

***The need for reports of new  
research to begin with up-to-date  
analyses of what is already known***

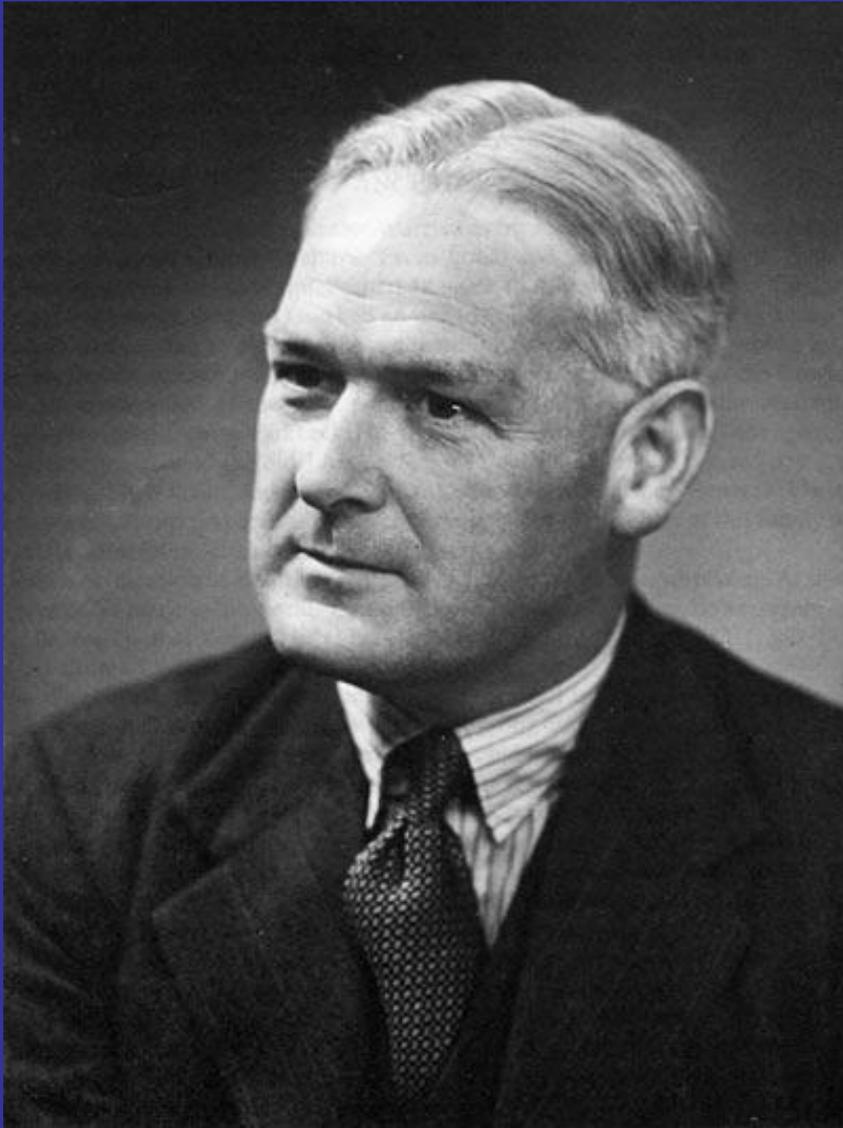
**Iain Chalmers**

Coordinator, James Lind Initiative

[www.jameslindlibrary.org](http://www.jameslindlibrary.org)



