

“Meeting the research information needs of patients and clinicians more effectively”

Iain Chalmers

Editor, *James Lind Library*

www.jameslindlibrary.org



equator
network

1st Annual Lecture

The problem

**People are suffering and dying
unnecessarily**

**because of insufficient
clinician and patient access**

**to reliable, up-to-date information
about completed and ongoing research**

*Why have I been obsessed for
forty years with the need to
meet the research information
needs of patients and clinicians
more effectively?*

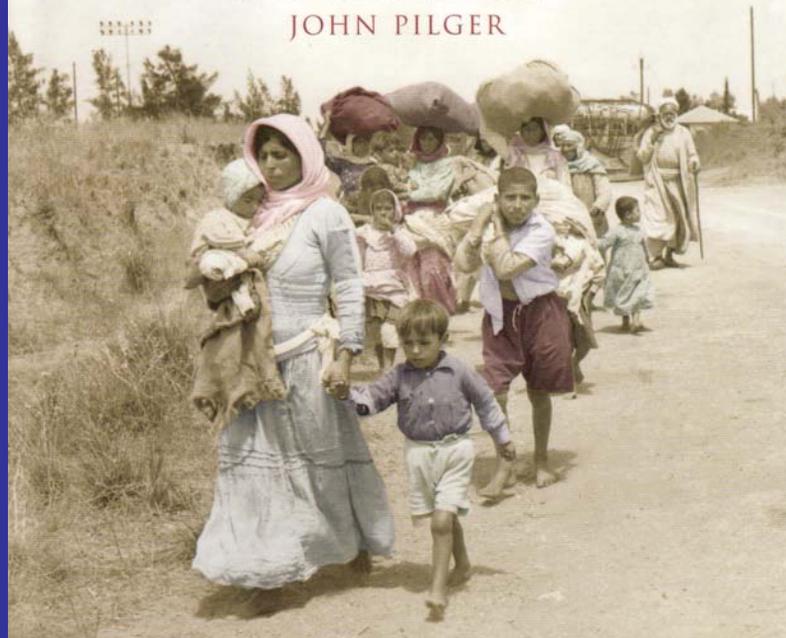
My experience as a clinician

ILAN PAPPE

The ETHNIC
CLEANSING *of*
PALESTINE

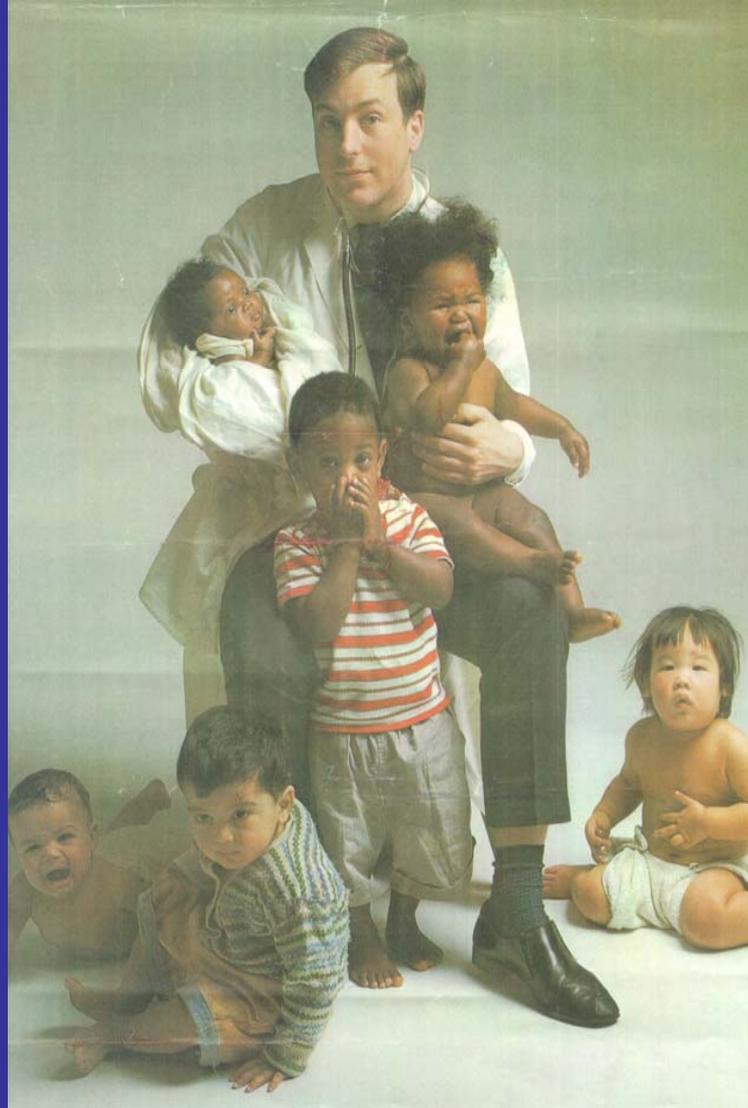
'Ilan Pappé is Israel's bravest, most principled,
most incisive historian.'

