Evidenzbasierte Studienplanung und Berichterstattung (CONSORT Statement)

PD Dr. Joerg Meerpohl

Institut für Evidenz in der Medizin
(für Cochrane Deutschland Stiftung)
Universitätsklinikum Freiburg

Dank an Anette Bluemle, IfEM

89. Jahresversammlung
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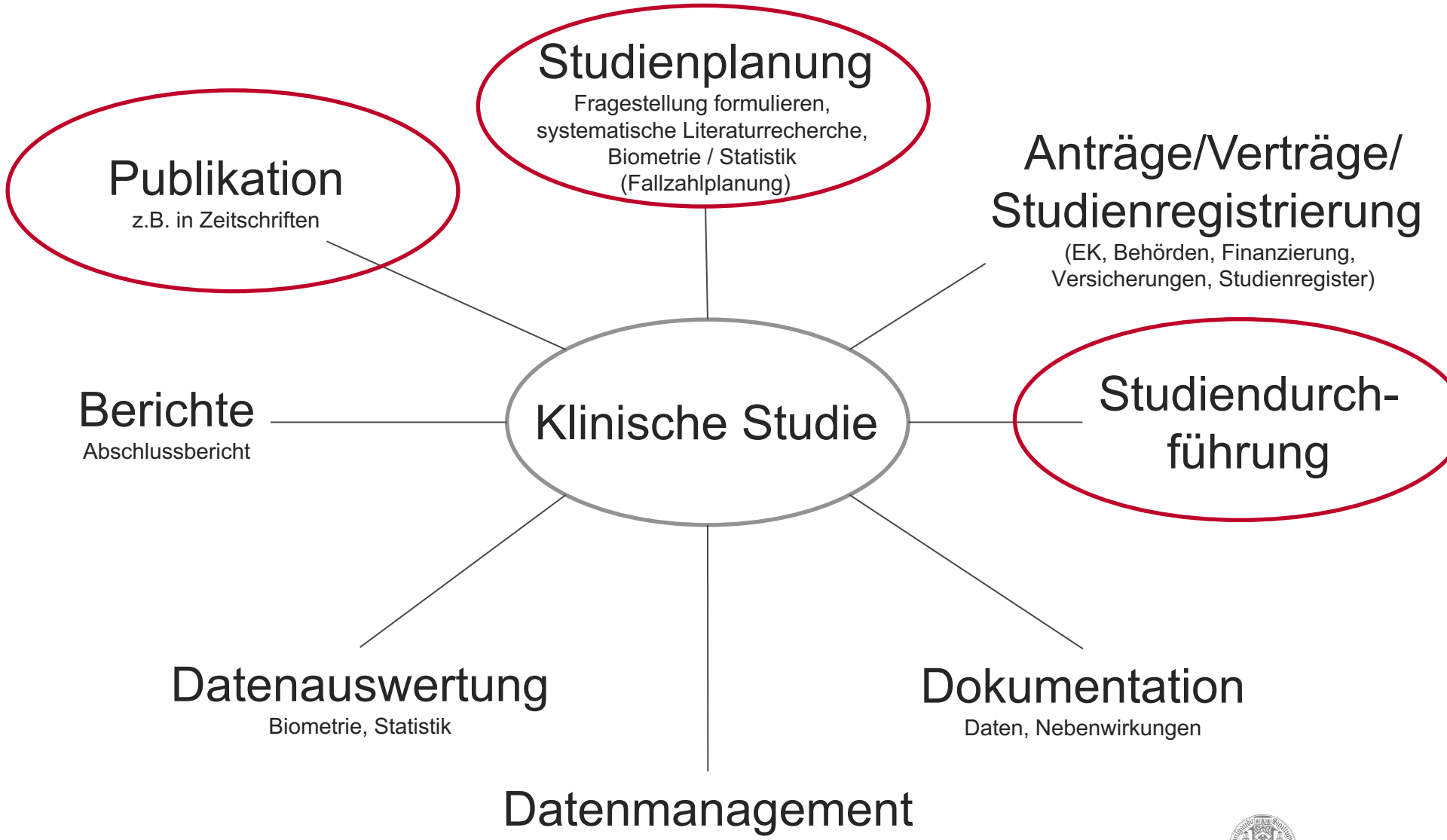
Lübeck

KLINISCHE STUDIE



Studienplanung auf Grundlage der bereits vorhandenen Evidenz – Gründe

- Es ist unethisch, Erkenntnisse aus Studien zu ignorieren

- Verantwortung gegenüber den Studienteilnehmern:
  - Studie muss notwendig sein
  - Schadensrisiko muss minimiert sein

- Sinnvolle Verwendung von Fördergeldern und Ressourcen, d.h. weniger Verschwendung!

Lesenswert!
Artikel-Serie zu mehr Wert und weniger Verschwendung in den medizinischen Wissenschaften: Research: increasing value, reducing waste 1-5; January 8, 2014 http://www.thelancet.com/series/research

Studienplanung im Kontext der bereits vorhandenen Evidenz – Gefordert von:

Bundesministerium für Bildung und Forschung

DFG Deutsche Forschungsgemeinschaft

Antragsstellung: BMBF / DFG-Förderrichtlinien: Leitfaden für die Antragstellung, Klinische Studien.

