The ethics of inefficiency

Shaun Treweek

Twitter: @shauntreweek

streweek@mac.com

Health Services Research Unit
University of Aberdeen

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MRC | Hubs for Trials Methodology Research

OK TO ASK about clinical research

NHS National Institute for Health Research

Trials Change Lives

"Clinical trials are the backbone of primary research that informs clinical practice in the NHS in the UK"

Prof Hywel Williams, Director, Health Technology Assessment Programme (NIHR)

Listen to the podcast

Clinical Trials for the NHS

www.methodologyhubs.mrc.ac.uk/trials-change-lives/

Photo reference,
Queen's University Belfast

Let’s do what we did last time..

‘There is a peculiar paradox that exists in trial execution - we perform clinical trials to generate evidence to improve patient outcomes; however, we conduct clinical trials like anecdotal medicine:

- **we do what we think works**
- **we rely on experience and judgement and..**
- **limited data to support best practices.’**

Monica Shah in ‘Site selection in global clinical trials in patients hospitalized for heart failure: perceived problems and potential solutions’. Heart Failure Review 2014; 19:135-52.

trialforge.org

TRIAL FORGE

HOME ABOUT WHATS NEW COLLABORATORS GET INVOLVED PATHWAY

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 LEARN MORE

Trials

Randomised controlled trials are the gold standard for evaluating healthcare

Essential

Randomised trials are the cornerstone of evidence-based healthcare because they

Inefficient

The evidence base for how to make the trials process efficient is remarkably thin.

Choosing the right research question

BMJ 2014;349:g5219 doi: 10.1136/bmj.g5219

RESEARCH

Ability of a meta-analysis to prevent redundant research: systematic review of studies on pain from propofol injection

Céline Habre *research fellow*[1], Martin R Tramèr *professor in anaesthesia*[2 3], Daniel M Pöpping *anaesthetist*[4], Nadia Elia *public health epidemiologist*[2 5]

[1]Department of Radiology, Geneva University Hospitals, 4 rue Gabrielle-Perret-Gentil, CH-1211 Geneva 14, Switzerland; [2]Division of Anaesthesiology, Geneva University Hospitals, Geneva, Switzerland; [3]Faculty of Medicine, University of Geneva, Geneva, Switzerland; [4]Department of Anaesthesiology and Intensive Care, University Hospital Münster, Münster, Germany; [5]Institute of Global Health, Faculty of Medicine, University of Geneva, Geneva, Switzerland

Abstract

Objective To examine whether, according to the conclusions of a 2000 systematic review with meta-analysis on interventions to prevent pain

of the new trials were considered clinically relevant since they used the most efficacious intervention as comparator or included a paediatric population.

Choosing the right research question

thebmj

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RESEARCH

Number of clinically irrelevant trials:

87 of 136 (64%)

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Choosing the right research question

'A survey of investigators of clinical trials generating data that others had used to update systematic reviews showed that less than half were even aware that relevant reviews of existing evidence were available when they designed their studies.'

Chalmers I, Bracken MB, Djulbegovic B, Garattini S, Grant J, Gülmezoglu AM, et al. How to increase value and reduce waste when research priorities are set. Lancet 2014;383:156–65. .

p53 as a prognostic marker in bladder cancer

Systematic review

- 168 published studies
- >10000 patients

"After 10 years of research, evidence is not sufficient to conclude whether changes in P53 act as markers of outcome in patients with bladder cancer."

[Malats et al, *Lancet Oncology* 2005]

equator network

p53 as a pr
in bla

Systematic review

- 168 published studi
- >10000 patients

"After 10 years of rese
to conclude whether
of outcome in patient

Our design choices

'…most therapeutic trials are inadequately formulated, and this from the earliest stages of their conception. Their inadequacy is basic..