JOHN PILGER



60 years ago

**This do-gooder
needs your help**



Fund raising advert for the United Nations Association



TEACH THY TONGUE TO
SAY I DO NOT KNOW
AND THOU SHALT PROGRESS

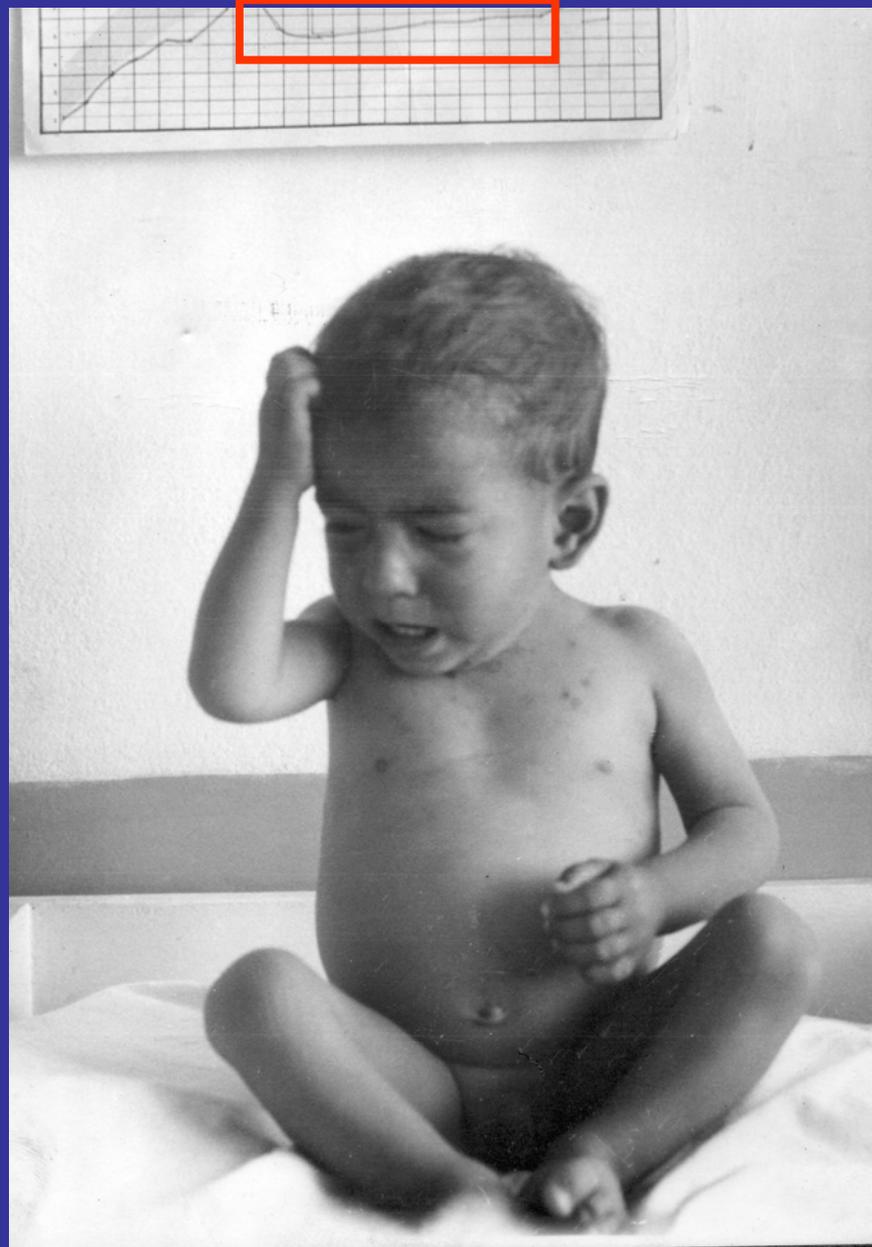
I could have served my Palestinian patients and their community better if I had had:

more humility

access to systematic reviews of relevant clinical trials.



UNRWA Clinic, Khan Younis Camp, Gaza Strip, 1969/70.



Severe malnutrition following measles

A systematic review of clinical trials reported between 1939 and 1967 shows that:

antibiotics prescribed for children with measles can reduce their risk of developing pneumonia

Which antibiotic should I use in the 21st century, and at which dose, frequency and duration?

Paul Glasziou et al. What is missing from treatment descriptions in trials and reviews? BMJ In press.

BMJ 23 October 2006

Prophylactic antibiotics to prevent pneumonia and other complications after measles: community based randomised double blind placebo controlled trial in Guinea-Bissau

May-Lill Garly, Carlitos Balé, Cesário Lourenco Martins, Hilton C Whittle, Jens Nielsen, Ida M Lisse, Peter Aaby

Interventions Sulfamethoxazole-trimethoprim (**co-trimoxazole**) or placebo for **seven days.**

Conclusions The group that received prophylactic antibiotics **had less pneumonia and conjunctivitis** and had significantly **higher weight gains** in the month after inclusion. The results indicate that prophylactic antibiotics may have an important role in the management of measles infection in low income countries.

Trial registration Clinical trials NCT001168532.

Are there any relevant ongoing controlled trials addressing these uncertainties?



World Health
Organization

INTERNATIONAL CLINICAL TRIALS REGISTRY PLATFORM
SEARCH PORTAL

[Home](#)

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[ICTRP website](#)

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[Search tips](#)

Results of the search for **measles AND antibiotics in the Title**, Main ID, Countries, Interventions and Condition fields.

