Experience and progress with developing guidance for the analysis of key topics in observational research

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for the STRATOS initiative

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http://stratos-initiative.org/

Launch of the STRATOS initiative 2013

The STRATOS initative was launched at a half-day Mini-Symposium on the last day of the ISCB2013 meeting in Munich, in August 2013.

There were three general talks by Willi Sauerbrei, Doug Altman and James Carpenter. James also introduced a route map by using TG1 (missing data) as an example.

In addition, there were specific talks discussing key issues of TG2 through TG7:

- TG2 Selection of variables and functional form, Michal Abrahamowicz
- TG3 Descriptive and initial data analysis, Saskia Le Cessie
- TG4 Measurement error, Helmut Küchenhoff
- TG5 Design, Doug Altman
- TG6 Evaluating diagnostic tests and prediction models, Petra Macaskill
- TG7 Causal Inference, Els Goetghebeur

TG8 Survival analysis and TG9 High-dimensional data started in 2015

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

Guidelines for observational studies

- **Several guidelines have outlined the essential elements of reporting observational studies of different designs (see equator-network.org)**
  - STROBE (epidemiological cohort, case-control, cross-sect) 2007
    - Extensions STREGA, STROBE-ME,…
  - REMARK (tumour marker prognostic studies) 2005
  - TRIPOD (multivariable prediction models) 2015
  - GRIPS (genetic risk prediction studies) 2011

- **There is a clear need for companion guidelines for research conduct**
  - Would be of particular benefit to those without formal training or limited experience

What should be our scope?

- **Observational studies cover a wide variety of research questions**
  - Effects of interventions
  - Incidence, Aetiology, Prognosis, Diagnosis, …

  … and study designs
  - Cohort, Case-control, Cross-sectional
  - Interrupted time series, Ecological, …

  … and data sources
  - Prospective planned studies
  - Routinely collected data
- **Guidance can be generic (e.g. missing data) or specific (e.g. design of case-control 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

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

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 two decades ago
- Machine learning approaches may be interesting alternatives to more traditional 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

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

Improvement

At least **two tasks** are essential

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

Aims of the initiative

- **Provide guidance documents** for highly relevant issues

- 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**

- For the **start** we will concentrate on **state-of-the-art** documents for experienced statisticians **(level 2)**
- Help to identify questions **requiring more primary research**

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

Short term aims

- For a small number of **highly relevant topics** we will try to assess the current **state of practice** and identify current documents which try provide some guidance
- Try to find **‘agreement’ what to recommend** within each of the three levels mentioned
- Documents have to be **understood** and at least broadly **accepted**
- **Positive examples** from the current literature will help to reach the latter goal

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: First 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.

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.

What about statistical guidance from journals?

