STRATOS initiative – progress with guidance in three topics in observational research

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http://stratos-initiative.org/

Launch of the STRATOS initiative 2013

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

Situation in 2013:

- Funding for a guidance initiative was (and still is) a problem
- Funders and journals prioritize novelty over incremental replication research
- 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
- ….

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Why we need guidance for the design and analysis of observational studies

"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**

- **Researchers have an obligation to do high quality research**
  - Scientific, ethical, financial considerations

- **These issues are most obvious for RCTs but apply also to observational studies**

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

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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

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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 three 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 are ignored in practical statistical analyses

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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

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Improvement

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 **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**

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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** with different levels of statistical expertise.

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

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.

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What about statistical guidance from journals?

## Statistical Guidance to Authors at Top-Ranked Journals across Scientific Disciplines

Tom E. Hardwicke[a,b], Maia Salholz-Hillel[c], Mario Malički[d], Dénes Szűcs[e], Theiss Bendixen[f], and John P. A. Ioannidis[d,g,h]

Statistical guidance at 15 journals (top ranked by IF) in each of 22 scientific disciplines
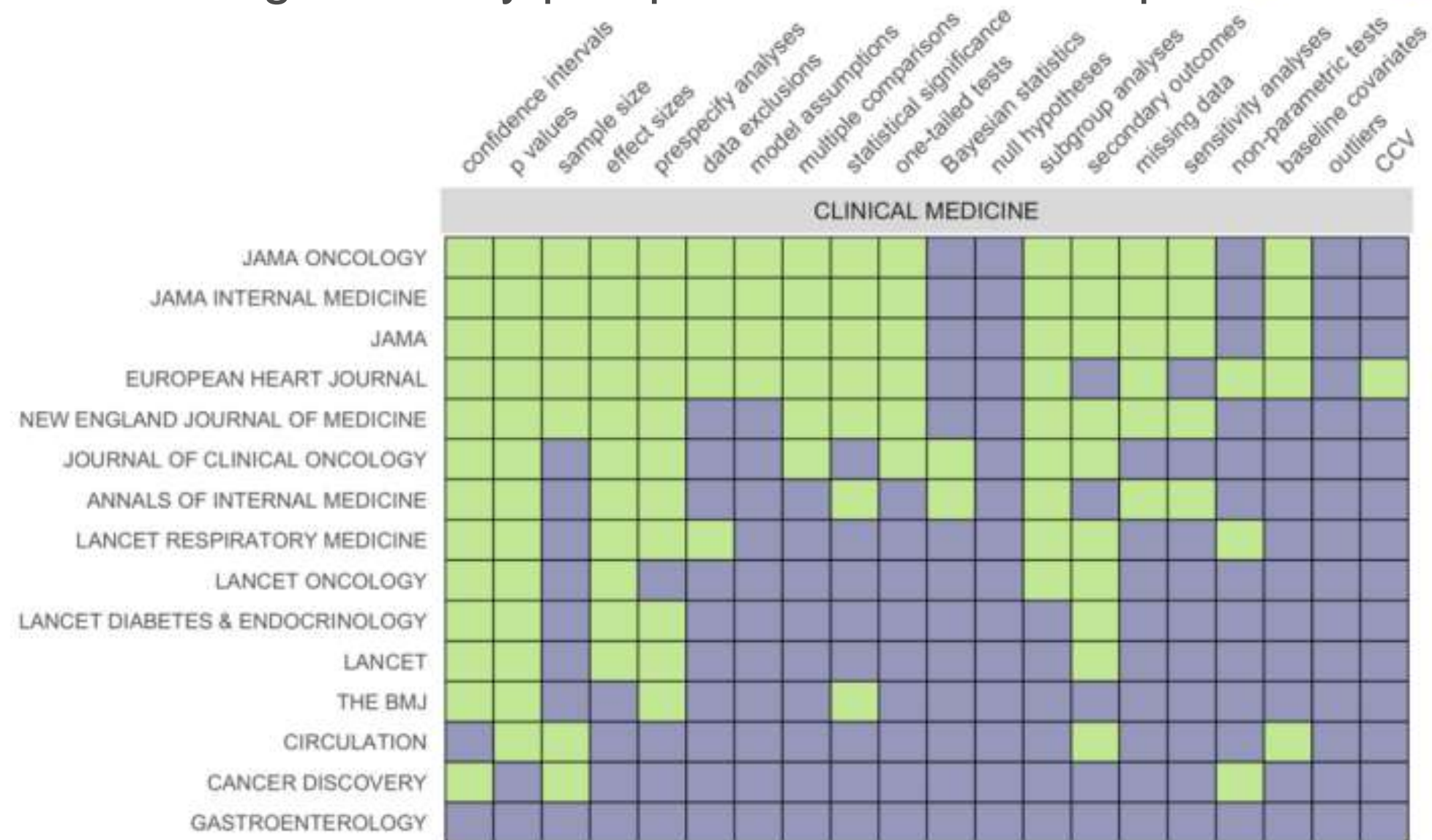n = 330 journals