No results found!

My experience as a patient

What do I want from health research and researchers when I am a patient?

Iain Chalmers

BRITISH MEDICAL JOURNAL, *20th May 1995, Vol. 310, Pages 1315-1318*

systematic reviews of carefully controlled research will be required to produce the kind of evidence that I am likely to believe, and that I would wish those offering me care to take into account.

Retained/impacted ear wax

a problem causing impaired hearing and localised eczema,
sometimes associated with serious complications,
which costs the NHS £50 million a year

Otolaryngology–Head and Neck Surgery (2007) 137, S69-S71

INVITED ARTICLE

Better information systems are needed to help patients and clinicians integrate clinical research within everyday clinical practice

Iain Chalmers, Oxford, UK



RESOURCES

Evidence Based Reviews

Bandolier, Cochrane Library, DARE, HTA Database, NHS EED

Guidance

CKS (incorporating Prodigy), National Library of Guidelines, NICE Guidance, Protocols and Care Pathways and selected International Guidelines

Specialist Libraries

Collections of the best available evidence for different communities of practice

Books, Journals and Healthcare

Databases

AMED, British Nursing Index, CINAHL, E-books, EMBASE, HMIC, MEDLINE, My Journals, PsycINFO, PubMed, Databases from Dialog



Burton MJ, Doree CJ. Ear drops for the removal of ear wax. *Cochrane Database of Systematic Reviews* 2003, Issue 3.

"...ear drops (of any sort) can help to remove ear wax..."

"...water and saline drops appear to be as good as more costly commercial products..."

"...The quality of the trials was generally low and more research is needed."

What do I want from health research and researchers when I am a patient?

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BRITISH MEDICAL JOURNAL, 20th May 1995, Vol. 310, Pages 1315-1318

systematic reviews of carefully controlled research will be required to produce the kind of evidence that I am likely to believe, and that I would wish those offering me care to take into account.

when the relative merits of alternative forms of care are uncertain, I want to be offered the opportunity to participate in properly controlled research

Welcome to the WHO International Clinical Trials Registry Platform

The mission of the WHO Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.

The registration of all interventional trials is a scientific, ethical and moral responsibility.

An evaluation of the self-use of bulb syringes for the self-treatment of ear wax and their impact on primary care workload - a randomised controlled trial

ISRCTN

ISRCTN71172551



MEDICAL EMERGENCY CARD

supplied by

VOLUNTARY EUTHANASIA SOCIETY

3 Prince of Wales Terrace London W8 5PG 0171 937 7770

My Full name is

IAIN GEOFFREY CHALMERS

If there is no reasonable prospect of recovery I do NOT wish to be resuscitated or my life to be artificially prolonged
My Advance Directive is lodged with

DR. ANDY CHIVERS
01865 - 558861

1. Medical Information eg. blood group

Invite me to participate in all randomized controlled trials for which I am potentially eligible

2. After my death my organs may be used for medical purposes

YES

3. Next of Kin

JAN CHALMERS
01865 - 554949

Signature

Date

Iain Chalmers 7/12/98

In summary

As a clinician and as a patient, I want reader access to:

- up-to-date, valid, systematic reviews
- with details sufficient to inform my decision making; and
- information about relevant unpublished and ongoing trials

Improving reports of research



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network



What guidance is available for reporting research studies?

In addition to the Uniform Requirements, a number of reporting guidelines were developed by groups of experts to facilitate reporting of research studies. Medical journals, including [BMJ](#), [JAMA](#), [Lancet](#), and [NEJM](#) often require compliance to all or some of the following reporting guidelines:

- [CONSORT Statement](#) (reporting of randomised controlled trials)
- [STARD](#) (reporting of diagnostic accuracy studies)
- [STROBE](#) (reporting of observational studies in epidemiology)
- [QUOROM](#), recently renamed [PRISMA](#) (reporting of systematic reviews)
- [MOOSE](#) (reporting of meta-analyses of observational studies)