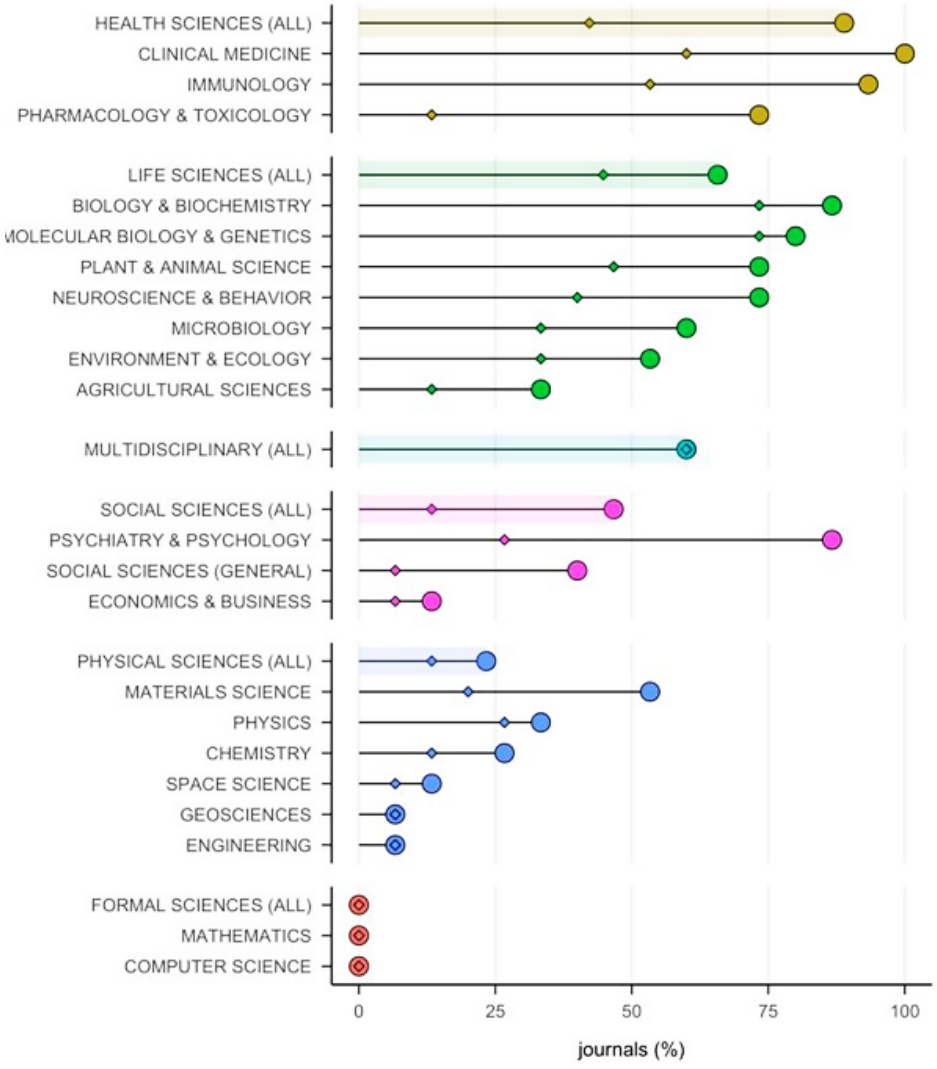
Statistical Guidance to Authors at Top-Ranked Journals across Scientific Disciplines

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]

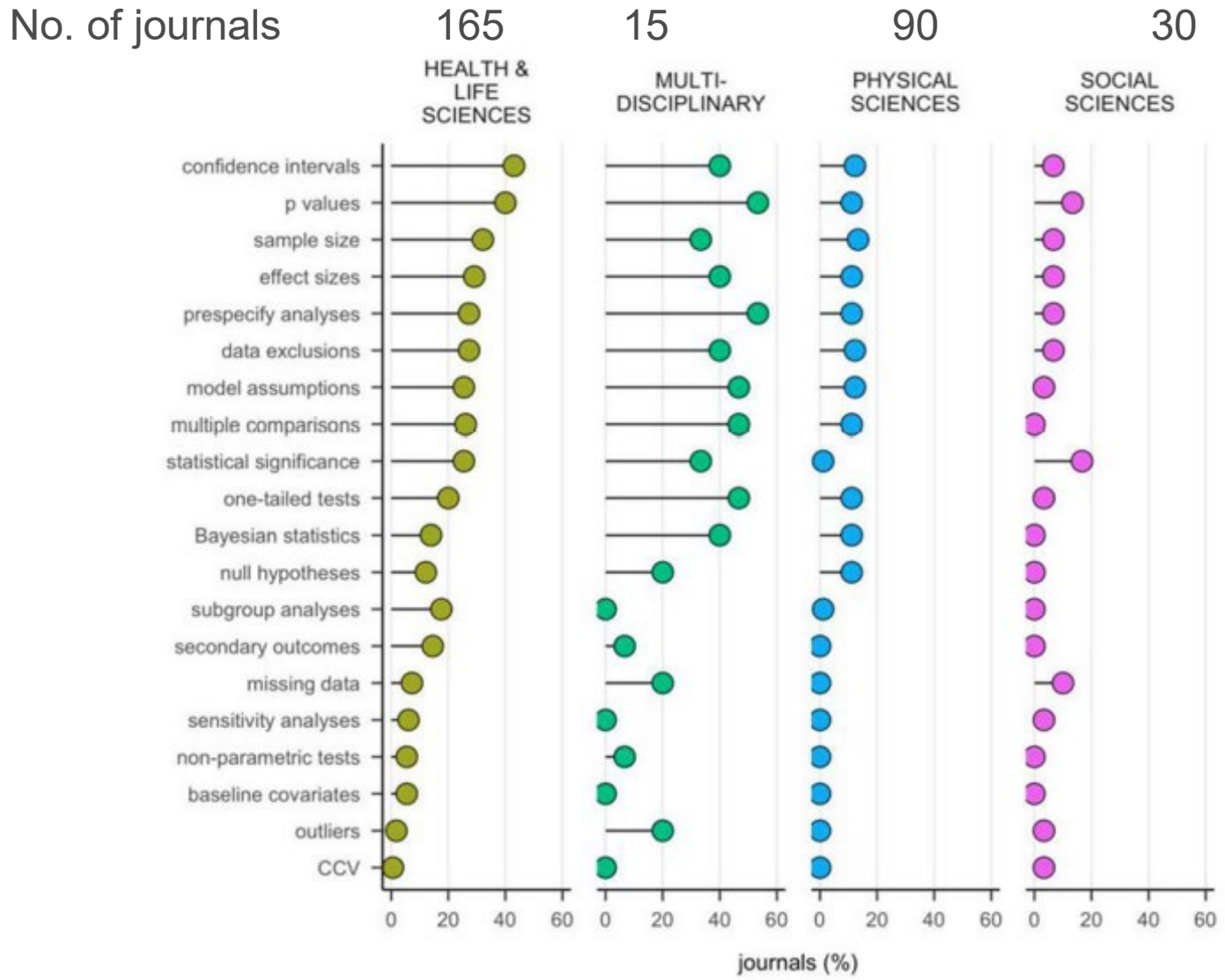
THE AMERICAN STATISTICIAN
2022, VOL. 00, NO. 0, 1–9: General
https://doi.org/10.1080/00031305.2022.2143897

