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

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CSM

Obligation

"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**

Observational studies

- **Most published research articles (towards 90%) report observational studies**
- **Evidence from numerous reviews of publications shows that design, analysis and reporting are often substandard**

BMJ

LONDON, SATURDAY 29 JANUARY 1994

The scandal of poor medical research

We need less research, better research, and research done for the right reasons

Ecological studies

Review of 125 articles in 6 major epidemiology journals [Dufault & Klar, *Am J Epidemiol* 2011]

- 18% prespecification of ecologic units
- in 23 of 36 papers, the investigators failed to adjust covariates for age or sex when the outcomes had been standardized for these potential confounders
- Investigators did not sufficiently inform the reader about the possibility of crosslevel bias; in 55 articles (44%), authors tempered their results in some fashion, whereas in 61 (49%) they did not

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EDITORIAL

Post hoc decision-making in observational epidemiology—is there need for better research standards?

Mika Kivimäki,[1]* Archana Singh-Manoux,[1,2] Jane E Ferrie[1,3] and G David Batty[1,4]

Why we need guidelines for study methods

- **Frequent use of weak or incorrect methods**
- **Most analyses are done by non-experts**
- **Rapid development of new methods**
- **Issues are common across wide areas of application**

- **More controversial than reporting guidelines**
- **Not saying how research *should* be done**
- **Rather:**
  - Issues to consider (options, with advantages and disadvantages)
  - Some things to avoid

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PLoS MEDICINE

Guidelines and Guidance

Guidance for Developers of Health Research Reporting Guidelines

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"Developing a reporting guideline is complex and time consuming, so a compelling rationale is needed. Most reporting guidelines have been developed because researchers are convinced of the need to improve the quality of reporting of a certain type of health research. For some study aspects there may be direct evidence that inadequate reporting is associated with biased reports or harmful consequences. At this early stage, the executive group needs to set out clearly and explicitly their objectives and consider the scope of recommendations."

Moher et al *PLoS Med* 2010

"Developing a conduct guideline is complex and time consuming, so a compelling rationale is needed. Most conduct guidelines have been developed because researchers are convinced of the need to improve the quality of conduct of a certain type of health research. For some study aspects there may be direct evidence that inadequate conduct is associated with biased results or harmful consequences. At this early stage, the executive group needs to set out clearly and explicitly their objectives and consider the scope of recommendations."

Moher et al *PLoS Med* 2010

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)
    - Extensions STREGA, STROBE-ME,…
  - REMARK (tumour marker prognostic studies)
  - TRIPOD (multivariable prediction models)
  - GRIPS (genetic risk prediction studies)

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

The example of SPIRIT

SPIRIT 2013 Statement: Defining Standard Protocol Items for Clinical Trials

Ann Intern Med. 2013;158:200-207.

An-Wen Chan, MD, DPhil; Jennifer M. Tetzlaff, MSc; Douglas G. Altman, DSc; Andreas Laupacis, MD; Peter C. Gøtzsche, MD, DrMedSci; Karmela Krleža-Jerić, MD, DSc; Asbjørn Hróbjartsson, PhD; Howard Mann, MD; Kay Dickersin, PhD; Jesse A. Berlin, ScD; Caroline J. Doré, BSc; Wendy R. Parulekar, MD; William S.M. Summerskill, MBBS; Trish Groves, MBBS; Kenneth F. Schulz, PhD; Harold C. Sox, MD; Frank W. Rockhold, PhD; Drummond Rennie, MD; and David Moher, PhD

SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials

An-Wen Chan,[1] Jennifer M Tetzlaff,[2] Peter C Gøtzsche,[3] Douglas G Altman,[4] Howard Mann,[5] Jesse A Berlin,[6] Kay Dickersin,[7] Asbjørn Hróbjartsson,[3] Kenneth F Schulz,[8] Wendy R Parulekar,[9] Karmela Krleža-Jeric,[10] Andreas Laupacis,[11] David Moher[2 10]

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equator network

SPIRIT

Preliminary activities

- Two systematic reviews were performed:
  - to identify existing protocol guidelines
  - To find empirical evidence supporting the importance of specific (potential) checklist items
- Delphi consensus survey (n=96)
- 2 face-to face consensus meetings

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)**