SPIRIT

Richtlinie zur Protokollerstellung:
SPIRIT Statement (Standard Protocol Items: Recommendations for Interventional Trials); (www.spirit-statement.org)

CONSORT TRANSPARENT REPORTING of TRIALS

Publikationsrichtlinien (www.equator-network.org):
z.B. CONSORT Statement (Consolidated Standards of Reporting Trials) (www.consort-statement.org)

THE LANCET

Autorenrichtlinien: «The Lancet» fordert seit 2010 die Einordnung von Forschungsergebnissen in den jeweiligen Kontext (Lancet 2010; 376: 10-11)

2. EVIDENCE

Set your trial into perspective. This section should detail the background of the starting hypotheses of the trial. Also give evidence why a confirmatory trial is justifiable at this stage.

A description of how you searched for the evidence (databases, search terms, limits) is mandatory: Please indicate the electronic databases searched. MEDLINE, Cochrane Central, the Cochrane library, clinicaltrials.gov, Deutsches Register Klinischer Studien (DRKS) and International Clinical Trials Search Portal (ICTRP) are recommended as a minimum, but other databases may be relevant in special occasions. Include search terms, limits, date of search and time period covered. Provide a narrative summary: Which trials have been conducted either by you or by others? What is the relevance of their results? Give references to any relevant systematic review(s)[6] and / or pilot studies, feasibility studies, relevant previous / ongoing trials, case reports / series. State what your study adds to the existing body of evidence. Also explain why a confirmatory trial is justified in this case.

A full electronic search strategy for one database, including any limits used, has to be presented in appendix 2 (max. one page). Guidance concerning search techniques can be found in the following document:

http://www.cochrane.de/sites/cochrane.de/files/uploads/20130523_Manual_Literaturrecherche_Final.pdf.

Please note that insufficient clinical evidence precludes funding.[7]

Derzeitige Praxis

Clarke, M, Hopewell, S. Many reports of randomised trials still don't begin or end with a systematic review of the relevant evidence. Bahrain Med Soc, Vol. 24, 145-48, 2013

Alle RCTs im Monat Mai in: 1997, 2001, 2005, 2009, 2012
Zeitschriften: BMJ, JAMA, Lancet, New Engl J Med, Ann Intern Med

1997: 76% **2012: 61%**

Studienergebnisse sind noch immer NICHT in den Kontext einer aktuellen systematischen Übersichtsarbeit oder anderer relevanter Evidenz gestellt!

DISCO-Projekt

Research

Original Investigation

Prevalence, Characteristics, and Publication of Discontinued Randomized Trials

Benjamin Kasenda, MD; Erik von Elm, MD, MSc; John You, MD, MSc; Anette Blümle, PhD; Yuki Tomonaga, MSc; Ramon Saccilotto, MD, MSc; Alain Amstutz, BSc; Theresa Bengough, BSc; Joerg J. Meerpohl, MD; Mihaela Stegert, MD; Kari A. O. Tikkinen, MD, PhD; Ignacio Neumann, MD, MSc; Alonso Carrasco-Labra, MD, MSc; Markus Faulhaber, MD, MSc; Sohail M. Mulla, BSc; Dominik Mertz, MD, MSc; Elie A. Akl, MD, PhD, MPH; Dirk Bassler, MD, MSc; Jason W. Busse, DC, PhD; Ignacio Ferreira-González, MD, PhD; Francois Lamontagne, MD, MSc; Alain Nordmann, MD, MSc; Viktoria Gloy, PhD; Heike Raatz, MD, MSc; Lorenzo Moja, MD, MSc; Rachel Rosenthal, MD, MSc; Shanil Ebrahim, PhD; Stefan Schandelmaier, MD; Sun Xin, PhD; Per O. Vandvik, MD, PhD; Bradley C. Johnston, PhD; Martin A. Walter, MD; Bernard Burnand, MD, MSc; Matthias Schwenkglenks, PhD; Lars G. Hemkens, MD; Heiner C. Bucher, MD, MPH; Gordon H. Guyatt, MD, MSc; Matthias Briel, MD, MSc

IMPORTANCE The discontinuation of randomized clinical trials (RCTs) raises ethical concerns and often wastes scarce research resources. The epidemiology of discontinued RCTs, however, remains unclear.

OBJECTIVES To determine the prevalence, characteristics, and publication history of discontinued RCTs and to investigate factors associated with RCT discontinuation due to poor recruitment and with nonpublication.

DESIGN AND SETTING Retrospective cohort of RCTs based on archived protocols approved by 6 research ethics committees in Switzerland, Germany, and Canada between 2000 and 2003. We recorded trial characteristics and planned recruitment from included protocols. Last follow-up of RCTs was April 27, 2013.

