the STRATOS Initiative\*


Annals of Internal Medicine 2023



# TG7 – Causal inference

## Formulating causal questions and principled statistical answers

Els Goetghebeur<sup>1,2</sup>  | Saskia le Cessie<sup>3</sup> | Bianca De Stavola<sup>4</sup> |

Erica EM Moodie<sup>5</sup>  | Ingeborg Waernbaum<sup>6</sup> | “on behalf of” the topic group Causal

Inference (TG7) of the STRATOS initiative

Statistics in Medicine 2020

### Biometric Bulletin

Introducing the Causal Inference Topic Group (TG7)

Waernbaum I, De Stavola B, Moodie E, le Cessie S, Goetghebeur E on behalf of STRATOS TG7, 4/2018

Some members are very active in the





**Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints (SISAQOL) consortium**

talks by Saskia le Cessie and Els Goetghebeur



# TG8 – Survival analysis

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

Per Kragh Andersen<sup>1</sup> | Maja Pohar Perme<sup>2</sup> | Hans C. van Houwelingen<sup>3</sup> | Richard J. Cook<sup>4</sup> | Pierre Joly<sup>5</sup> | Torben Martinussen<sup>1</sup> | Jeremy M. G. Taylor<sup>6</sup> | Michal Abrahamowicz<sup>7</sup> | Terry M. Therneau<sup>8</sup>

Statistics in Medicine 2020

Joint project with TG6

### *Biometric Bulletin*

Introducing the Survival Analysis Topic Group (TG8)

Andersen PK, Abrahamowicz M, Therneau TM on behalf of STRATOS TG8, 3/2019

## Biometric Bulletin - short overview from panels

### Introducing the Simulation Panel

Boulesteix AL, Morris T, Sauerbrei W, Abrahamowicz M  
on behalf of the Simulation Panel, 2/2020

### Introducing the Visualisation Panel (SP)

Baillie M, Vandemeulebroecke M on behalf of the  
Visualisation Panel, 3/2020

### Glossary Panel (GP) – Defining common meaning for statistical terms

Boeker M, Tippmann P, Day S, Huebner M, Sauerbrei  
W on behalf of the Glossary Panel, 4/2020

### Introducing the Open Science Panel

Hoffmann S, Luijken K, Sauerbrei W, Shaw P,  
Boulesteix AL, 2/2023

## Biometric Bulletin - further papers

### On the importance of Data Quality Assessments and Initial Data Analysis

Schmidt C.O., Heinze G, Lusa L and Huebner M for  
the STRATOS initiative 4/2022

### Guidance for analysts with limited statistical knowledge

Heinze G, Boulesteix AL, Dunkler D, Gail M, Lee KJ,  
van Calster B, Wallace M, Sauerbrei W, 1/2023

# What have we learned?

- Improvements needed
- Next steps – discussion at the end  
(based on last week's discussion at ISCB)

# Interested to become a member?

Visit website and send an email:

<https://stratos-initiative.org/de/contact>

Please send us some information about your professional background, statistical expertise and your interest to join STRATOS. Please send the completed [contact form and a two page CV](#) including a list of max. 10 publications from the last 10 years via email to: [contact@stratos-initiative.org](mailto:contact@stratos-initiative.org).

TG and panel chairs will decide about your application

# 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, but which?) 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