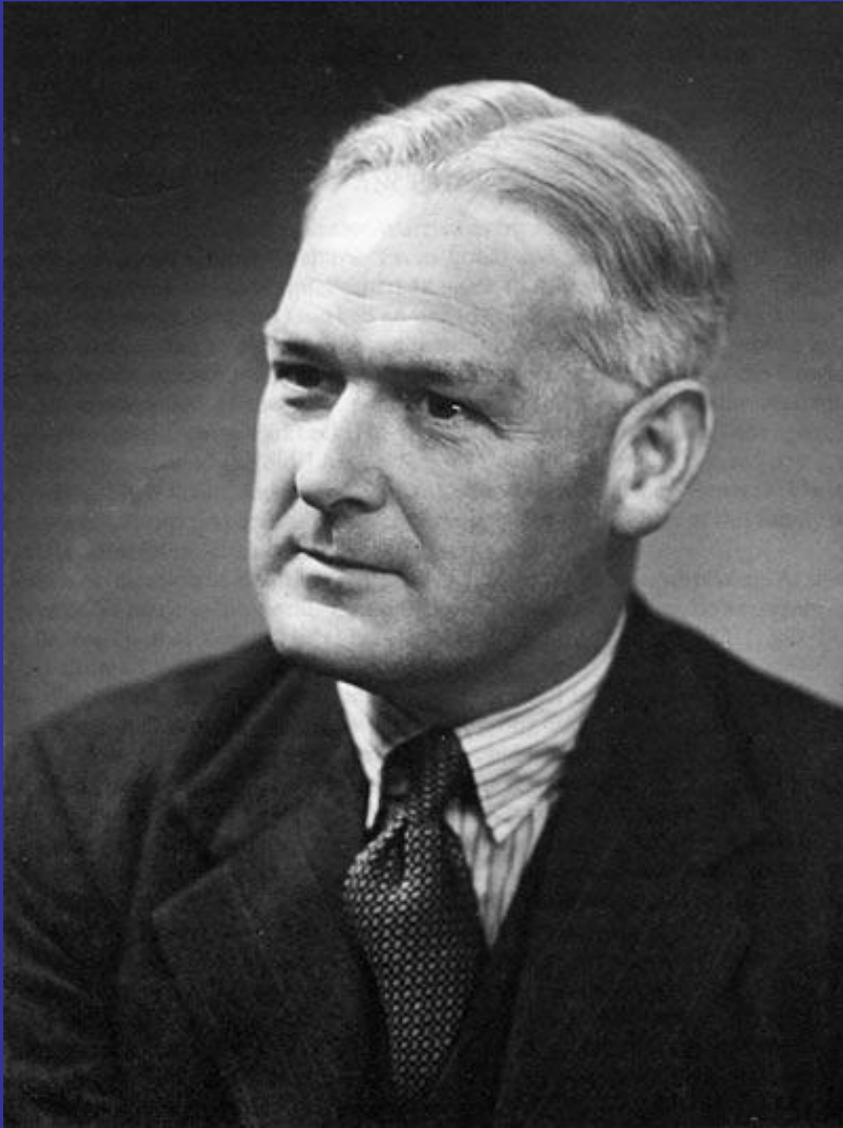
Freiburg i. Br, 11 October 2012



## **Austin Bradford Hill, 1965**

**Four questions to which readers want answers when reading reports of research.**

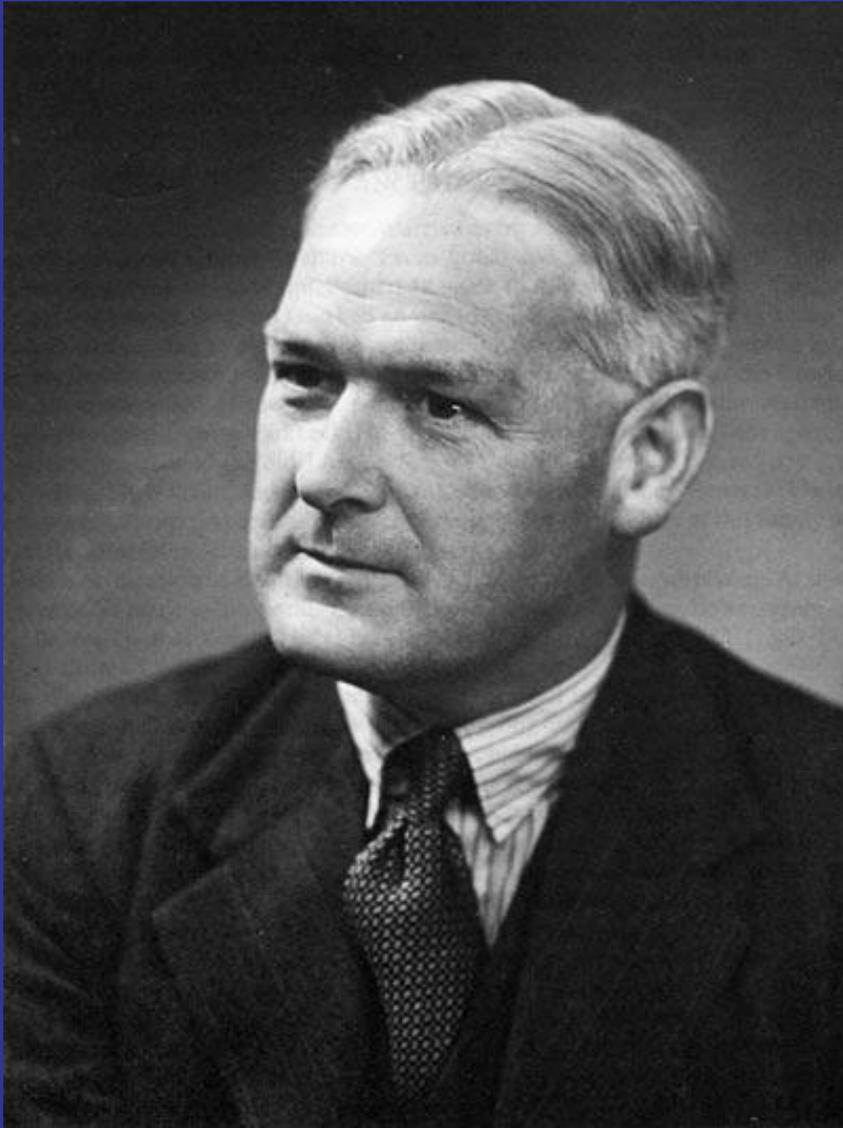
- 1.** Why did you start?
- 2.** What did you do?
- 3.** What answer did you get?
- 4.** And what does it mean anyway?



## Austin Bradford Hill, 1965

Four questions to which readers want answers when reading reports of research.