Formal sources of evidence

Published
Clinical
Studies

Referenced

Captured

Systematic
Reviews

Quality
Labelled

Summaries

Pathways,
Guidelines &
Standards

Tailored Content

Models &
Tools

Quality Labelled

Captured

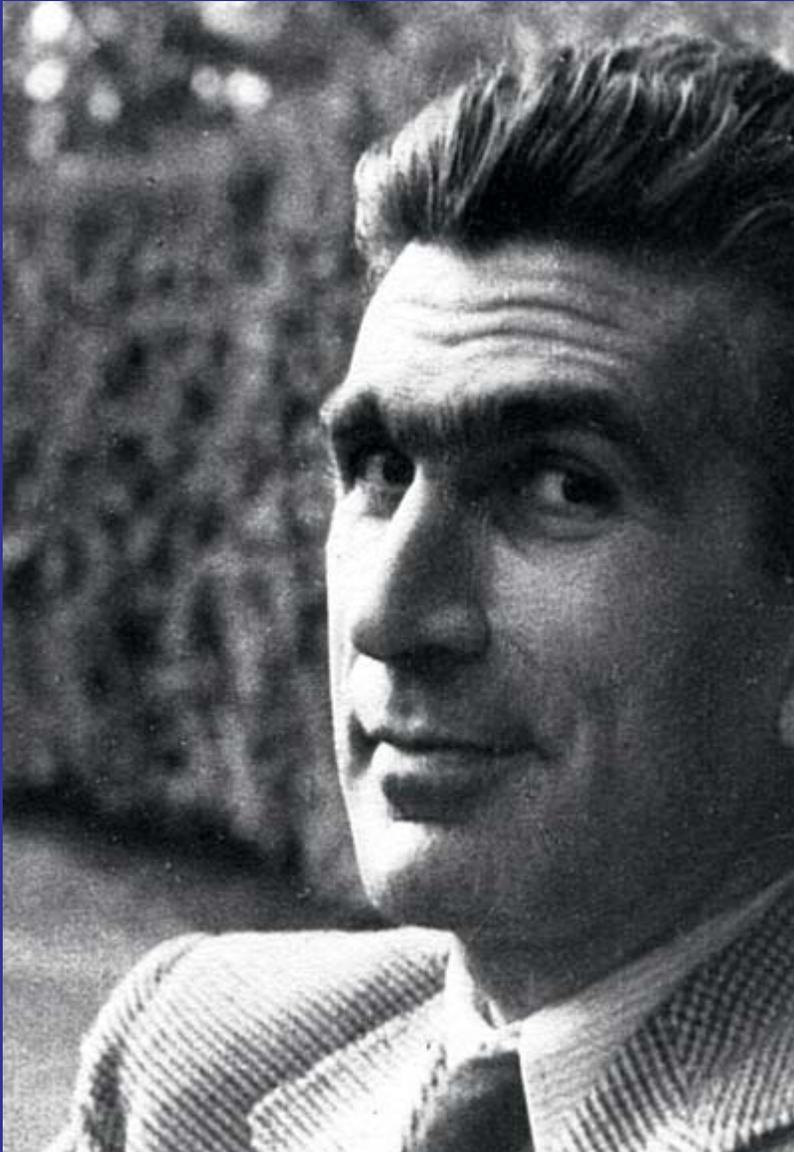
Referenced

"Local Experience"



CONSORT, STARD,
and STROBE

QUOROM/PRI SMA
and MOOSE



Marc Daniels, 1950

“...Some essential details are omitted from the report, possibly because of required brevity. This leads one to consider if it is possible, in planning a trial, in reporting the results, or in assessing the published reports of trials, to apply criteria which must be satisfied in the analysis is to be entirely acceptable.”

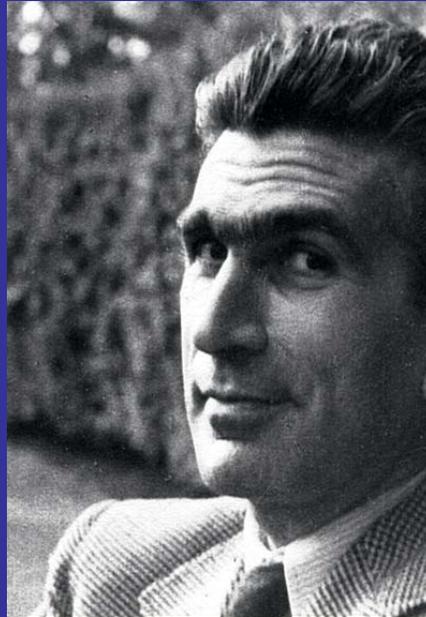
Scientific appraisal of new drugs in tuberculosis. American Review of Tuberculosis 61:751-756.

The team responsible for designing, coordinating and reporting the MRC randomised trial of streptomycin for pulmonary tuberculosis, 1947-1948

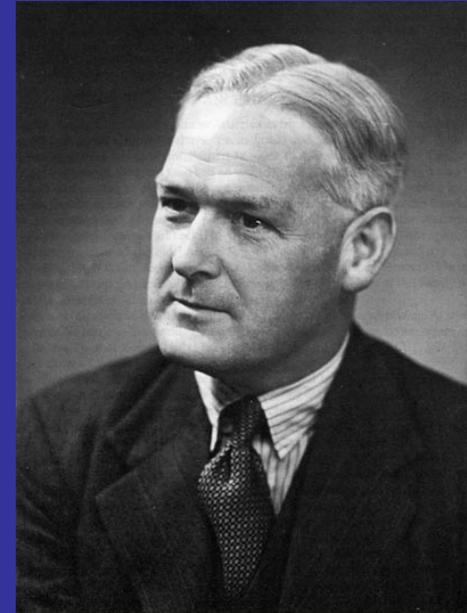
(with administrative assistance from Mrs Chirene Agnew)