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

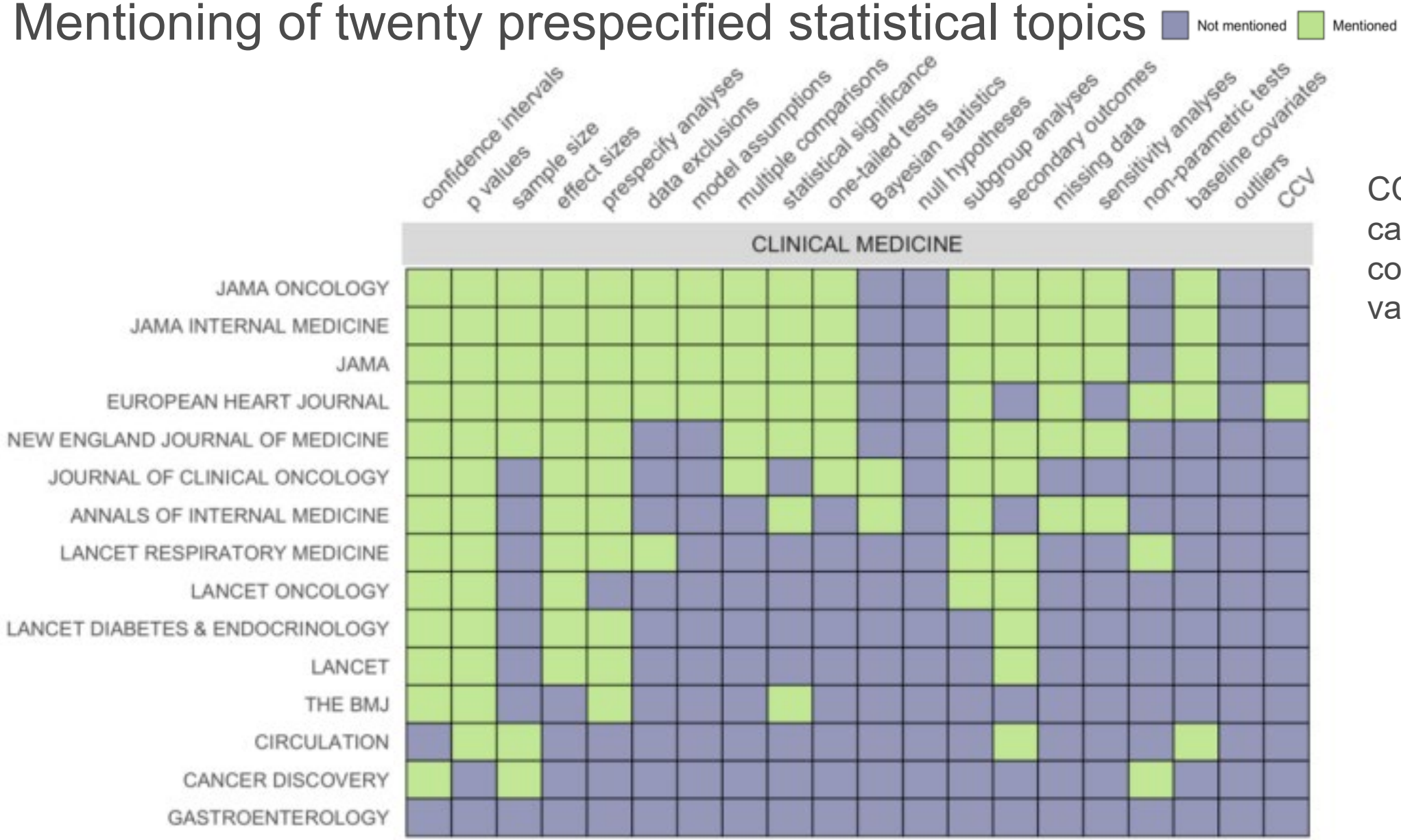
Frequency of journals offering some statistical guidance (circles) or having a dedicated statistical guidance section(diamonds)



