

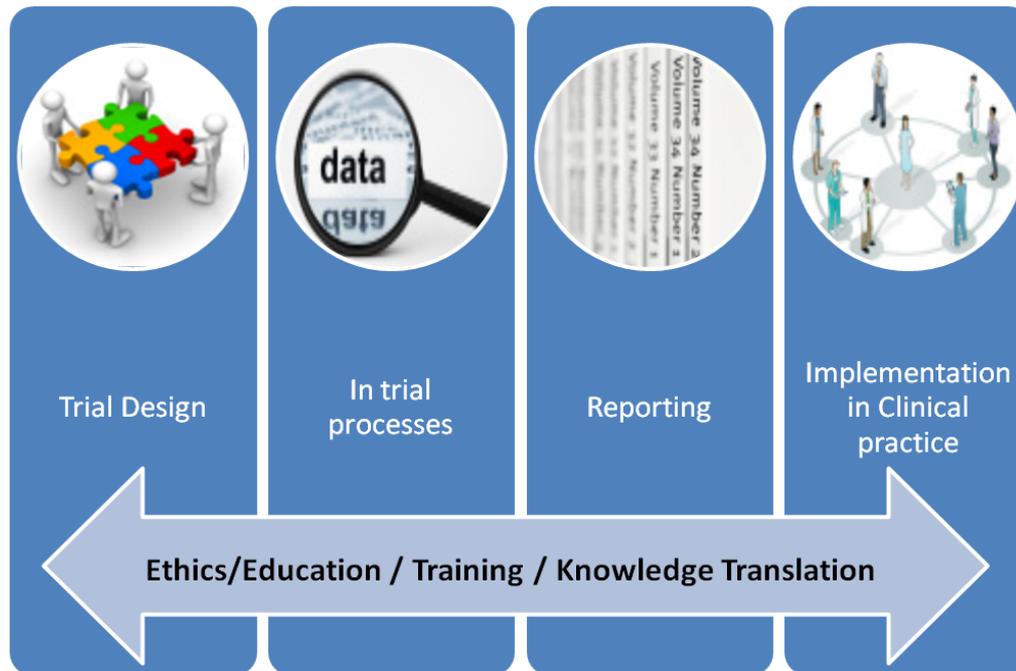
PRO assessment in stroke trials: challenges and opportunities.



Melanie Calvert, PhD
Professor of Outcomes Methodology

PRO Research Group, University of Birmingham

Aim: to develop best practice for PROs in trials to improve patient care.



<http://www.birmingham.ac.uk/patient-reported-outcomes>

UNIVERSITY OF
BIRMINGHAM



Overview

Challenges: Trial Design, Conduct, Reporting

- Ensuring a clear rationale and hypothesis.
- Selecting of PROs (Drs Sara Brookes/Kerry Avery).
- Content of trial PROocols.
- 'In-trial' practices including dealing with PRO Alerts.
- Analysing & reporting PRO results in a meaningful way to inform clinical practice.

Opportunities to improve practice and patient care.

The Ultimate Challenge

'We must do all that we can to make patient reported outcome assessment feasible and credible. If we fail in our task we will have left out the heart of all health-care research: the patient.'

Sloan 2007

Challenge

Trial Design

Challenge: Ensuring a clear PRO rationale & hypothesis.

- What outcome/domain/time-point?
- What' the rationale?
- What's the evidence?
- Risk of multiple statistical testing and selective reporting of significant results.



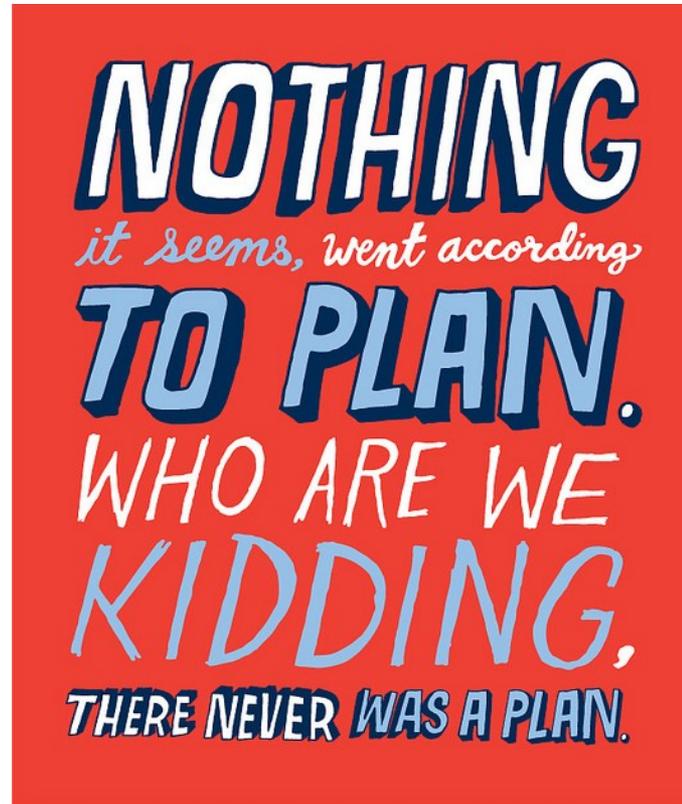
Opportunity: Ensuring a clear PRO rationale & hypothesis.