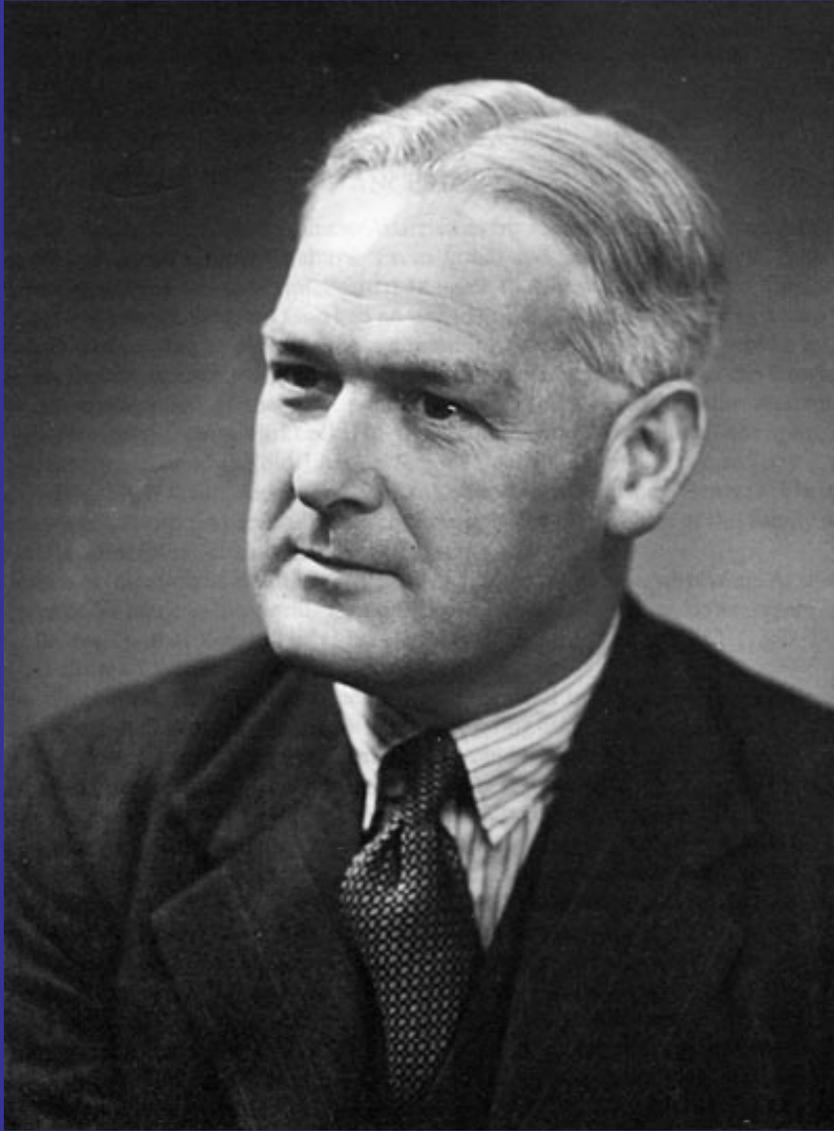
Philip D'Arcy Hart



Marc Daniels



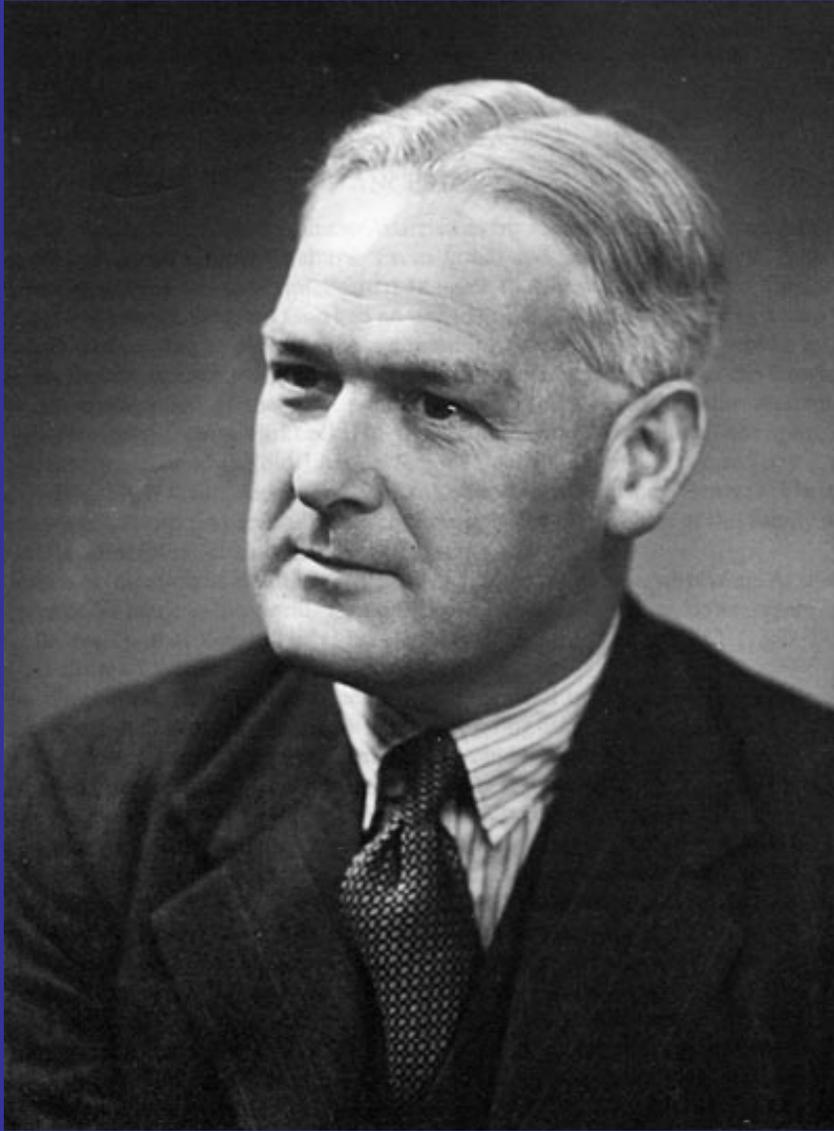
Austin Bradford Hill



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

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

Is the study worth doing?