MAIN OUTCOMES AND MEASURES Completion status, reported reasons for discontinuation, and publication status of RCTs as determined by correspondence with the research ethics

Editorial page
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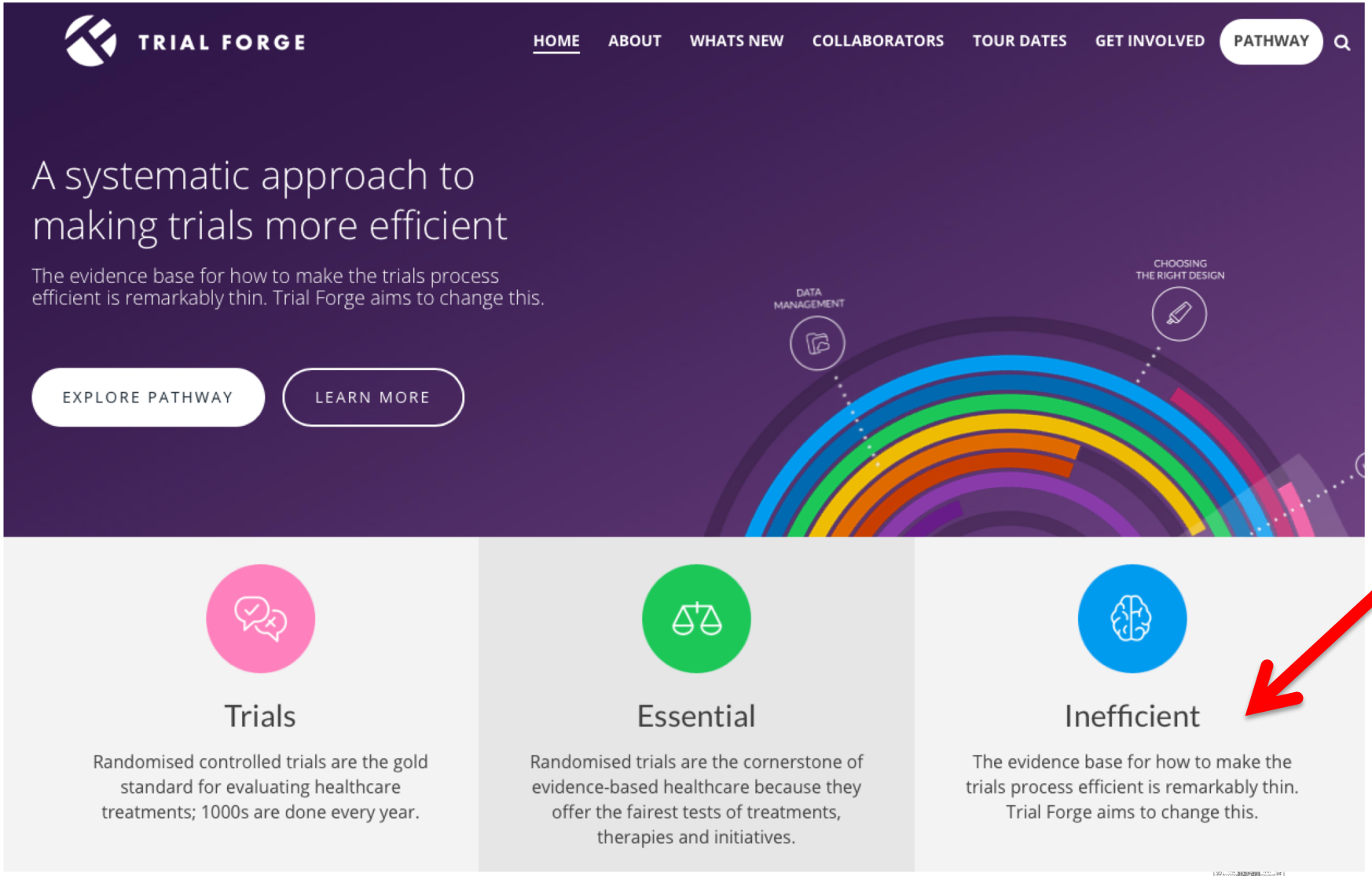
Supplemental jama.com