A clearly defined rationale and hypothesis will:

1. minimise multiple statistical testing
2. reduce the risk of selective reporting
3. aid interpretation of results
4. may facilitate the use of results to inform patient care.



Challenge: Content of trial PROocols



Evidence: Systematic Review of PRO Guidance for Protocol Writers

- Searched MEDLINE, EMBASE, CINAHL, the Cochrane Library databases from inception until February 2013 for PRO specific guidance for trial protocol writers. Plus grey literature.
- 21,175 citations identified and screened from which 54 met our inclusion criteria.
- >150 unique PRO related recommendations for protocol writers.
- **Funded by NIHR SPCR**

Evidence: Review of NIHR HTA Protocols

- Many protocols, including stroke trials, lack PRO specific information.
- Rationale, hypothesis, data collection, timing of assessment, methods to minimise missing data, analysis.

- **Funded by NIHR SPCR**

Opportunity: Improve the content of trial protocols.

- Guideline development underway lead by the PRO Research Group and ISOQOL Task force.
- Include PRO experts as part of the trial team.
- Consider ways to optimise PRO data collection.
- Stakeholder engagement & involvement in the above activities.



Challenge: Inconsistencies in quality of life data collection in clinical trials

OPEN ACCESS Freely available online

PLOS ONE

Inconsistencies in Quality of Life Data Collection in Clinical Trials: A Potential Source of Bias? Interviews with Research Nurses and Trialists

Derek Kyte¹, Jonathan Ives², Heather Draper², Thomas Keeley^{1,3}, Melanie Calvert^{1,3*}

1 Primary Care and Clinical Sciences, University of Birmingham, Birmingham, United Kingdom, **2** Medicine, Ethics, Society and History, University of Birmingham, Birmingham, United Kingdom, **3** MRC Midland Hub for Trial Methodology Research, University of Birmingham, Birmingham, United Kingdom

October 2013 | Volume 8 | Issue 10 | e76625

UNIVERSITY OF
BIRMINGHAM

Evidence:

26 Semi-structured interviews of trials staff involved in PRO data collection/management.

Results:

- Theme 1: Inconsistent PRO measurement.
- Theme 2: Dealing with 'concerning PRO data'.
- Theme 3: Emotional or ethical burden for trial staff.
- Theme 4: Lack of training and guidance.
- **D. Kyte Doctoral Research NIHR SPCR Doctoral Fellowship**

Opportunity: Optimal data collection

- Guideline development (underway).
- Training for staff.
- Improved protocols (see previous).
- Pre-specified methods to deal with PRO Alerts.

Challenge: 'PRO Alerts' in clinical trials

“worrying levels of psychological distress or physical symptoms that may require an immediate response.”

JAMA The Journal of the
American Medical Association

[Home](#) [Current Issue](#) [All Issues](#) [Online First](#) [Specialties & Topics](#) [CME](#) [Mul](#)

September 25, 2013, Vol 310, No. 12 >

[< Previous Article](#) [Next Article >](#)

Viewpoint | September 25, 2013

Patient-Reported Outcome Alerts Ethical and Logistical Considerations in Clinical Trials

Derek Kyte, MSc¹; Heather Draper, PhD²; Melanie Calvert, PhD^{1,3}

[\[+\] Author Affiliations](#)

JAMA. 2013;310(12):1229-1230. doi:10.1001/jama.2013.277222.