1. Why did you start?
2. **What did you do?**
3. **What answer did you get?**
4. And what does it mean anyway?



## **Austin Bradford Hill, 1965**

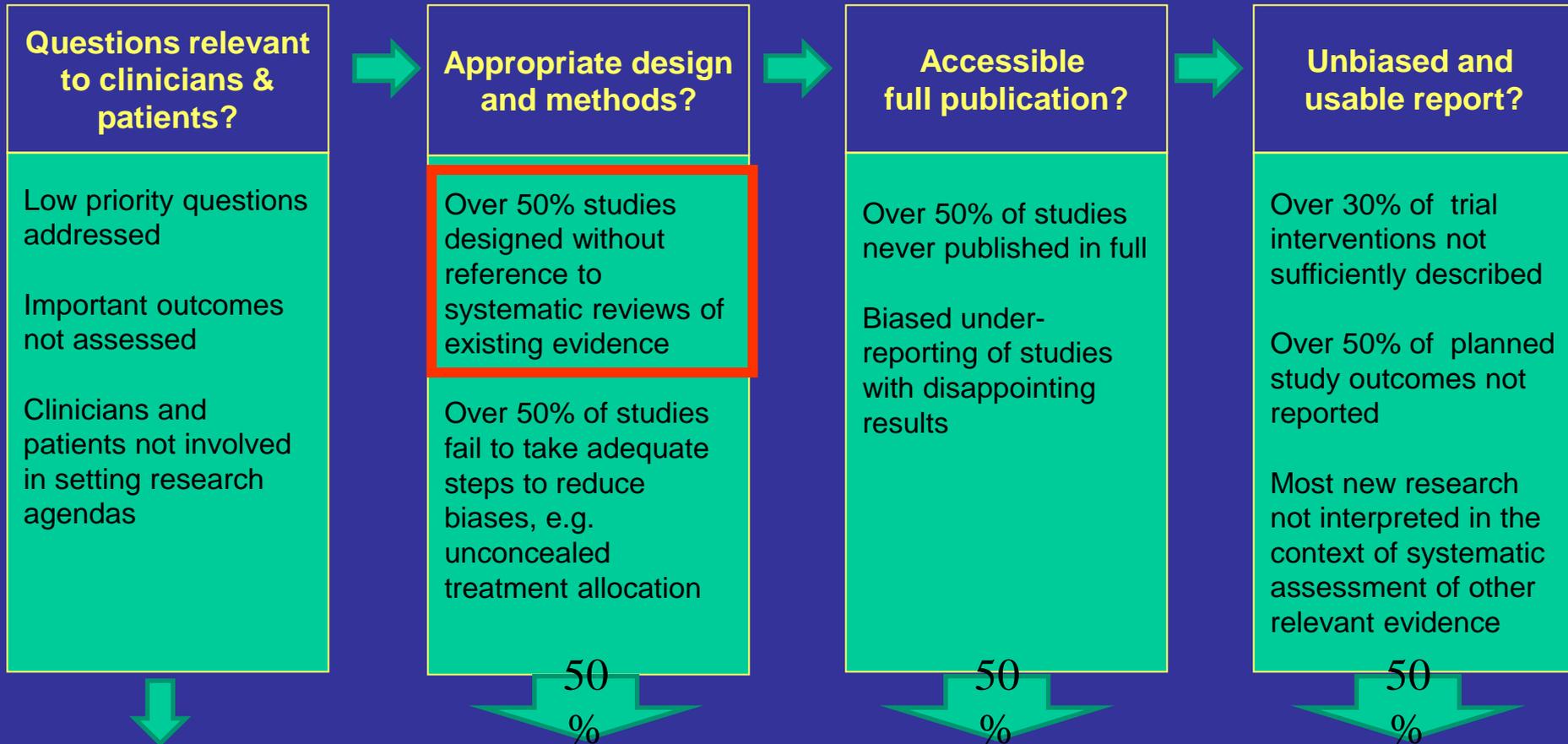
**Four questions to which readers want answers when reading reports of research.**

- 1. Why did you start?**
2. What did you do?
3. What answer did you get?
4. And what does it mean anyway?

# Avoidable waste in the production and reporting of research evidence

Iain Chalmers, Paul Glasziou

Lancet 2009; 374: 86-89



**85% Research waste = over \$85 Billion / year**

Reprinted from the **BMJ**, 30 November 1996, Vol 313, p 1390-1393

---

## **Are research ethics committees behaving unethically?**

### **Some suggestions for improving performance and accountability**

Julian Savulescu, Iain Chalmers, Jennifer Blunt

**The results of recent empirical investigations in research synthesis imply that research ethics committees are behaving unethically by endorsing new research which is unnecessary and by acquiescing in biased under-reporting of research which they have approved.**

"It is essential that existing sources of evidence, especially systematic reviews, are considered carefully prior to undertaking research.

"Research which duplicates other work unnecessarily, or which is not of sufficient quality to contribute something useful to existing knowledge, is in itself unethical."

Department of Health. Research Governance Framework for Health and Social Care, **2001**, para 2.3.1

**People have suffered and died unnecessarily, and resources for health care and health research have been wasted, because existing research evidence has not been reviewed systematically**



## TGN 1412



# Establishing risk of human experimentation with drugs: lessons from TGN1412

M J H Kenter, A F Cohen

*Lancet* 2006; 368: 1387-91

## Discussion

The above risk analysis, undertaken with data available in the research file and public domain before the TGN1412 trial started, shows that essential information was absent and the antibody was a high-risk compound unlikely to be suitable for administration to healthy people without additional preclinical experiments.

Patients have suffered and died unnecessarily, and resources for health care and health research have been wasted, because existing research evidence has not been reviewed systematically

# Is the study worth doing?

Lancet **1993**; 342:221-223.

*Lucy M Carpenter*

**“Good systematic reviews provide a valuable foundation for new research initiatives.”**

## STUDIES IN ANIMALS

### **Nimodipine in Animal Model Experiments of Focal Cerebral Ischemia**

#### **A Systematic Review**

J. Horn, MD; R.J. de Haan, PhD; M. Vermeulen, MD; P.G.M. Luiten, PhD; M. Limburg, MD

**20 animal studies: “The results of this review did not show convincing evidence to substantiate the decision to perform trials with nimodipine in large numbers of patients.**

Stroke 2001;32:2433-8.