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Frequency of journals offering some statistical guidance (circles) or having a dedicated statistical guidance section(diamonds)
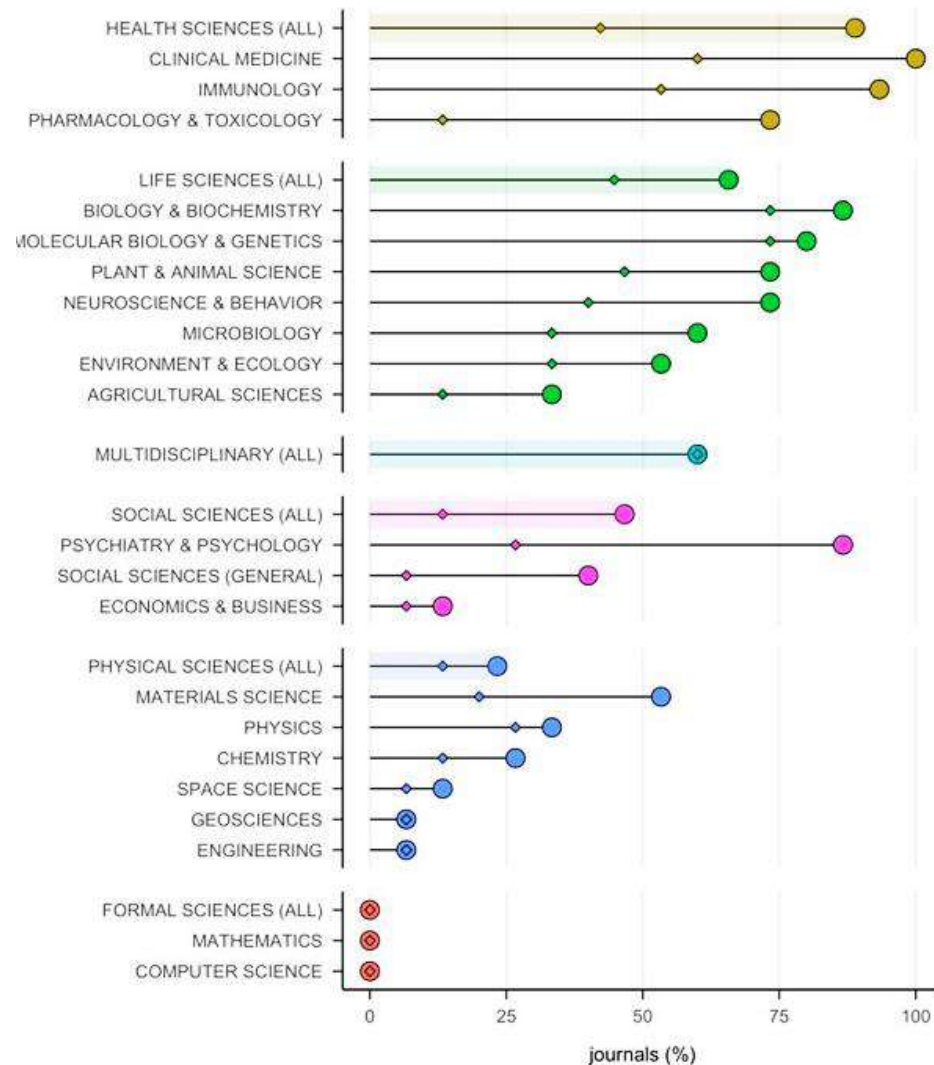
Frequency of journals offering guidance on 20 prespecified statistical topics
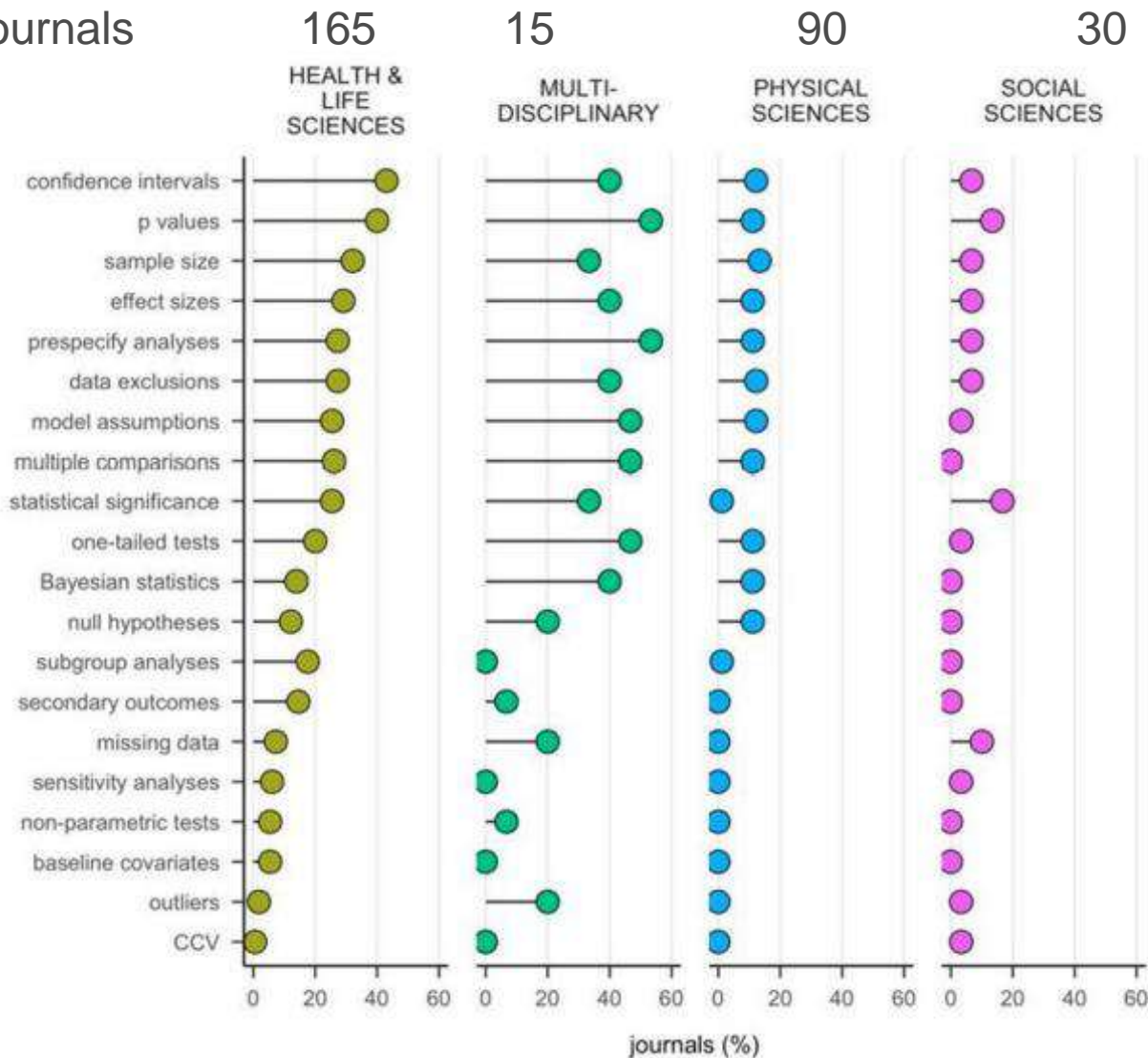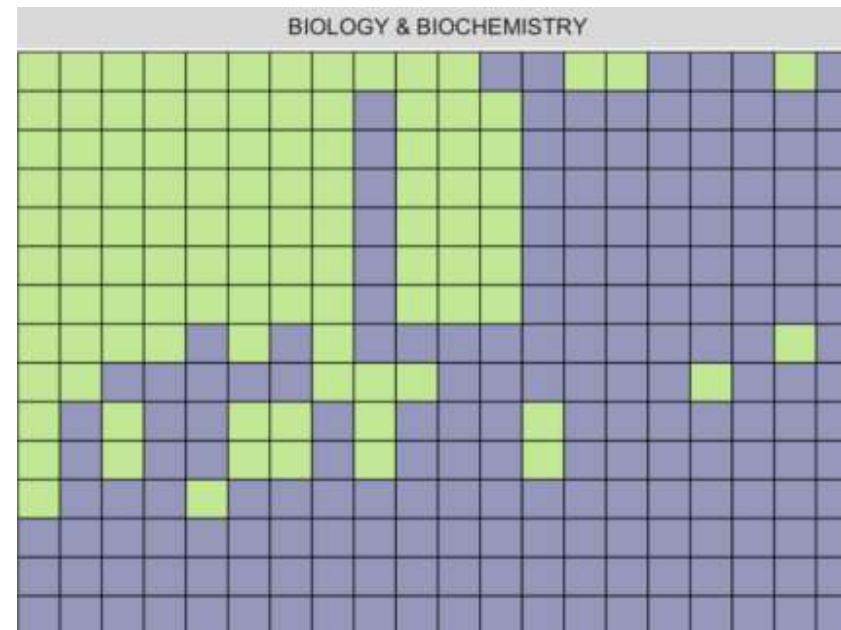