Text Size: [A](#) [A](#) [A](#)

Challenge: 'PRO Alerts' in clinical trials

- Potential for co-intervention bias.
- Trial participants 'in-need' may receive suboptimal care.
- Confidentiality & consent.

Evidence:

- 26 Semi-structured interviews of trials staff involved in PRO data collection/management.
- Survey of >600 trialists (Derek Kyte doctoral research, manuscript in preparation).

Funding:

- **D. Kyte: Doctoral Research NIHR SPCR Doctoral Fellowship**
- **M. Calvert, H Draper: MRC MHTMR**

Opportunities:

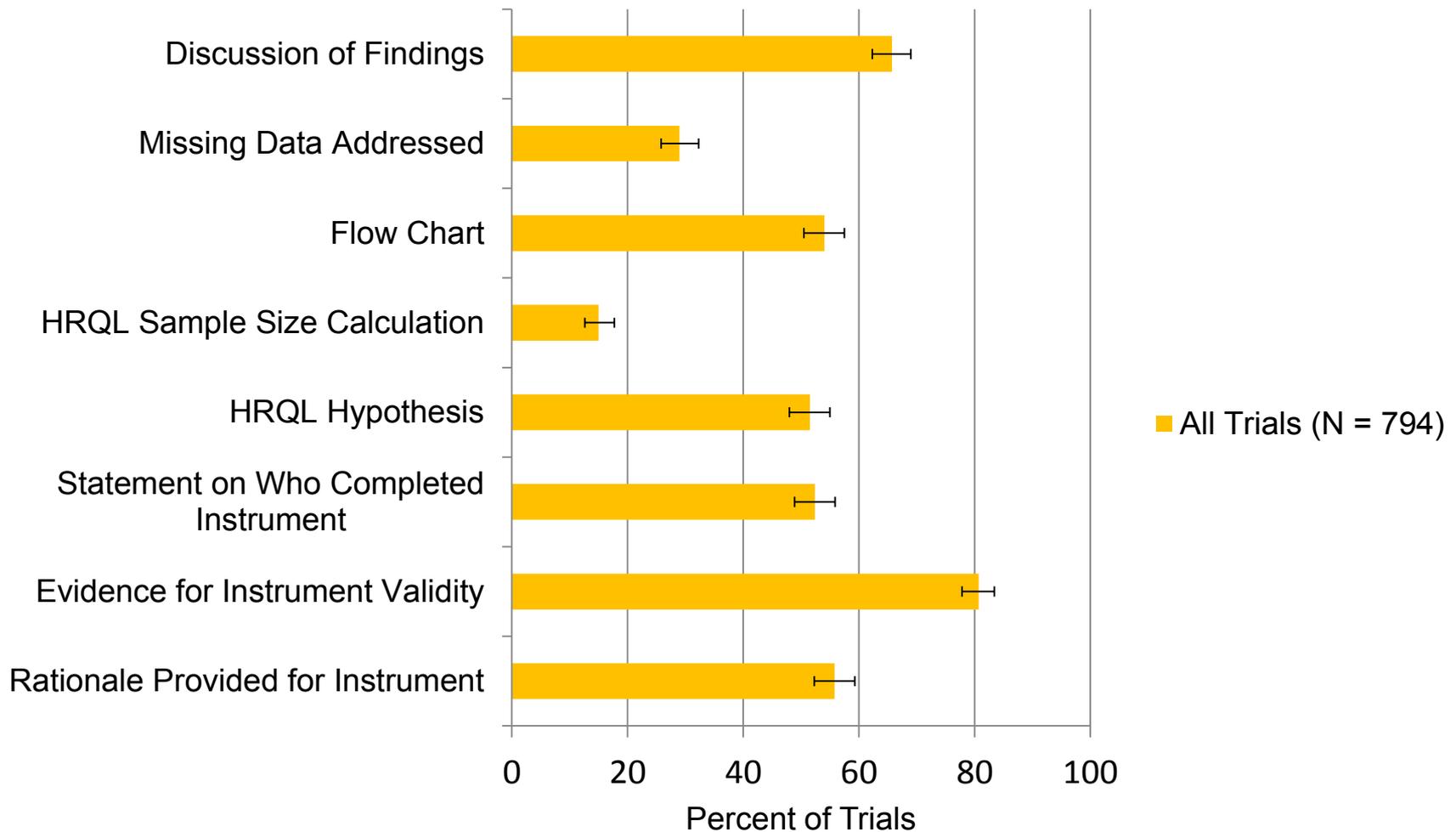
- To ensure trial participants are fully informed on **how** their data will be used to inform their care and **who** will access the data.
- Researchers should be aware of potential 'PRO alerts' and pre-specify management in the protocol and supporting trials documentation.