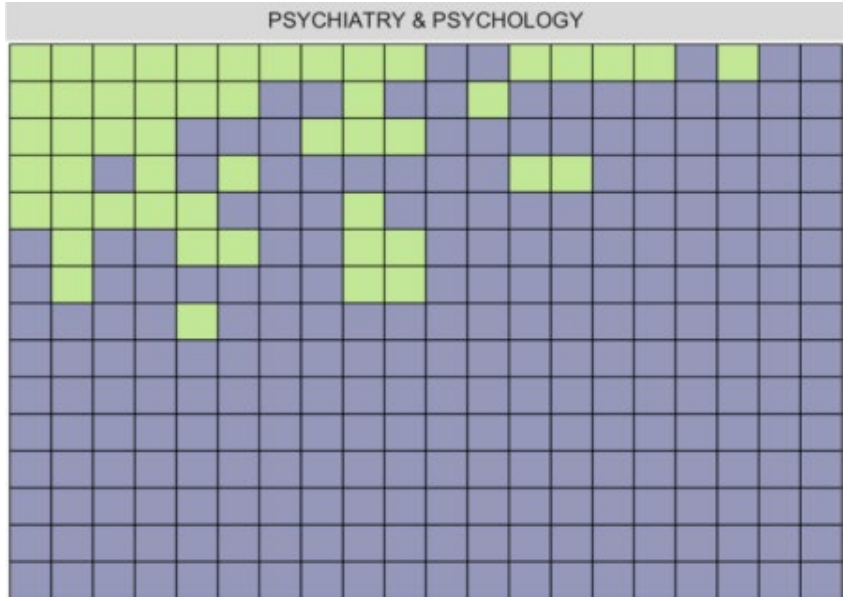
Frequency of journals offering guidance on 20 prespecified statistical topics