Table 2. Prevalence of Randomized Clinical Trial (RCT) Discontinuation

	RCTs Involving Patients			
	Sponsorship			
	Industry (n = 551)	Investigator (n = 343)	All (n = 894)	Full Journal Publication (n = 530)
Completion status				
Completed	394 (71.5) [68.1-75.2]	181 (52.8) [47.3-58.1]	575 (64.3) [61.1-67.4]	417 (78.7) [75.0-82.0] [
Discontinued	119 (21.6) [18.3-25.3]	130 (37.9) [32.8-43.3]	249 (27.9) [25.0-30.9]	113 (21.3) [18.1-25.0]
Unclear	38 (6.9) [5.0-9.4]	32 (9.3) [6.6-13.0]	70 (7.8) [6.2-9.8]	0 [0.0-0.9]
Reason for discontinuation				
Poor recruitment[a]	40 (7.3) [5.3-9.8]	60 (17.5) [13.7-22.0]	100 (11.2) [9.2-13.5]	40 (7.5) [5.5-10.2]
Futility[b]	25 (4.5) [3.0-6.7]	12 (3.5) [1.9-6.2]	37 (4.1) [3.0-5.7]	18 (3.4) [2.1-5.4]
Administrative reasons[c]	20 (3.6) [2.3-5.7]	16 (4.7) [2.8-7.6]	36 (4.0) [2.9-5.6]	8 (1.5) [0.7-3.1]
Harm	17 (3.1) [1.9-5.0]	7 (2.0) [0.9-4.3]	24 (2.7) [1.8-4.0]	12 (2.3) [1.2-4.0]
Unknown reason[d]	6 (1.1) [0.4-2.5]	18 (5.3) [3.2-8.3]	24 (2.7) [1.8-4.0]	21 (4.0) [2.6-6.0]
Benefit	2 (0.4) [0.06-1.5]	7 (2.0) [0.9-4.2]	9 (1.0) [0.5-2.0]	9 (1.7) [0.8-3.3]
External evidence	6 (1.1) [0.4-2.5]	2 (0.6) [0.1-2.3]	8 (0.9) [0.4-1.8]	2 (0.4) [0.0-1.5]
Lack of funding	1 (0.2) [0.01-1.2]	4 (1.2) [0.4-3.2]	5 (0.6) [0.2-1.4]	0 [0.0-0.9]
Other	2 (0.4) [0.06-1.5]	4 (1.2) [0.4-3.2]	6 (0.7) [0.3-1.5]	3 (0.6) [0.2-1.7]

Kasenda, B., E. von Elm, J. You, A. Blumle, Y. Tomonaga, R. Saccilotto, A. Amstutz, T. Bengough, J.J. Meerpohl, M. Stegen Bassler, J.W. Busse, I. Ferreira-Gonzalez, F. Lamontagne, A. Nordmann, V. Gloy, H. Raatz, L. Moja, R. Rosenthal, S. Ebrah Schwenkglenks, L.G. Hemkens, H.C. Bucher, G.H. Guyatt, and M. Briel, Prevalence, characteristics, and publication of disco

Trial Forge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A systematic approach to making trials more efficient
The evidence base for how to make the trials process efficient is remarkably thin. Trial Forge aims to change this.
EXPLORE PATHWAY
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DATA MANAGEMENT
CHOOSING THE RIGHT DESIGN
Trials
Randomised controlled trials are the gold standard for evaluating healthcare treatments; 1000s are done every year.
Essential
Randomised trials are the cornerstone of evidence-based healthcare because they offer the fairest tests of treatments, therapies and initiatives.
Inefficient
The evidence base for how to make the trials process efficient is remarkably thin. Trial Forge aims to change this.

Cochrane Library

Cochrane Database of Systematic Reviews

Strategies to improve recruitment to randomised trials (Review)

Treweek S, Pitkethly M, Cook J, Fraser C, Mitchell E, Sullivan F, Jackson C, Taskila TK, Gardner H

Authors' conclusions

The literature on interventions to improve recruitment to trials has plenty of variety but little depth. Only 3 of 72 comparisons are supported by high-certainty evidence according to GRADE: having an open trial and using telephone reminders to non-responders to postal interventions both increase recruitment; a specialised way of developing participant information leaflets had little or no effect. The methodology research community should improve the evidence base by replicating evaluations of existing strategies, rather than developing and testing new ones.

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Treweek, S., M. Pitkethly, J. Cook, C. Fraser, E. Mitchell, F. Sullivan, C. Jackson, T.K. Taskila, and H. Gardner, Strategies to improve recruitment to randomised trials. Cochrane Database Syst Rev, 2018. **2**: p. MR000013.

Studien zu methodischen Aspekten der Durchführung von „Trials“

Gillies *et al. Trials* (2018) 19:197
https://doi.org/10.1186/s13063-018-2572-0

Trials

STUDY PROTOCOL Open Access

Systematic Techniques to Enhance rEtention in Randomised controlled trials: the STEER study protocol

Katie Gillies[1*], Peter Bower[2], Jim Elliott[1], Graeme MacLennan[3], Rumana S. N. Newlands[4], Margaret Ogden[1], Shaun P. Treweek[1], Mary Wells[5], Miles D. Witham[6], Bridget Young[7] and Jill J. Francis[8]

Abstract

Background: Non-retention of participants seriously affects the credibility of clinical trial results and significantly reduces the potential of a trial to influence clinical practice. Non-retention can be defined as instances where participants leave the study prematurely. Examples include withdrawal of consent and loss to follow-up and thus outcome data cannot be obtained. The majority of existing interventions targeting retention fail to describe any theoretical basis for the observed improvement, or lack of improvement. Moreover, most of these interventions lack involvement of participants in their conception and/or design, raising questions about their relevance and acceptability. Many of the causes of non-retention involve people performing a behaviour (e.g. not returning a questionnaire). Behaviour change is difficult, and the importance of a strong theoretical basis for interventions that aim to change behaviour is increasingly recognised. This research aims to develop and pilot theoretically informed, participant-centred, evidence-based behaviour change interventions to improve retention in trials.