## STUDIES IN HUMANS

Horn J, Limburg M.

**Calcium antagonists for acute ischemic stroke.**

*The Cochrane Database of Systematic Reviews, 2000*

“46 trials were identified of which 28 were included (7521 patients). No effect of calcium antagonists on poor outcome at the end of follow-up (OR 1.07, 95% CI 0.97/1.18), or on death at end of follow-up (OR 1.10, 95% CI 0.98/1.24) was found.”

These problems are still not  
being adequately addressed

# A Systematic Examination of the Citation of Prior Research in Reports of Randomized, Controlled Trials

Karen A. Robinson, PhD, and Steven N. Goodman, MD, MHS, PhD

**Conclusion:** In reports of RCTs published over 4 decades, fewer than 25% of preceding trials were cited, comprising fewer than 25% of the participants enrolled in all relevant prior trials. A median of 2 trials was cited, regardless of the number of prior trials that had been conducted. Research is needed to explore the explanations for and consequences of this phenomenon. Potential implications include ethically unjustifiable trials, wasted resources, incorrect conclusions, and unnecessary risks for trial participants.

*Ann Intern Med.* 2011;154:50-55.

# The use\* of systematic reviews when designing studies

\*actually, **the non-use**

*Nicola J Cooper\*, David R Jones\* and Alex J Sutton*

Only 11 of 24 responding authors of trial reports that had been added to existing systematic reviews were even aware of the relevant reviews when they designed their new studies.

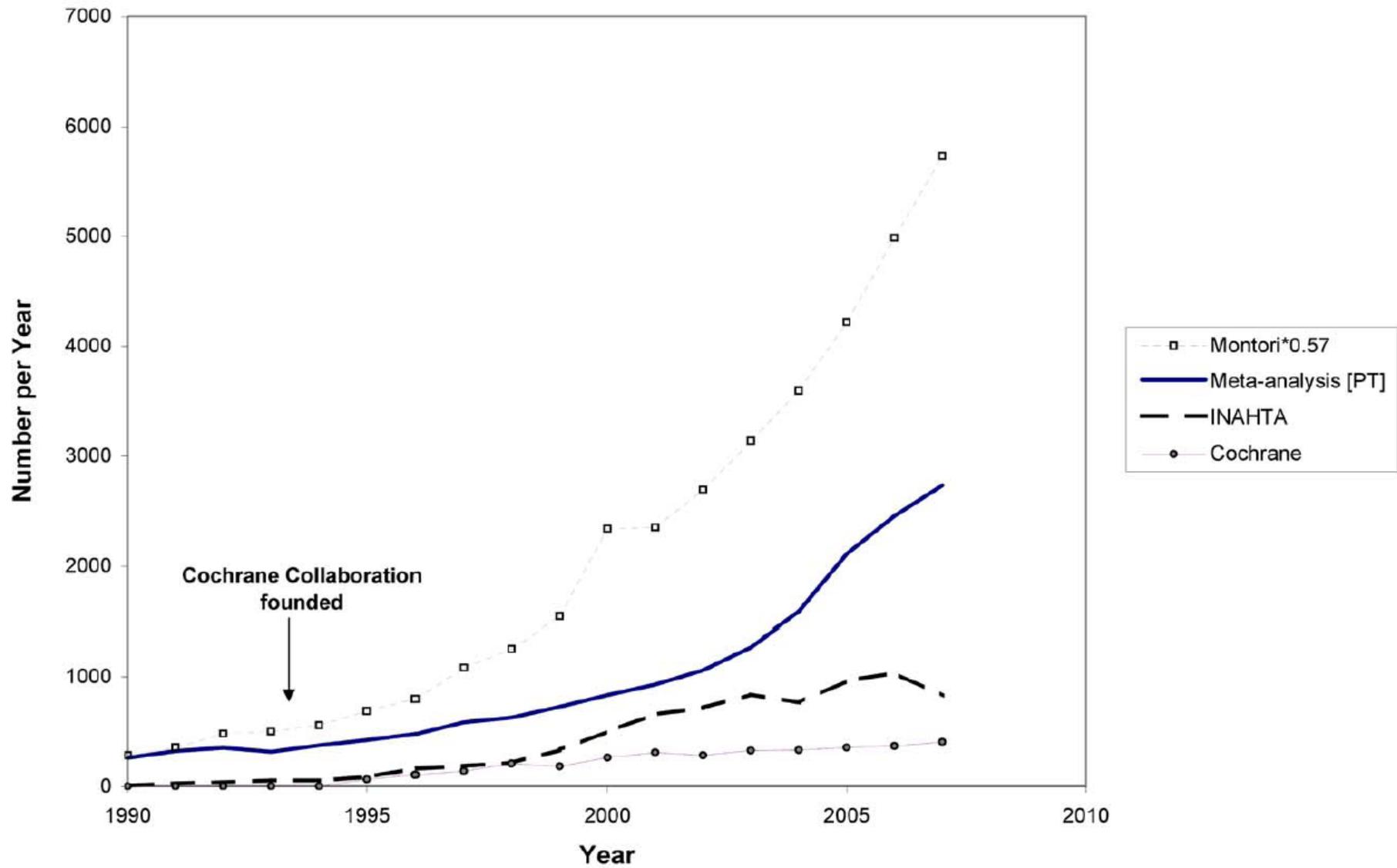
**Conclusions** Cautious interpretation of these results is necessary, but it is apparent that the proportion of study investigators using Cochrane or other systematic reviews in designing their new studies was very limited. Inclusion of encouragement in publication or application guidelines to consider and cite review results is desirable. *Clinical Trials* 2005; 2: 260–264. [www.SCTjournal.com](http://www.SCTjournal.com)

