

Sample size calculations and data analyses: Comparison of publications with protocols

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Background

- Discrepancies between protocols and publications
 - Primary outcomes
 - Allocation concealment
 - Blinding
 - Handling of adverse events
 - Subgroup analyses

Hróbjartsson A et al (submitted); Al-Marzouki S et al, *Lancet* 2008;
Chan AW et al, *JAMA* 2004; Scharf O, *J Clin Oncol* 2006; Pildal J et al, *BMJ* 2005;
Soares HP et al, *BMJ* 2004.

Discrepancies in power calculations & statistical analyses

- 70 published, parallel group, randomized trials approved in 1994-95 in Denmark
 - Comparison of protocols with publications
 - Duplicate data extraction
 - Power calculation parameters
 - Statistical methods

AW Chan et al, BMJ, in press

Discrepancies in power calculations

- 53% of trials had at least 1 discrepancy
 - Outcome measure
 - Clinically relevant effect size or event rates
 - Standard deviation
 - Alpha
 - Power
 - Sample size estimate

AW Chan et al, BMJ, in press

Examples of discrepancies

■ Changed delta

- Outcome: Disease progression or death rate
- Protocol: Delta 10%, Event rates unspecified
- Publication: Delta 6%, Event rates 16% and 10%

■ Changed power

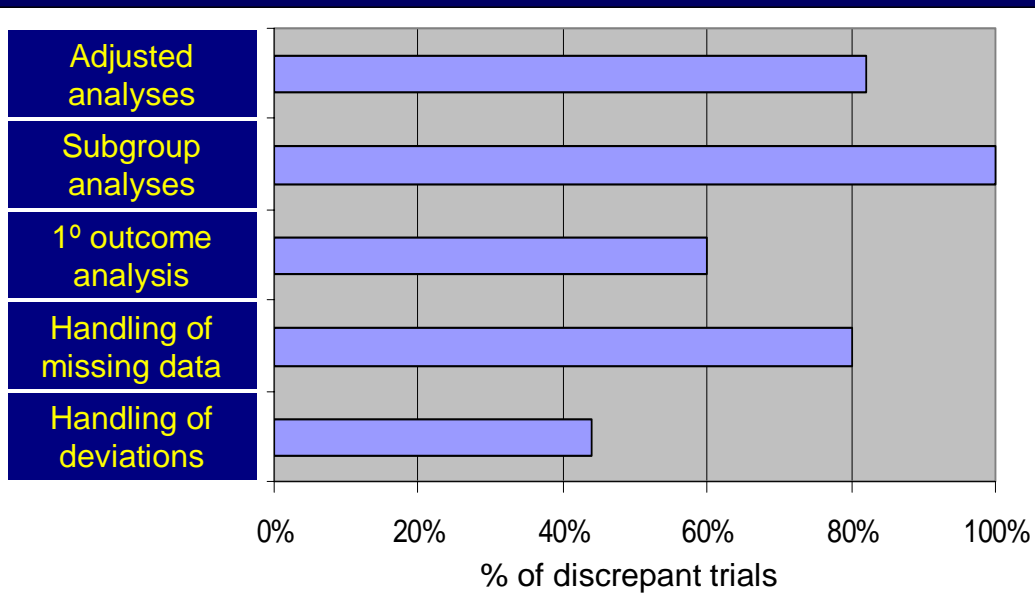
- Outcome: Survival without disease progression
- Protocol: 90%
- Publication: 80%

■ Changed sample size estimate

- Outcome: Thromboembolic complication rate
- Protocol: 2200
- Publication: 1500

AW Chan et al, BMJ, in press

Discrepancies in statistical analyses



Examples of discrepancies

- **New subgroups added to publication**
 - Outcome: Time to progression or death
 - Protocol: Baseline disease severity
 - Publication: Duration of prior therapy, type of prior therapy, blood count, disease severity
- **Omitted covariates for adjusted analysis in publication**
 - Outcome: Neurologic score at 6 months
 - Protocol: Baseline neurologic score, pupil reaction, age, CT scan classification, shock, hemorrhage
 - Publication: No adjusted analysis reported

AW Chan et al, BMJ, in press

Interim analyses & DSMB

Interim analyses

- Pre-specified in 13 protocols
 - 38% (5/13) publications
- Reported in 2 publications whose protocols explicitly stated that none would be performed

DSMB

- Described in 12 protocols
 - 42% (5/12) publications

AW Chan et al, BMJ, in press

Conclusions

- Power calculations and analyses differ between protocols and publications
- Unclear reasons
- Access to full protocols and regulatory agency submissions would improve transparency

Collaborators

University of Oxford

- Doug Altman

Nordic Cochrane Centre

- Peter Gøtzsche
- Asbjørn Hróbjartsson
- Karsten Jørgensen