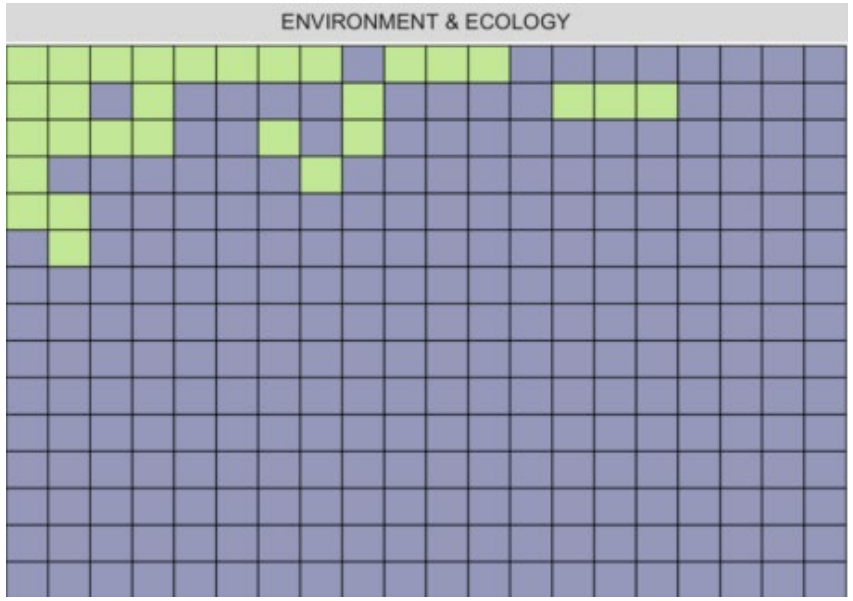


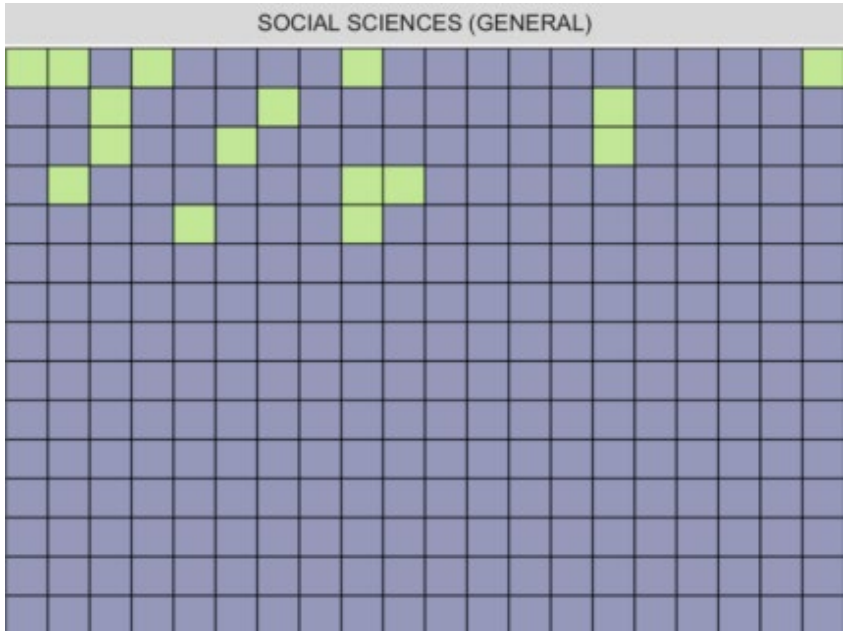
Mentioning of twenty prespecified statistical topics

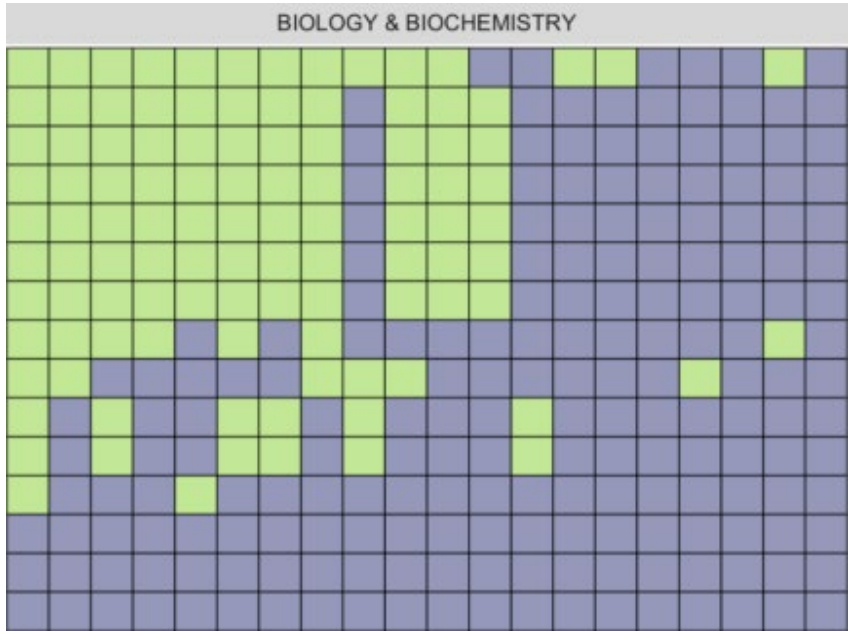


CCV categorizing continuous variables


PSYCHIATRY & PSYCHOLOGY


ENVIRONMENT & ECOLOGY


SOCIAL SCIENCES (GENERAL)


BIOLOGY & BIOCHEMISTRY

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