Trial Reporting

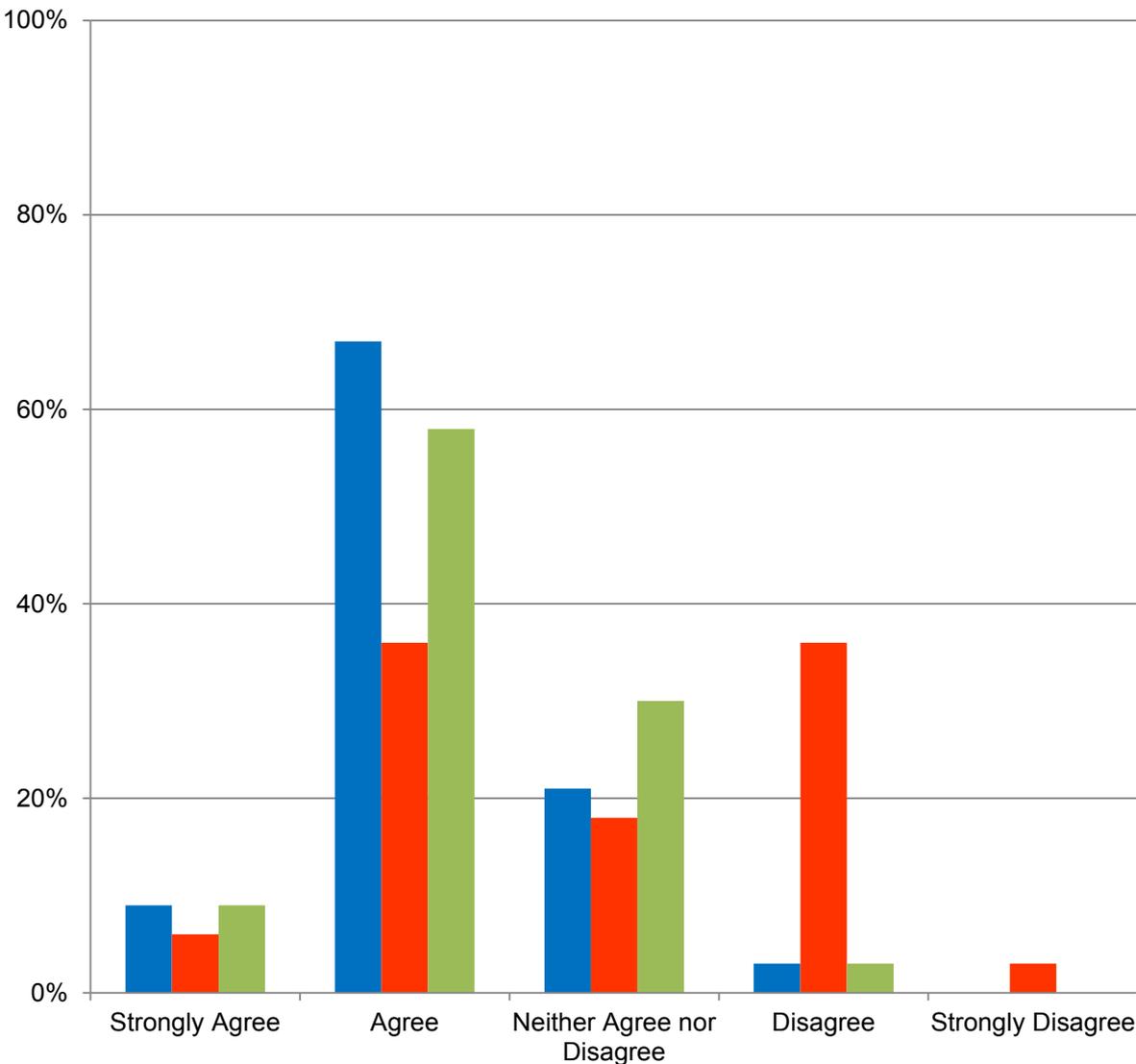
Challenges:

- Current reporting of PROs is poor quality.
- Poor reporting hampers the use of PRO trial data to inform clinical practice.

Evidence: current reporting of PRO data is poor quality.