Policy Forum

# Seventy-Five Trials and Eleven Systematic Reviews a Day: How Will We Ever Keep Up?

**Hilda Bastian<sup>1\*</sup>, Paul Glasziou<sup>2</sup>, Iain Chalmers<sup>3</sup>**

**1** German Institute for Quality and Efficiency in Health Care (IQWiG), Cologne, Germany, **2** Centre for Research in Evidence-Based Practice, Faculty of Health Sciences, Bond University, Gold Coast, Australia, **3** James Lind Library, James Lind Initiative, Oxford, United Kingdom



**Two new resources that will  
help the EQUATOR Network  
to help others to address  
these serious problems**



What works?  
Clinical effectiveness.

In partnership with:



**PubMedHealth specializes in reviews of clinical effectiveness research, with easy-to-read summaries for consumers as well as full technical reports.**



Home

Register a review

My PROSPERO records

My details

Search PROSPERO

Search CRD databases

About PROSPERO

Help with registration

Support for PROSPERO

References and resources

Contact

Disclaimer

Home

Sign in or Join



### PROSPERO, looking good one year on

PROSPERO, the first open access online facility to prospectively register systematic reviews reports a successful first year with researchers from 27 countries around the world registering reviews.

We are delighted to announce that BMJ and BMJ Open have joined PLoS in supporting the principle of protocol registration and the aims of PROSPERO. In addition, the new BMC journal *Systematic Reviews* launched with a featured series of articles supporting systematic review registration and PROSPERO including a commentary on the NIHR position by Dame Sally Davies.

[Read more...](#)

### Register your review protocol details

Registration is free and open to anyone undertaking systematic reviews of the effects of interventions and strategies to prevent, diagnose, treat, and monitor health conditions, for which there is a health related outcome.

Register your review when the protocol (or equivalent) has been completed but before screening studies for inclusion begins.

Simply:

- Sign in
- Click on 'Register a review'
- Complete the required fields
- Click submit

# **The problem of continuing academic opposition**

## WELLCOME TRUST FUNDING FOR CLINICAL TRIALS

In the UK and Ireland

Interventions against health problems of developing countries

---

### **In the UK and Ireland**

Clinical trials will be considered by the Science Funding Division of the Wellcome Trust when, in addition to evaluating the efficacy of an intervention, they also provide insight into the underlying biology and mechanisms.

The Trust will not consider applications to support systematic reviews of clinical trials.

**Can this policy be defended on scientific, ethical, or economic grounds?**

## Academia's failure to support systematic reviews

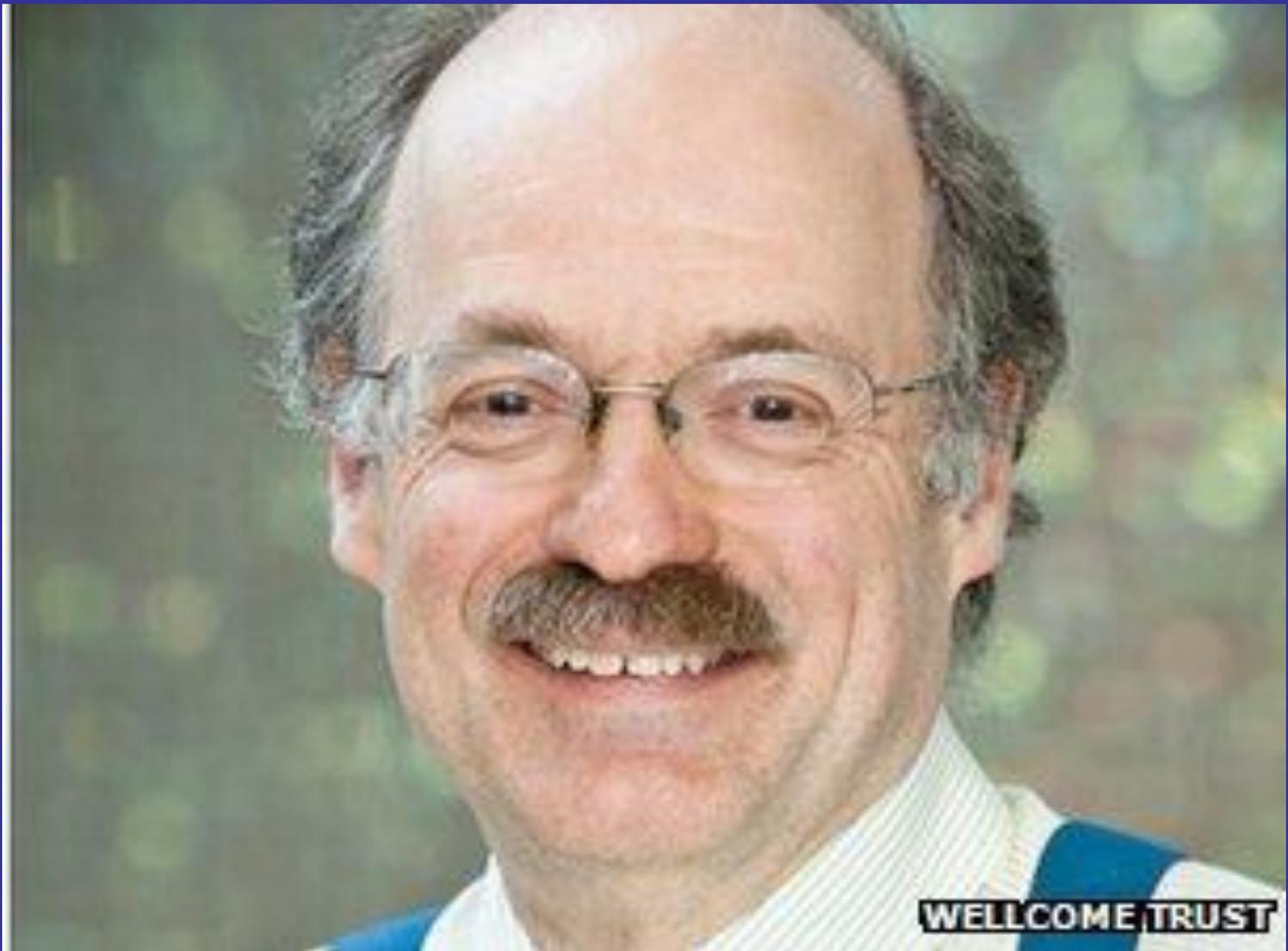
www.thelancet.com Vol 365 February 5 2005