Lucy M Carpenter

Department of Public Health and Primary Care, University of Oxford,
Gibson Building, Radcliffe Infirmary, Oxford OX2 6HE, UK
(L M Carpenter PhD)

Vol 342 • July 24, 1993

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

Lancet 1993;342:221-223.

The use of systematic reviews when designing studies

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

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

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

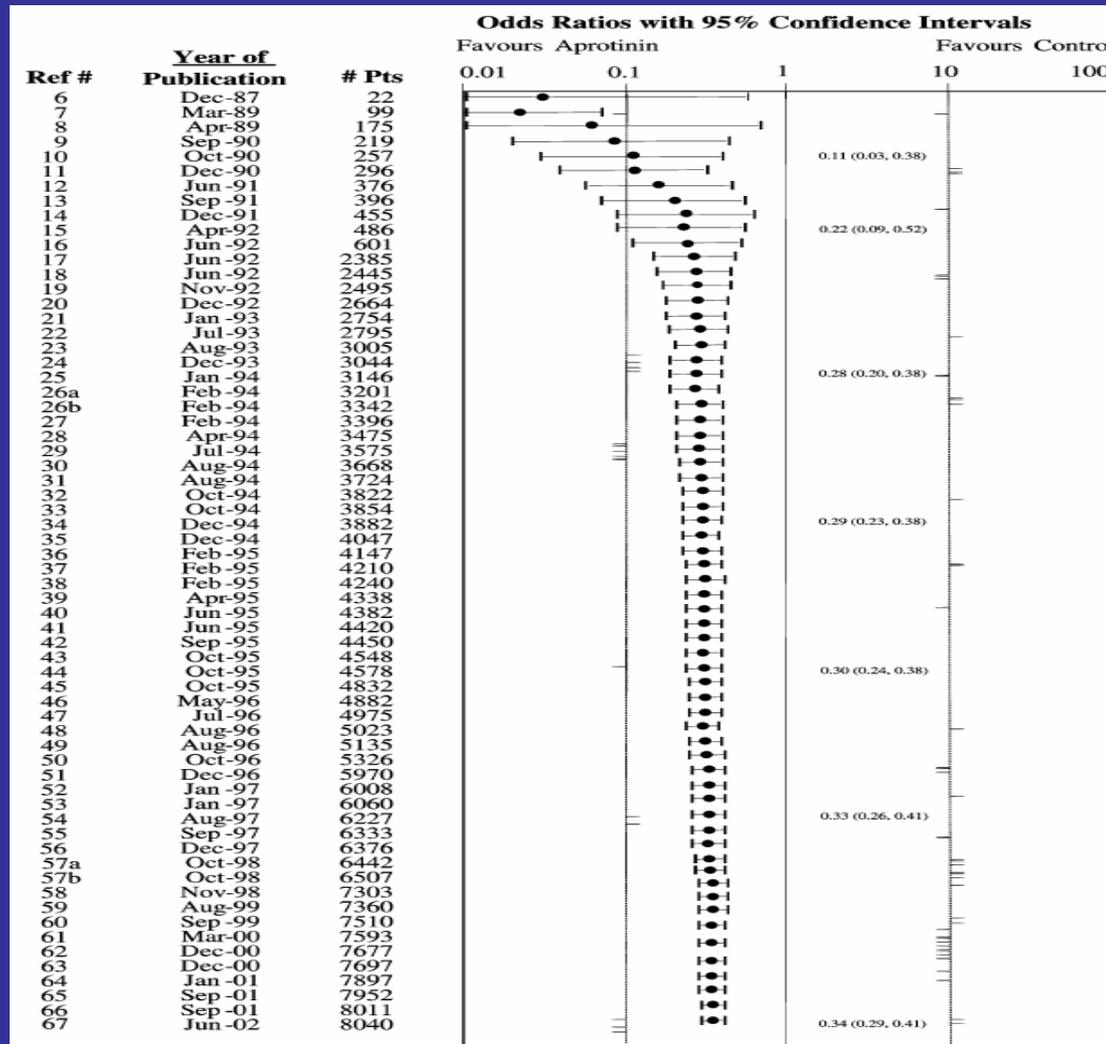
Conclusions: Thirty years of clinical investigation of patients with prion disease has resulted in little progress in either defining or evaluating potential treatments. Disease course and treatment of all patients must be evaluated within a structured framework, preferably within randomized controlled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

Randomized controlled trials of aprotinin in cardiac surgery: could clinical equipoise have stopped the bleeding?

Dean Fergusson^{a,b}, Kathleen Cranley Glass^{b,c}, Brian Hutton^a and Stan Shapiro^{b,c,d}

Clinical Trials 2005; 2: 218–232

Cumulative estimate of the effect of aprotinin on perioperative blood transfusion, 1987-2002.