Methods: This research will generate data through semi-structured interviews on stakeholders' perspectives of the reasons for trial non-retention. It will identify perceived barriers and enablers to trial retention using the Theoretical Domains Framework. The intervention development work will involve identification of behaviour change techniques, using recognised methodology, and co-production of retention interventions through discussion groups with end-users. An evaluation of intervention acceptability and feasibility will be conducted in focus groups. Finally, a ready-to-use evaluation framework to deploy in Studies Within A Trial as well as an explanatory retention framework will be developed for identifying and tackling modifiable issues to improve trial retention.

Discussion: We believe this to be one of the first studies to apply a theoretical lens to the development of interventions to improve trial retention that have been informed by, and are embedded within, participants' experiential accounts. By developing and identifying priority interventions this study will support efforts to reduce research waste.

Keywords: Trials, Retention, Non-retention, Dropout, Theory, Intervention, Interviews

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Gillies, K., P. Bower, J. Elliott, G. MacLennan, R.S.N. Newlands, M. Ogden, S.P. Treweek, M. Wells, M.D. Witham, B. Young, and J.J. Francis, Systematic Techniques to Enhance rEtention in Randomised controlled trials: the STEER study protocol. Trials, 2018. **19**(1): p. 197.

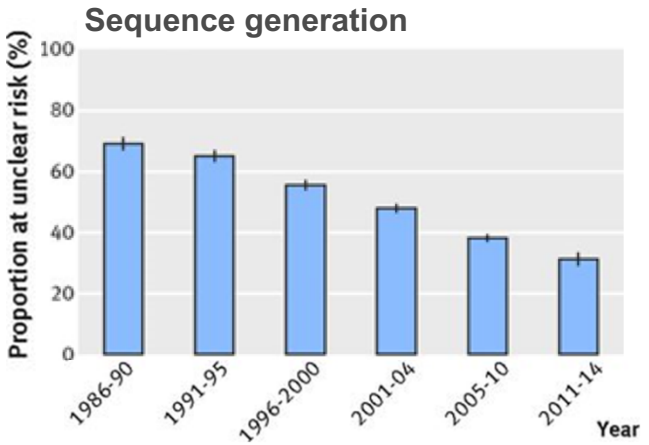
PUBLIKATION

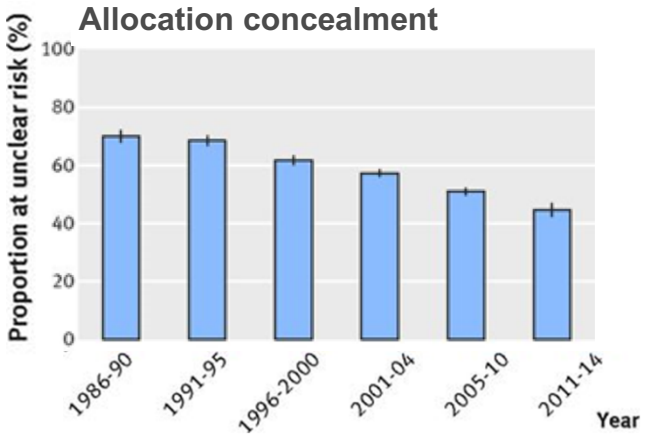
WICHTIG!

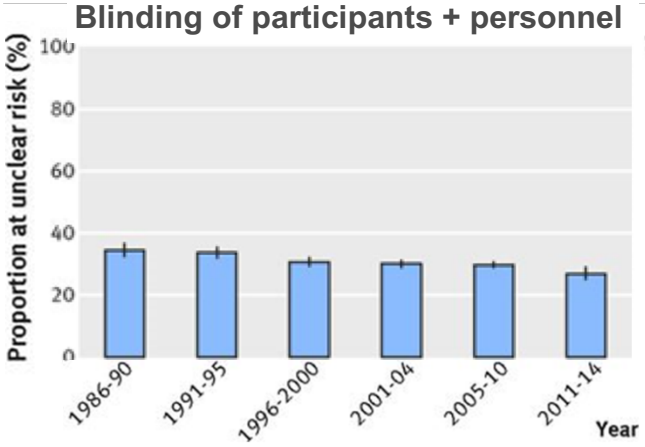
- Publikation aller Studien(-ergebnisse)
- Publikationen sind verfügbar und auffindbar
- Publikationen enthalten alle relevanten Informationen