In view of the now widespread appreciation outside academia and many research funding agencies of the need for systematic reviews of research, I challenge decision makers within those spheres who continue to frustrate efforts to promote this form of research to come out from behind their closed doors and defend their attitudes and policies in public. There is now plenty of evidence to show how patients are suffering unnecessarily as a result of their pervasive influence.

I declare that I have no conflict of interest.

*Iain Chalmers*

[ichalmers@jameslindlibrary.org](mailto:ichalmers@jameslindlibrary.org)



**Sir Mark Walport**, Director, The Wellcome Trust, and Government Chief Scientific Advisor elect.



# The ethics of research involving animals

2005

NUFFIELD  
COUNCIL ON  
BIOETHICS

“...there is a relative scarcity of systematic reviews...”  
“...it would therefore be desirable to undertake further systematic reviews and meta-analyses to evaluate more fully the predictability and transferability of animal models.”

# Why animal research needs to improve



**Many of the studies that use animals to model human diseases are too small and too prone to bias to be trusted, says Malcolm Macleod.**

Malcolm Macleod

*Nature* 477, 511 (2011) | doi:10.1038/477511a



Collaborative Approach to Meta Analysis and

•C•A•M•A•R•A•D•E•S•

Review of Animal Data from Experimental Studies

Dopamine agonists in animal models of Parkinson's disease: A systematic review and meta-analysis☆

Evelien D.M. Rooke<sup>1</sup>, Hanna M. Vesterinen<sup>1</sup>, Emily S. Sena, Kieren. J. Egan, Malcolm R. Macleod\*



The **Academy of  
Medical Sciences**

10 Carlton House Terrace  
London SW1Y 5AH  
Tel: 020 7969 5288  
Fax: 020 7969 5298  
Email: [apollo@acmedsci.ac.uk](mailto:apollo@acmedsci.ac.uk)  
Web: [www.acmedsci.ac.uk](http://www.acmedsci.ac.uk)

Professor Richard Hughes FMedSci  
Professor of Neurology  
Guy's, King's and St Thomas' School of  
Medicine

Department of Neuroimmunology  
Hodgkin Building  
Guy's Campus  
London SE1 1UL

8 March 2002

Dear Professor Hughes

**Scientific Meeting proposal**

Thank you for your response to the Academy's recent Call for Proposals.

The Officers considered *Research Synthesis* at their meeting on Monday. Though they received your draft outline with interest, they reached the decision that the whole of the meeting programme requires review, and therefore events proposed for 2003 are 'on hold' for the time being.

I hope that this news is not too disappointing. I will contact you again in due course when a possible new format for the Academy's future meetings programme is agreed.

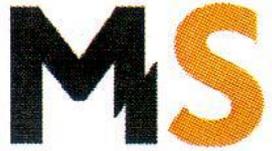
Yours sincerely

  
Susan Wicks  
Fellowship and Events Officer

**No subsequent contact made.**

Richard Hughes, personal communication,  
30 Nov 2011

RECEIVED  
12 MAR 2002



Multiple Sclerosis Society

# Research Strategy Committee

# Find out what's known already before embarking on new research

## Systematic review of therapeutic interventions in human prion disease

Lesley A. Stewart, Larysa H.M. Rydzewska, Geraldine F. Keogh and Richard S.G. Knight

*Neurology* 2008;70;1272-1281

DOI: 10.1212/01.wnl.0000308955.25760.c2

**Conclusions:** Thirty years of clinical investigation of patients with prion disease has resulted in little progress in either defining or evaluating potential treatments. Disease course and treatment of all patients must be evaluated within a structured framework, preferably within randomized controlled trials. *Neurology*<sup>®</sup> 2008;70:1272-1281



Multiple Sclerosis Society

# Research Strategy Committee



## Professor Julian Jack FRS, FMedSci, FRCP

Professor Jack was Professor of Physiology, University of Oxford from 1996-2003, and a Governor of the Wellcome Trust from 1987-2003 (Deputy Chairman of the Governors from 1994-99). He is distinguished for his outstanding theoretical and experimental contributions to the understanding of synaptic transmission in the central nervous system.