Evidence: Poor reporting hampers the use of PRO data in clinical practice



■ I have a good understanding of the concept of quality of life.

■ I feel comfortable interpreting quality of life data as it is reported in the clinical trial literature.

■ I feel a need to improve or increase my use of clinical trial quality of life data in my clinical practice.

Brundage et al Qual Life Res. 20(7): 979-985, 2011.

Opportunity: To Improve the Reporting of HRQL/PRO data from stroke trials

- Improved reporting of PROs in clinical trials will enable robust evidence to inform patient choice, aid clinical decision making, and inform health policy.



Opportunity: The CONSORT PRO Extension

THE LANCET

Search for in All Fields [Advanced](#)

[Home](#) | [Journals](#) | [Specialties](#) | [Clinical](#) | [Global Health](#) | [Audio](#) | [Conferences](#) | [Information for](#) | [Health](#)

The Lancet, [Volume 378, Issue 9804](#), Pages 1684 - 1685, 12 November 2011
doi:10.1016/S0140-6736(11)61256-7 [Cite or Link Using DOI](#)

[< Previous Article](#) | [Next Article >](#)

Reporting quality of life in clinical trials: a CONSORT extension

[Melanie Calvert](#) ^a, [Jane Blazeby](#) ^b, [Dennis Revicki](#) ^c, [David Moher](#) ^d, [Michael Brundage](#) ^e

Results for health-related quality of life (HRQoL) from clinical trials are increasingly used for clinical decision making as well as comparative effectiveness, health policy, and reimbursement decisions. Research suggests that HRQoL information can be used to establish treatment preferences because patients value HRQoL data and can interpret HRQoL findings accurately. ¹Trials that incorporate HRQoL as an outcome should therefore be designed, analysed, and reported well.



Reporting of Patient-Reported Outcomes in Randomized Trials The CONSORT PRO Extension

Melanie Calvert, PhD
 Jane Blazeby, MD
 Douglas G. Altman, DSc
 Dennis A. Revicki, PhD
 David Moher, PhD
 Michael D. Brundage, MD
 for the CONSORT PRO Group

The CONSORT (Consolidated Standards of Reporting Trials) Statement aims to improve the reporting of randomized controlled trials (RCTs); however, it lacks guidance on the reporting of patient-reported outcomes (PROs), which are often inadequately reported in trials, thus limiting the value of these data. In this article, we describe the development of the CONSORT PRO extension based on the methodological framework for guideline development proposed by the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network. Five CONSORT PRO checklist items are recommended for RCTs in which PROs are primary or important secondary end points. These recommendations urge that the PROs be identified as a primary or secondary outcome in the abstract, that a description of the hypothesis of the PROs and relevant domains be provided (ie, if a multidimensional PRO tool has been used), that evidence of the PRO instrument's validity and reliability be provided or cited, that the statistical approaches for dealing with missing data be explicitly stated, and that PRO-specific limitations of study findings and generalizability of results to other populations and clinical practice be discussed. Examples and an updated CONSORT flow diagram with PRO items are provided. It is recommended that the CONSORT PRO guidance supplement the standard CONSORT guidelines for reporting RCTs with PROs as primary or secondary outcomes. Improved reporting of PRO data should facilitate robust interpretation of the results from RCTs and inform patient care.

JAMA. 2013;309(8):814-822

www.jama.com

THE CONSORT (CONSOLIDATED Standards of Reporting Trials) Statement, first published in 1996 and most recently revised in 2010,^{1,2} provides evidence-based recommendations to improve the completeness of reporting of randomized controlled trials (RCTs). The statement focuses on parallel-group trials, but a number of extensions for reporting other trial designs (cluster, noninferiority, and equivalence), interventions (nonpharmacologic and herbal therapies), and for specific data, such as harms have been developed.³ The CONSORT Statement is endorsed by major journals and editorial groups, such as the Interna-

- **Funded by MRC & CIHR**

Summary

Need to improve PRO trial design analysis and reporting to:

- ensure high quality ethical data,**
- minimise research waste**
- and produce high quality data to inform care.**

Opportunities for help and advice:

PRO Research Group <http://www.birmingham.ac.uk/patient-reported-outcomes>

Design:

- NIHR Research Design Service
- MRC Hubs Trials Methodology Research
- Clinical Trials Units

Analysis:

- Clinical Trials Units

Reporting:

- CONSORT PRO Extension