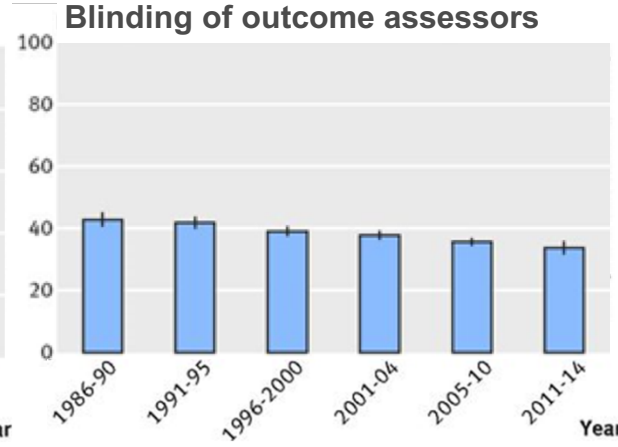
STUDIEN SIND UNZUREICHEND BERICHTET

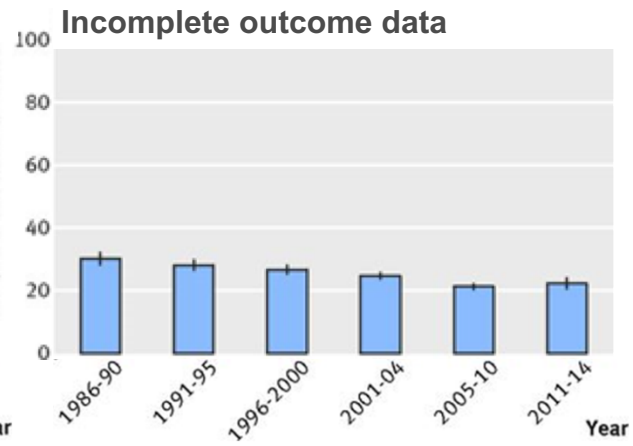
Dechartres A, Trinquart L, Atal I, Moher D, Dickersin K, Boutron I, et al. Evolution of poor reporting and inadequate methods over time in 20 920 randomised controlled trials included in Cochrane reviews: research on research study BMJ 2017; 357 :j2490











Evolution of poor reporting over time in 20 920 trial articles

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CONSORT 2010 checklist of information to include when reporting a randomised trial

Section/Topic	Item No	Checklist item
Title and abstract		
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
Sample size	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines
Randomisation:		
Sequence generation	8a	Method used to generate the random allocation sequence
	8b	Type of randomisation; details of any restriction (such as blocking and block size)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions

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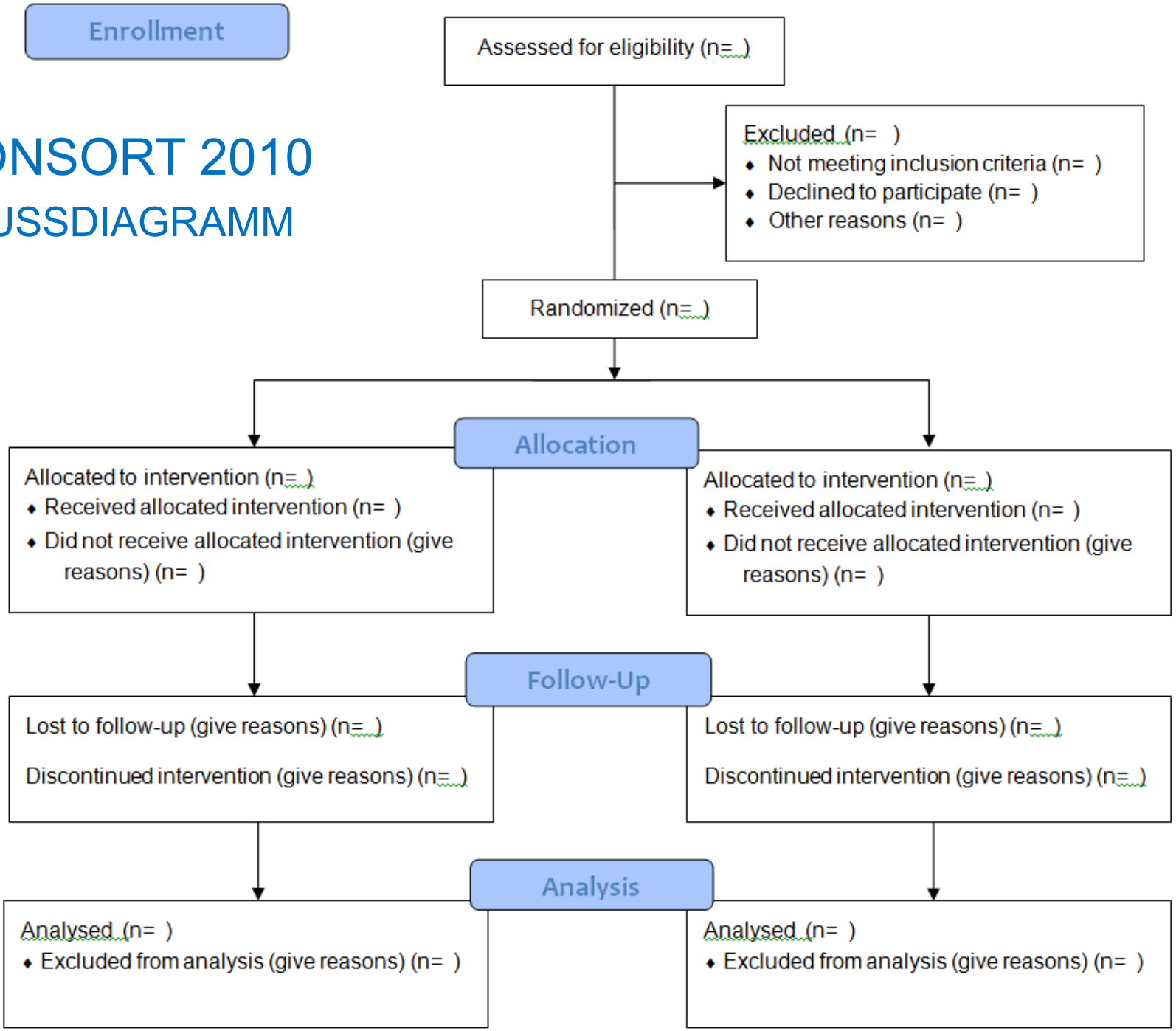
CONSORT 2010 checklist of information to include when reporting a randomised trial