Multiple Sclerosis Society

Board of Trustees

8 December 2010

Open

**Title of paper:**

BD.5.10.F

Report of the Research Strategy Committee

**Recommendation 5:** The Society should work with its partners to promote the development of new systematic reviews in MS, and where appropriate, the updating of existing reviews. This should include the development of a framework for identifying and agreeing priority areas for review.

# Improving the translational hit of experimental treatments in multiple sclerosis

Hanna M. Vesterinen, Emily S. Sena,  
Charles ffrench-Constant, Anna Williams,  
Siddharthan Chandran and Malcolm R. Macleod

*Multiple Sclerosis*

0(00) 1–12

© The Author(s) 2010

Reprints and permissions:

[sagepub.co.uk/journalsPermissions.nav](http://sagepub.co.uk/journalsPermissions.nav)

DOI: 10.1177/1352458510379612

[msj.sagepub.com](http://msj.sagepub.com)



**Methods:** A systematic review of the literature describing experiments testing the effectiveness of interventions in animal models of multiple sclerosis was carried out. Data were extracted for reported study quality and design and for

**Conclusions:** EAE has proven to be a valuable model in elucidating pathogenesis as well as identifying candidate therapies for multiple sclerosis. However, there is an inconsistent application of measures to limit bias that could be addressed by adopting methodological best practice in study design. Our analysis provides an estimate of sample size required for different levels of power in future studies and suggests a number of interventions for which there are substantial animal data supporting efficacy.

How can we expect patients and the public to trust that we have their interests at heart if we and our professional institutions continue to acquiesce in such massive waste of the very substantial resources that they make available for medical research?

Foreword by Ben Goldacre – author of 'Bad Science'

# TESTING TREATMENTS

BETTER RESEARCH FOR BETTER HEALTHCARE

SECOND EDITION



Imogen Evans, Hazel Thornton, Iain Chalmers and Paul Glasziou

About the authors

Acknowledgements

Foreword by Ben Goldacre

Foreword to the first edition by Nick Ross

Preface

Introduction

New – but is it better?

Hoped-for effects that don't materialize

More is not necessarily better

Earlier is not necessarily better

Dealing with uncertainty about the effects of treatments

Fair tests of treatments

Taking account of the play of chance

Assessing all the relevant, reliable evidence

Regulating tests of treatments: help or hindrance?

Research – good, bad, and unnecessary

Getting the right research done is everybody's business

So what makes for better healthcare?

Research for the right reasons: blueprint for a better future

References

Additional resources

List of Vignettes

List of Key Points

Index

# AN ACTION PLAN – THINGS YOU CAN DO

## Promote research on the effects of treatments...

Encourage and work with health professionals, researchers, research funders, and others who are trying to promote research addressing inadequately answered questions about the effects of treatment which you regard as important.

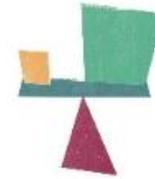
# AN ACTION PLAN – THINGS YOU CAN DO

## Promote research on the effects of treatments...

Encourage and work with health professionals, researchers, research funders, and others who are trying to promote research addressing inadequately answered questions about the effects of treatment which you regard as important.

## ...but only if it meets scientific and ethical principles

Agree to participate in a clinical trial only on condition (i) that the study protocol has been registered and made publicly available (ii) that the protocol refers to systematic reviews of existing evidence showing that the trial is justified; and (iii) that you receive a written assurance that the full study results will be published, and sent to all participants who indicate that they wish to receive them.



## Welcome to Testing Treatments interactive

How do you know whether one treatment is better than another, or whether the evidence about a treatment's benefits and harms is reliable?

Does current research address what you want to know? If not, what can you do to make treatment research more relevant to you?

Testing Treatments *interactive* (TTi) is for patients, health professionals and anyone else who is interested in these questions.

It will help you to understand the importance of having fair tests of the effects of treatments, and [how you can help make them a reality](#).



### What's new?

#### New resources

- [The placebo effect](#)
- [The Risky Business of Medical Reporting](#)
- [What did James Lind do in 1747?](#)

#### Recent comments

- [JD](#) Thanks for the link to the download!  
[Feedback](#) · 22 hours ago
- [Douglas Badenoch](#) Thanks for point this out JD, I have now rectified matters. The PDF of...  
[Feedback](#) · 2 days ago

### Share this page



### Getting started

1. [Welcome from Iain Chalmers](#)
2. [Watch the introductory video](#)
3. [Jump to the main text](#)
4. [Get more help](#)

### Translations of this website

This website has been professionally translated into the following languages:

Select Language

New translations are being added all the time. [Find out more](#).

### Other stuff

Find out [about the book](#) that provides the core content of Testing Treatments *interactive*.

Find out about the [funding, management and day-to-day running](#) of Testing Treatments *interactive*.

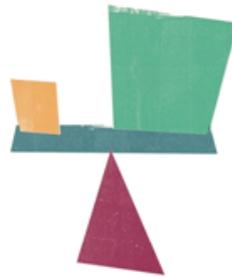


**Gerd Antes**  
Freiburg i. Br

## Willkommen beim Test Behandlungen interaktiv!

Dieses aufregende neue Entwicklung nimmt als Ausgangspunkt die [Buch-prüfung Behandlungen](#) , die vor kurzem in einer zweiten Auflage der Kritik gefeierten aktualisiert. In Kürze wird der vollständige Text dieses Buches sein, die auf dieser Website, mit der Möglichkeit zur Diskussion und Hinzufügen neuer Ressourcen. Unsere Redaktionen bereiten sich auf alle von diesem Recht nun zu verwalten.