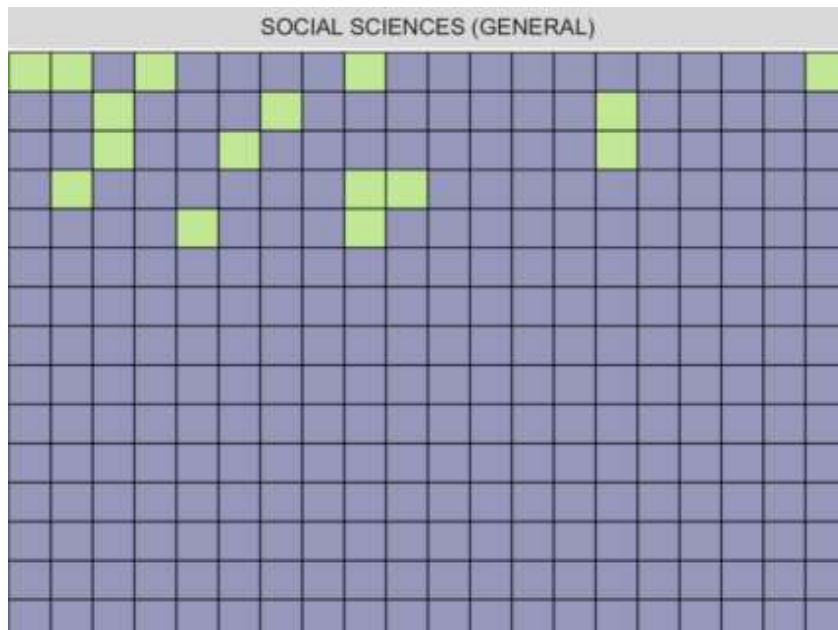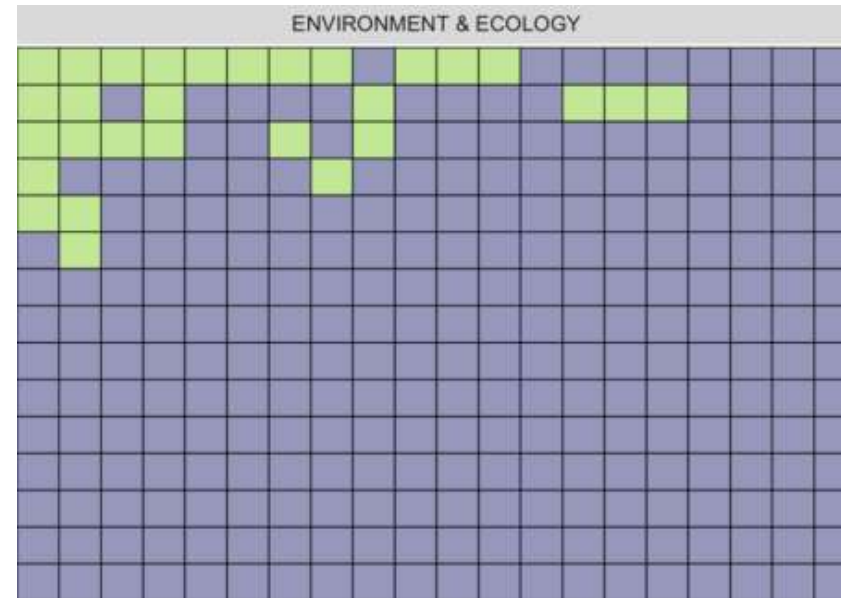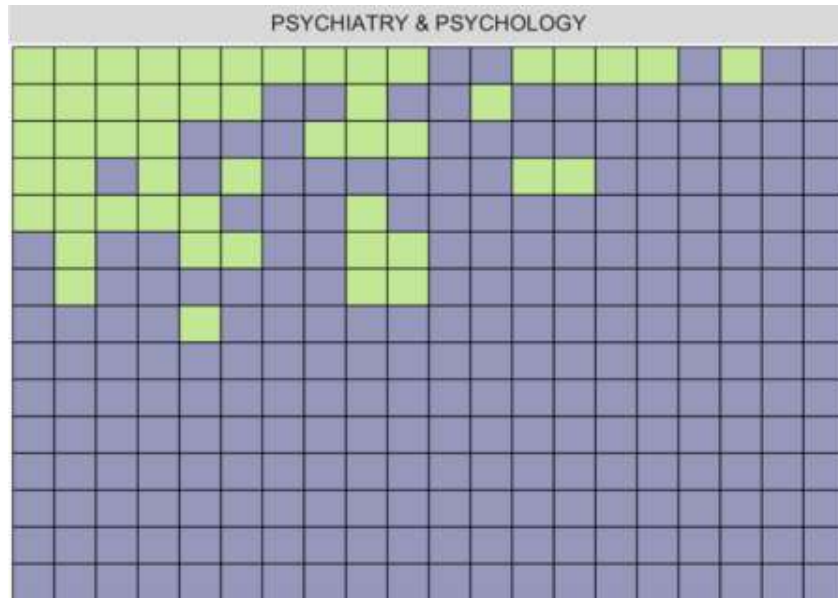
Mentioning of twenty prespecified statistical topics