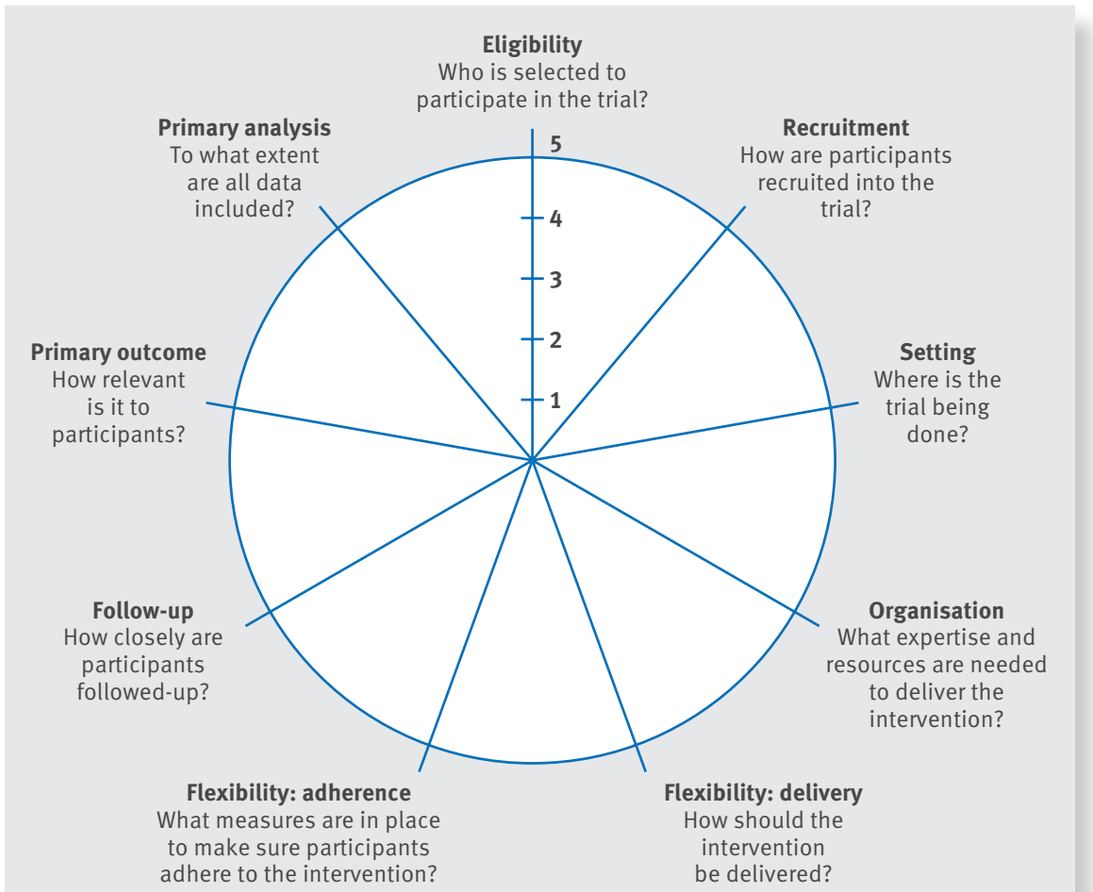
..the resulting ambiguity affects the definition of the treatments, the assessment of the results, the choice of subjects and the way in which the treatments are compared.'

Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutical trials. Journal of chronic diseases 1967; 20: 637–48.

Design: who are you trying to help?

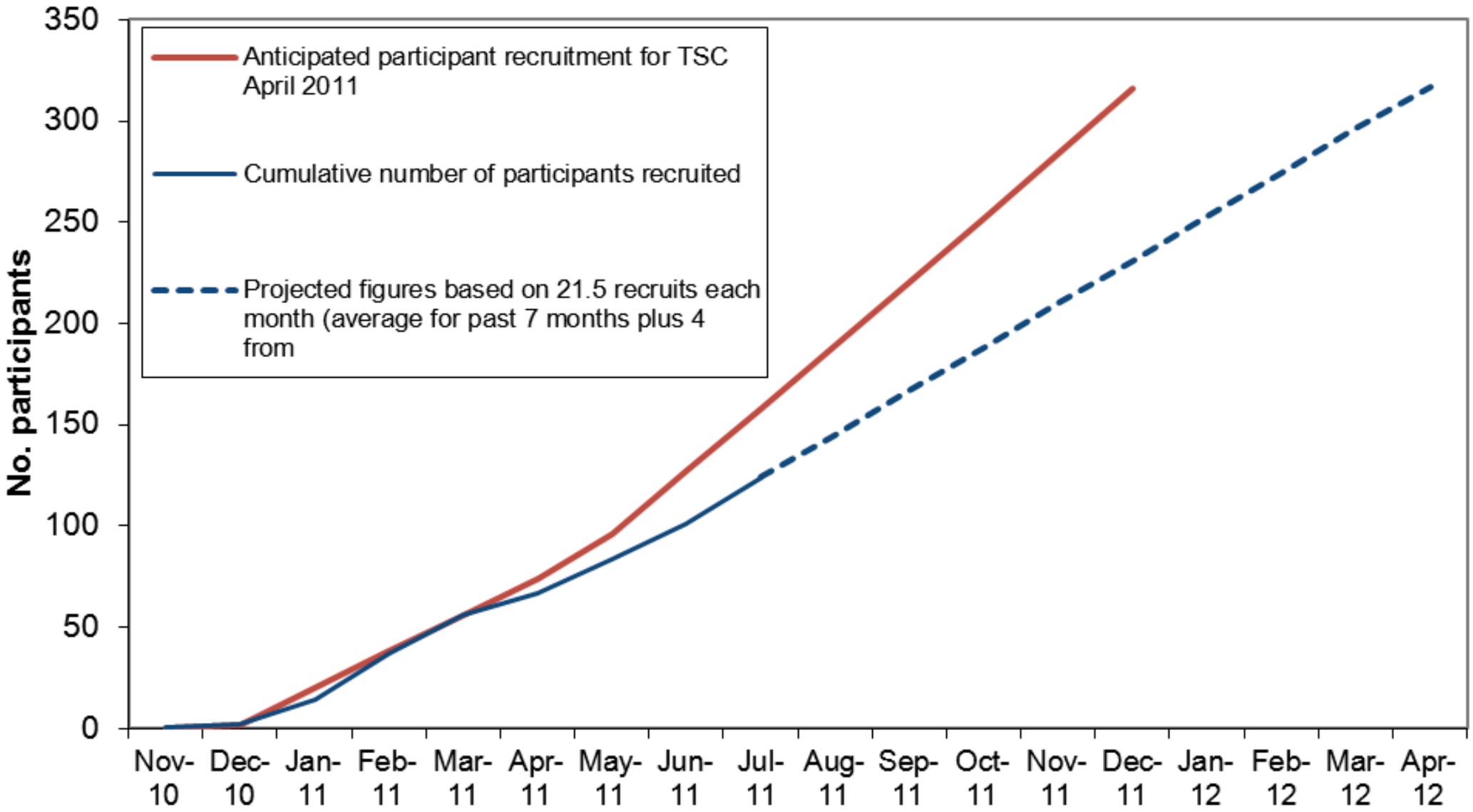
Who am I designing my trial for and what have I done to make sure they don't have to dismiss my trial as irrelevant?