- [Registrieren](#) , wenn Sie uns eine E-Mail an Sie, wenn wir live gehen wollen.
- Sie können auch [folgen Sie uns auf Twitter](#) .



**Woher wissen wir, ob ein bestimmtes Medikament, Therapie oder Operation wirklich funktioniert, und wie gut?**

**Wie zuverlässig ist der Beweis?**

**Klinische Studien sind wirklich unvoreingenommen?**

**Und ist aktueller Forschung auf die wirklichen Bedürfnisse der Patienten ausgerichtet?**

Mit dieser Website wollen wir mit unseren Lesern engagieren, um ein besseres Verständnis dieser Fragen. Mit anderen Worten, wir brauchen Ihre Hilfe, um zu illustrieren, zu kommunizieren und die Anwendung der Grundsätze des fairen Tests von Behandlungen.

- [Erfahren Sie mehr darüber, wie wir es tun](#) .

Testing Treatments interaktiven wird auch in einer Reihe von verschiedenen Sprachen verfügbar.

Sie können auch den vollständigen Text PDF des Buches, auch Übersetzungen lesen Sie Berichte in [der Books-](#) Sektion.

Finally, however, we need to be more efficient in preparing and updating systematic reviews.

## Policy Forum

# Seventy-Five Trials and Eleven Systematic Reviews a Day: How Will We Ever Keep Up?

Hilda Bastian<sup>1\*</sup>, Paul Glasziou<sup>2</sup>, Iain Chalmers<sup>3</sup>

**1** German Institute for Quality and Efficiency in Health Care (IQWiG), Cologne, Germany, **2** Centre for Research in Evidence-Based Practice, Faculty of Health Sciences, Bond University, Gold Coast, Australia, **3** James Lind Library, James Lind Initiative, Oxford, United Kingdom

To meet the needs of patients, clinicians, and policymakers, unnecessary trials need to be reduced, and systematic reviews need to be prioritised. Streamlining and innovation in methods of systematic reviewing are necessary to enable valid answers to be found for most patient questions. Finally, clinicians and patients require open access to these important resources.

# The steps in a Systematic Review

- What is current time for each step?
- How can we make each easier/faster?
  - Standardize
  - Streamline
  - Computerize

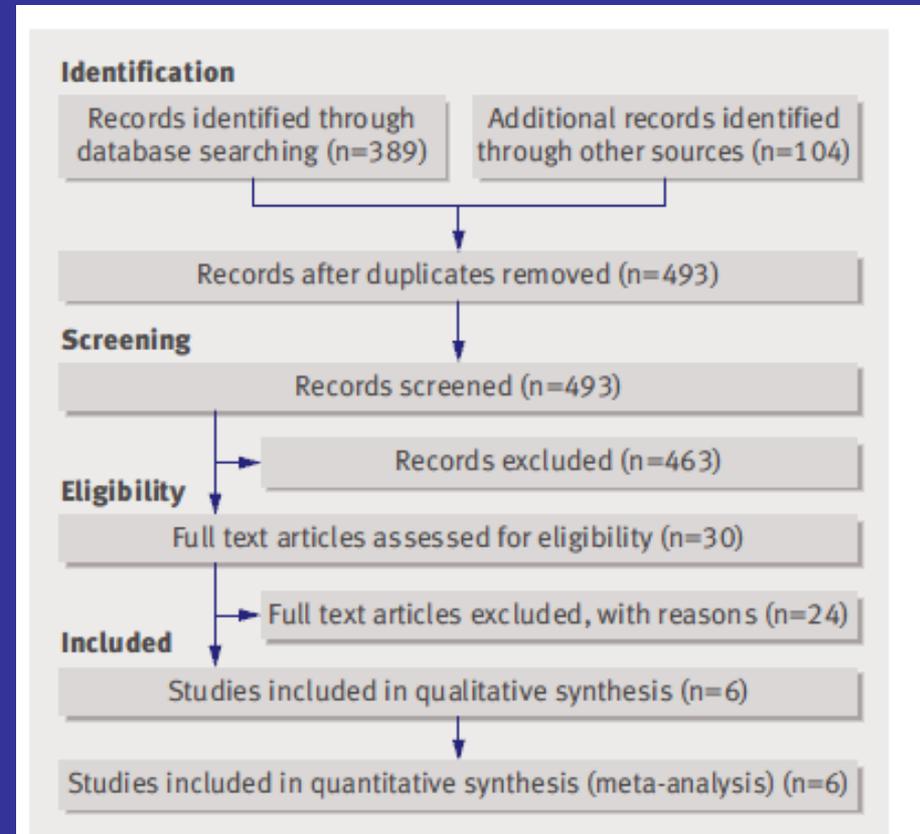


Fig 1 | Search strategy to identify trials of screening for prostate cancer

METHODOLOGY

Open Access

# Expediting systematic reviews: methods and implications of rapid reviews

Rebecca Ganann\*, Donna Ciliska and Helen Thomas

“[I]t is important that researchers undertaking reviews within the rapid to systematic continuum provide detailed descriptions of methods used and discuss the implications of their chosen methods in terms of **potential bias** introduced”.

# Your ideas please!

For any review step, do you have tips to:

- Standardize?
- Streamline?
- Automate?

**Ideas, please, to:**

[pglaszio@bond.edu.au](mailto:pglaszio@bond.edu.au)