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
	13b	For each group, losses and exclusions after randomisation, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)
Discussion		
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses
Generalisability	21	Generalisability (external validity, applicability) of the trial findings
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
Other information		
Registration	23	Registration number and name of trial registry
Protocol	24	Where the full trial protocol can be accessed, if available
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders

CONSORT 2010 FLUSSDIAGRAMM



Einfluss von CONSORT:
Unterstützende vs nicht-unterstützende Zeitschriften

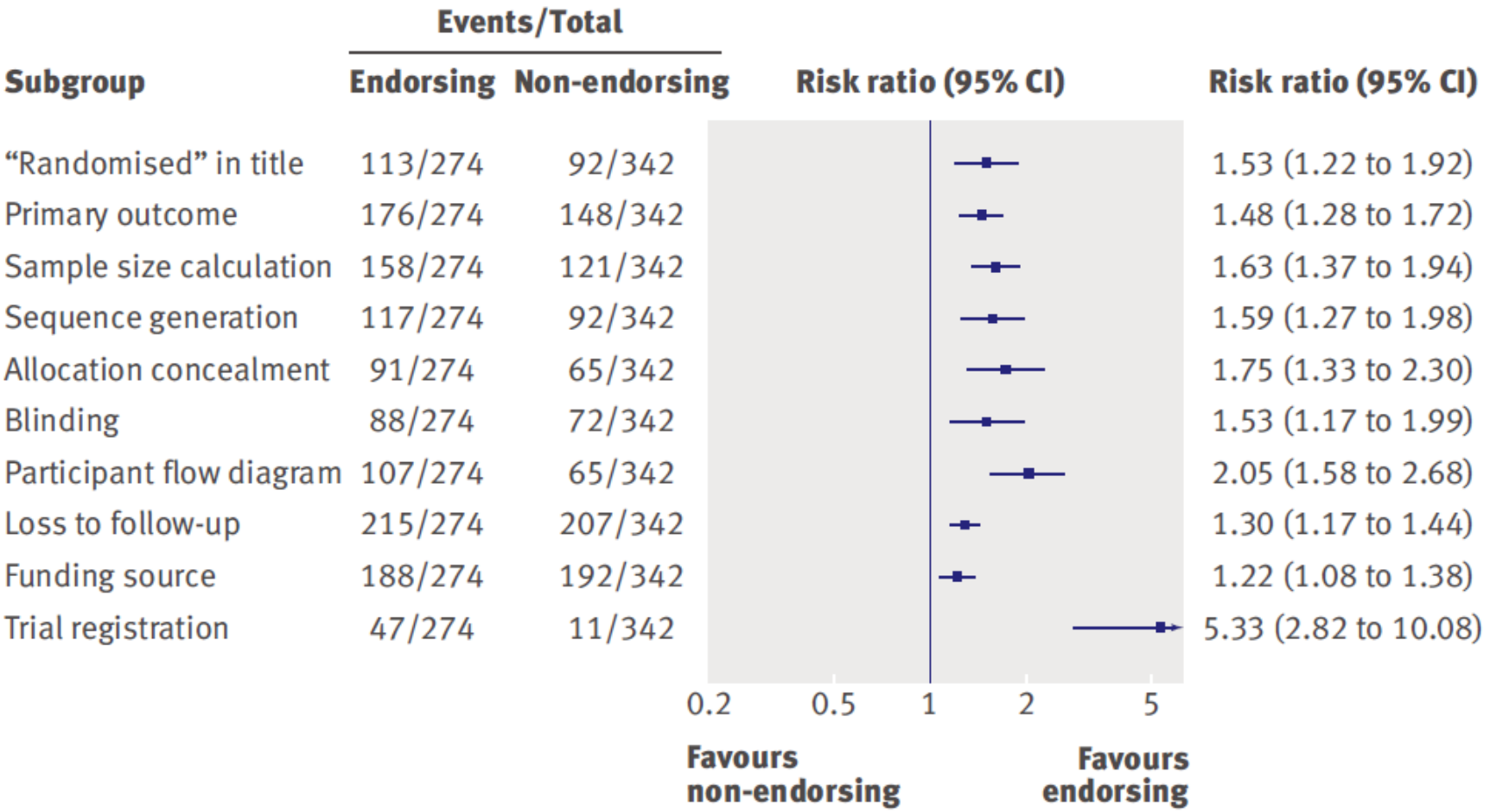
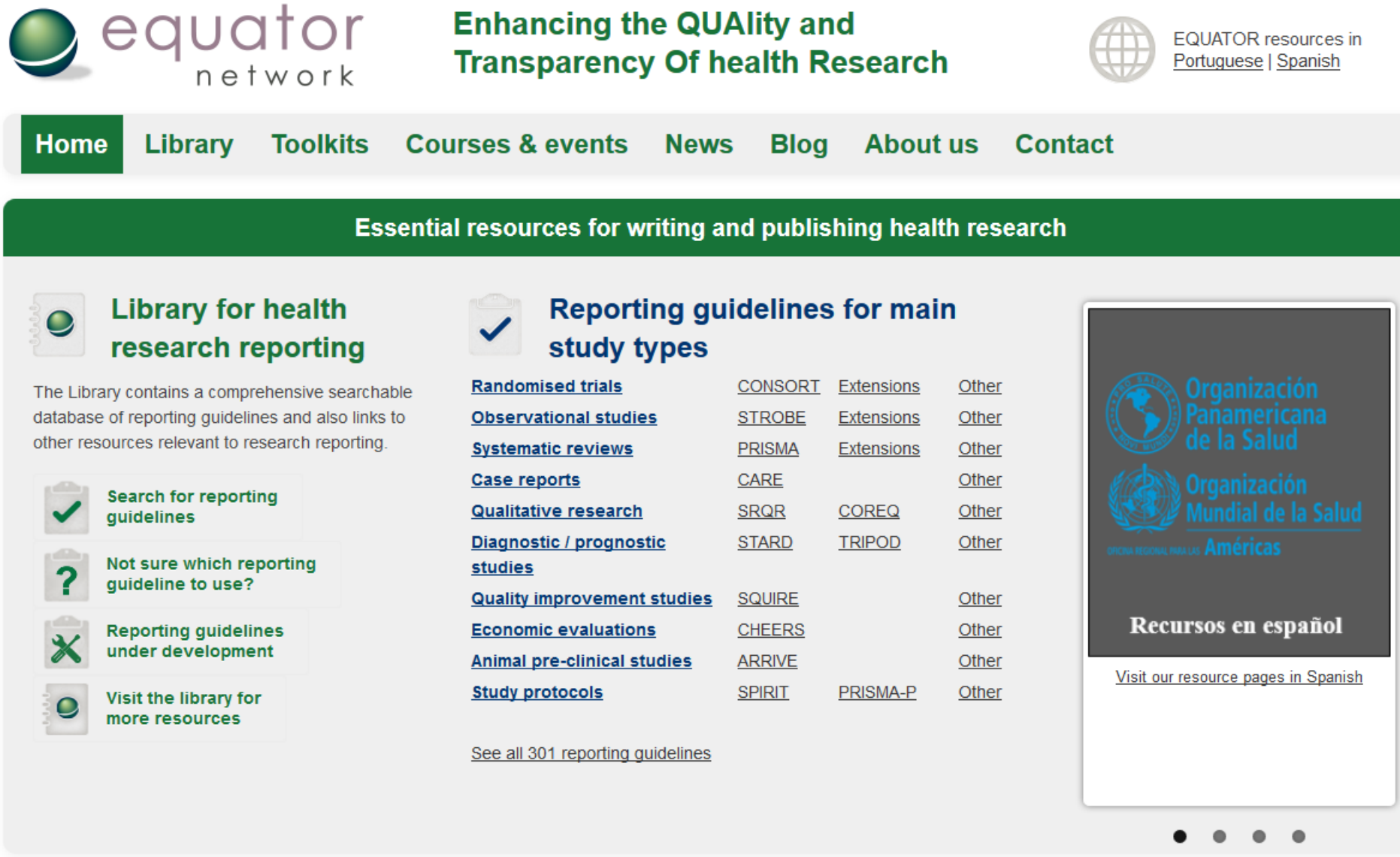


Fig 3 | Differences in reporting of methodological items between CONSORT endorsing and non-endorsing journals in 2006

www.equator-network.org



Zusammenfassung

1. Vorbestehende Evidenz (SR) konsequent nutzen
   - Notwendigkeit einer Studie
   - Exakte Fragestellung

2. Optimale, evidenzbasierte Studiendurchführung
   - Wirksame Strategien für effiziente Studien; Fehler vermeiden
   - Besonderheiten des Forschungsgebiets beachten

3. Vollständiges, transparentes Berichten von Studienergebnissen
   - Methodik (Biasbewertung)
   - Ergebnisse (Einschluss in SR/MA) möglich