CCV categorizing continuous variables

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Statistical guidance – mainly from reporting guidelines!

Supplementary Material J. External sources of statistical guidance.

Supplementary Table J1. Number of journals referring to specific reporting guidelines.

Reporting guideline	Journals (n)
Consolidated Standards of Reporting Trials (CONSORT)	95
Animal Research: Reporting of In Vivo Experiments (ARRIVE)	80
Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)	47
REporting recommendations for tumour MARKer prognostic studies (REMARK)	40
The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)	39
Standards for Reporting Diagnostic accuracy studies (STARD)	36
International Committee of Medical Journal Editors (ICMJE) Recommendations	21
Consolidated Health Economic Evaluation Reporting Standards (CHEERS)	18
STrengthening the REporting of Genetic Association Studies (STREGA)	16
National Institutes of Health (NIH) Recommendations	14
Meta-analysis Of Observational Studies in Epidemiology (MOOSE)	12
CAse REport (CARE)	11
Minimum Information About a Microarray Experiment (MIAME)	11
Consolidated criteria for reporting qualitative research (COREQ)	9
Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)	9
Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD)	9

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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)

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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
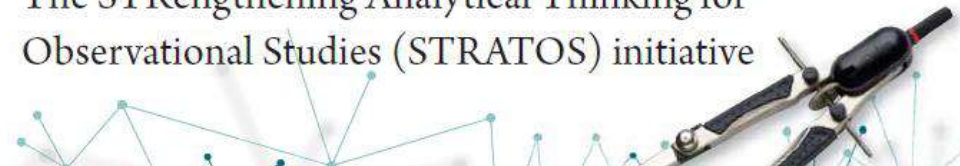
STRATOS INITIATIVE

Willi Sauerbrei[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

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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

2024: General Meeting, Lorentz Center in Leiden, Netherlands

… 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, RSS, SER, CEN, DAGStat

since 3/2017: Series in Biometric Bulletin with 30 short overviews published

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 2025: >100 members from 20 countries on 5 continents

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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 (SLO), Carsten Oliver Schmidt (GER)
4	**Measurement error and misclassification**	Paul Gustafson (CAN), 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**	Federico Ambrogi (ITA), Lisa McShane (US), Riccardo de Bin (NOR)

Chairs from 11 countries and 4 continents

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STRATOS Cross-cutting Panels

Panel		Chairs
MP	Membership	James Carpenter (UK), Willi Sauerbrei (GER)
PP	Publications	Mitchell Gail (US), Lisa McShane (US),Pam Shaw (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)
DP	Data Sets	Georg Heinze (AUT), Carsten Schmidt (GER), 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)

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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 inititative 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[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.

Biometric Bulletin 2017(3)

Each author represents one TG

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

Biometric Bulletin 2022(3)

Authors: members of ExCom and chairs of the Publication Panel

Introducing the Visualisation Panel (SP)

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

Introducing the Open Science Panel

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

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

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Summary: Guidance is needed, research is required!!

- 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

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