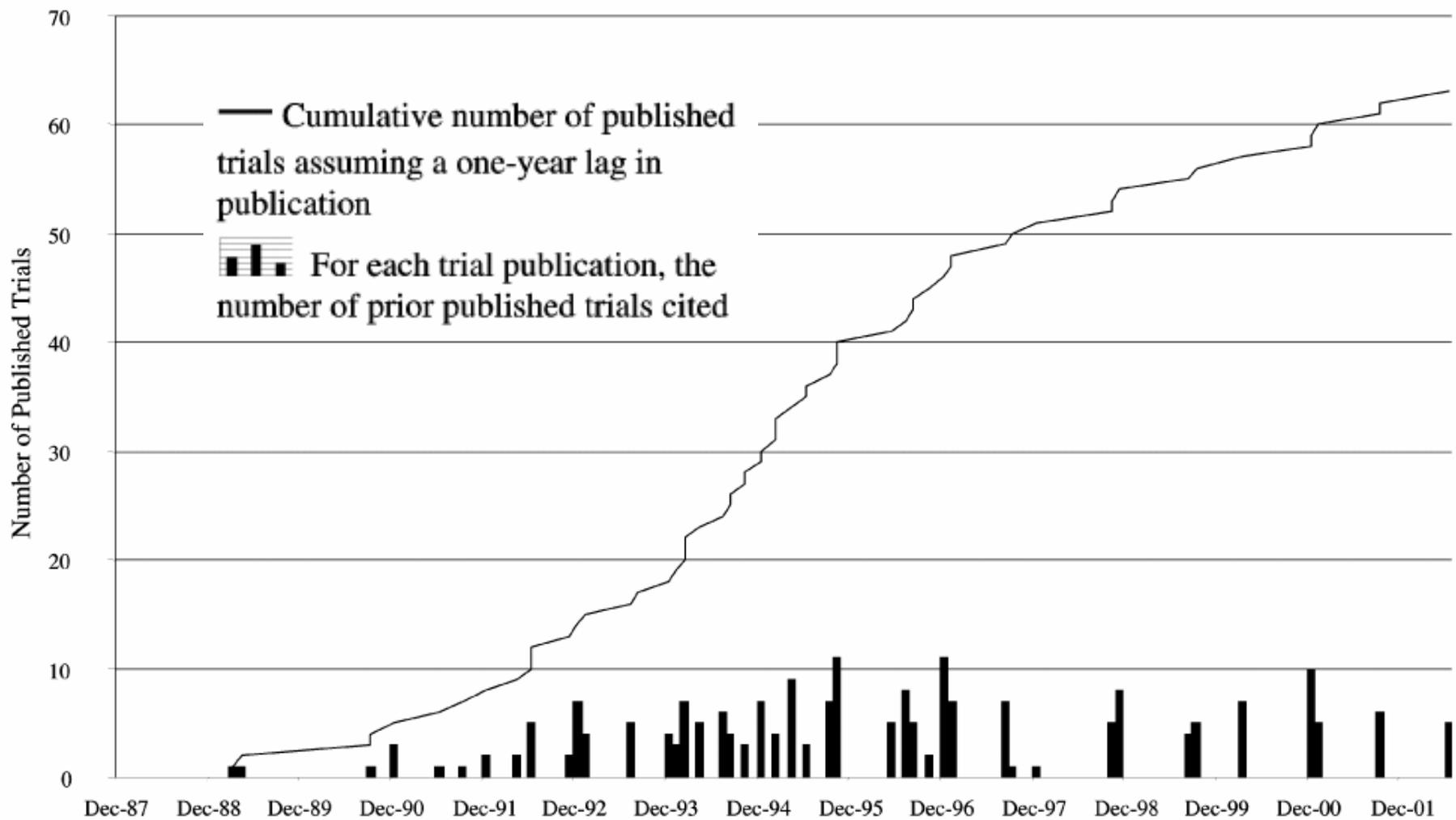


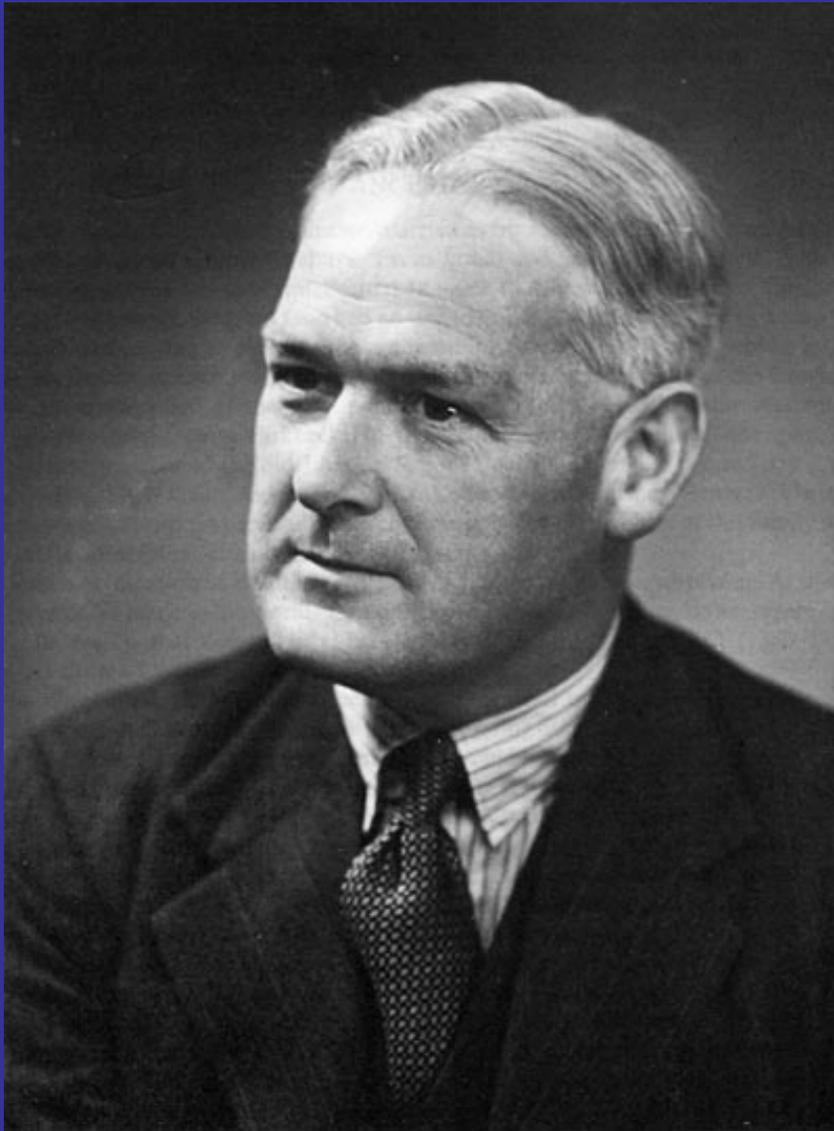
Figure 6 Citations of prior publications.