Kirsty Loudon, Stirling



The PRECIS-2 wheel

The challenge of recruitment



What helps recruitment?

Strategies to improve recruitment to randomised controlled trials (Review)

Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrøm M, Johansen M, Taskila TK, Sullivan F, Wilson S, Jackson C, Jones R, Lockhart P

THE COCHRANE COLLABORATION®

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THE COCHRANE COLLABORATION®

The cost of poor recruitment

The Prevalence and Economic Impact of Low-Enrolling Clinical Studies at an Academic Medical Center

Darlene R. Kitterman, MBA, Steven K. Cheng, PhD, David M. Dilts, PhD, MBA, and Eric S. Orwoll, MD

Abstract

Purpose
The authors assessed the prevalence and associated economic impact of low-enrolling clinical studies at a single academic medical center.

Method
The authors examined all clinical studies receiving institutional review board (IRB) review between FY2006 and FY2009 at Oregon Health & Science University (OHSU) for recruitment performance and analyzed them by type of IRB review (full-board, exempt, expedited), funding mechanism, and academic unit. A low-enrolling study included those with zero or one participant at the time of study termination. The authors calculated the costs associated with IRB review, financial setup, contract negotiation, and department study start-up activities and the total economic impact on OHSU of low-enrolling studies for FY2009.

Results
A total of 837 clinical studies were terminated during the study period, 260 (31.1%) of which were low-enrolling. A greater proportion of low-enrolling studies were government funded than industry funded ($P = .006$). The authors found significant differences among the various academic units with respect to percentages of low-enrolling studies (from 10% to 67%). The uncompensated economic impact of low-enrolling studies was conservatively estimated to be nearly $1 million for FY2009.

Conclusions
A substantial proportion of clinical studies incurred high institutional and departmental expense but resulted in little scientific benefit. Although a certain percentage of low-enrolling studies can be expected in any research organization, the overall number of such studies must be managed to reduce the aggregate costs of conducting research and to maximize research opportunities. Effective, proactive interventions are needed to address the prevalence and impact of low enrollment.

Editor's Note: A commentary on this article appears on page 1334.

Academic medical centers (AMCs), or institutions with the core mission of conducting clinical research, play a vital

communities.[1] One critical role of an AMC is to conduct research that advances basic scientific observations to applications in medical practice. The National Institutes of Health (NIH) has made translational research a priority, in

recruited less than 75% of their planned enrollment goals.[4] A sampling of 13 studies sponsored by the National Heart, Lung, and Blood Institute found that planned enrollment was completed for only two of the studies (15.4%),[5] and

Academic Medicine, Vol. 86, No. 11 / November 2011

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Institutional Issues

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Cost of 260 studies with zero or 1 participant at trial termination in 2011: almost $1 million

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Telephone reminders..

Telephoning people who do not respond to postal invitations increases recruitment:

- **Our best estimate is that recruitment increases by 6%.**
- **There is some uncertainty so the increase could be as low as 3% or as high as 9%.**

The certainty in this evidence is High.

A similar issue for the TwiCs design

What are the chances that a trial will work at all, or be as efficient, if the trial team doesn't use this design?

How big are the benefits compared to the harms?

Conclusion

- **Inefficiency is an ethical problem.**
- **There is a lot of it.**
- **Inefficiency wastes participant goodwill and time, resources and the opportunity of doing a different trial.**
- **When making ethical judgements, we should also consider the ethics issues of not doing something, as well as the ethics of doing it.**

Thank you!

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HEALTH SERVICES RESEARCH UNIT

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