The failure of clinical scientists to prepare and refer to systematic reviews of existing evidence has resulted in:

harm and wasted resources in health care

and

wasted resources in health research



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?**

Discussion Sections in Reports of Controlled Trials Published in General Medical Journals

Islands in Search of Continents?

Michael Clarke, DPhil; Iain Chalmers, MSc

JAMA. 1998;280:280-282

Classification of Discussion sections in RCT reports published in May issues of *Ann Int Med*, *BMJ*, *JAMA*, *Lancet*, and *N Eng J Med*

	1997 n=26		
First trial addressing the question	1		
Contained an updated systematic review integrating the new results	2		
Discussed a previous review but did not attempt to integrate new results	4		
No apparent systematic attempt to set new results in context of other trials	19		

The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19 435 patients with acute ischaemic stroke

*International Stroke Trial Collaborative Group**

Taking the IST together with the comparably large Chinese Acute Stroke Trial, aspirin produces a small but real reduction of about 10 deaths or recurrent strokes per 1000 during the first few weeks.

Discussion Sections in Reports of Controlled Trials Published in General Medical Journals

Mike Clarke, DPhil

Phil Alderson, MBChB

Iain Chalmers, DSc

JAMA. 2002;287:2799-2801

Classification of Discussion sections in RCT reports published in May issues of *Ann Int Med*, *BMJ*, *JAMA*, *Lancet*, and *N Eng J Med*

	1997 n=26	2001 n=33	
First trial addressing the question	1	3	
Contained an updated systematic review integrating the new results	2	0	
Discussed a previous review but did not attempt to integrate new results	4	3	
No apparent systematic attempt to set new results in context of other trials	19	27	

Reports of clinical trials should begin and end with up-to-date systematic reviews of other relevant evidence: a status report

Mike Clarke¹ Sally Hopewell¹ Iain Chalmers²

J R Soc Med 2007;**100**:187-190

Classification of Discussion sections in RCT reports published in May issues of *Ann Int Med*, *BMJ*, *JAMA*, *Lancet*, and *N Eng J Med*

	1997 n=26	2001 n=33	2005 n=18
First trial addressing the question	1	3	3
Contained an updated systematic review integrating the new results	2	0	0
Discussed a previous review but did not attempt to integrate new results	4	3	5
No apparent systematic attempt to set new results in context of other trials	19	27	10

Why promote the findings of single research studies?

PERSONAL VIEW **Paul Wilson, Mark Petticrew**

"Since when has a single scientific study constituted 'the truth' about anything?"

Medical journals can do more to ensure that researchers actually do discuss the findings of primary studies in the context of the existing and relevant evidence base. The Academy of Medical Sciences in London has recently argued that researchers, funders, and institutions should take greater responsibility for the accurate communication of non-experimental research. In truth, the research community as a whole needs to be more circumspect when it comes to the active promotion of primary research. Although all research has an audience, and should be made accessible, not all research can or should have an impact on practice or policy.

Putting clinical trials into context

In recognition that journal editors have a key part to play in ensuring that published research is presented in a way that clearly illustrates why it was necessary and what impact a particular trial has on the existing state of knowledge, *The Lancet* has decided to update its policies in this area. From August, 2005, we will require authors of clinical trials submitted to *The Lancet* to include a clear summary of previous research findings, and to explain how their trial's findings affect this summary.

Charles Young, Richard Horton
The Lancet, London NW1 7BY, UK

www.thelancet.com Vol 366 July 9, 2005

Improving syntheses of research findings (systematic reviews)



1987

Cynthia Mulrow.

**The medical review article:
state of the science.**

Ann Int Med 10:485-88.



1988

Andy Oxman, Gordon Guyatt.

**Guidelines for reading literature
reviews.**

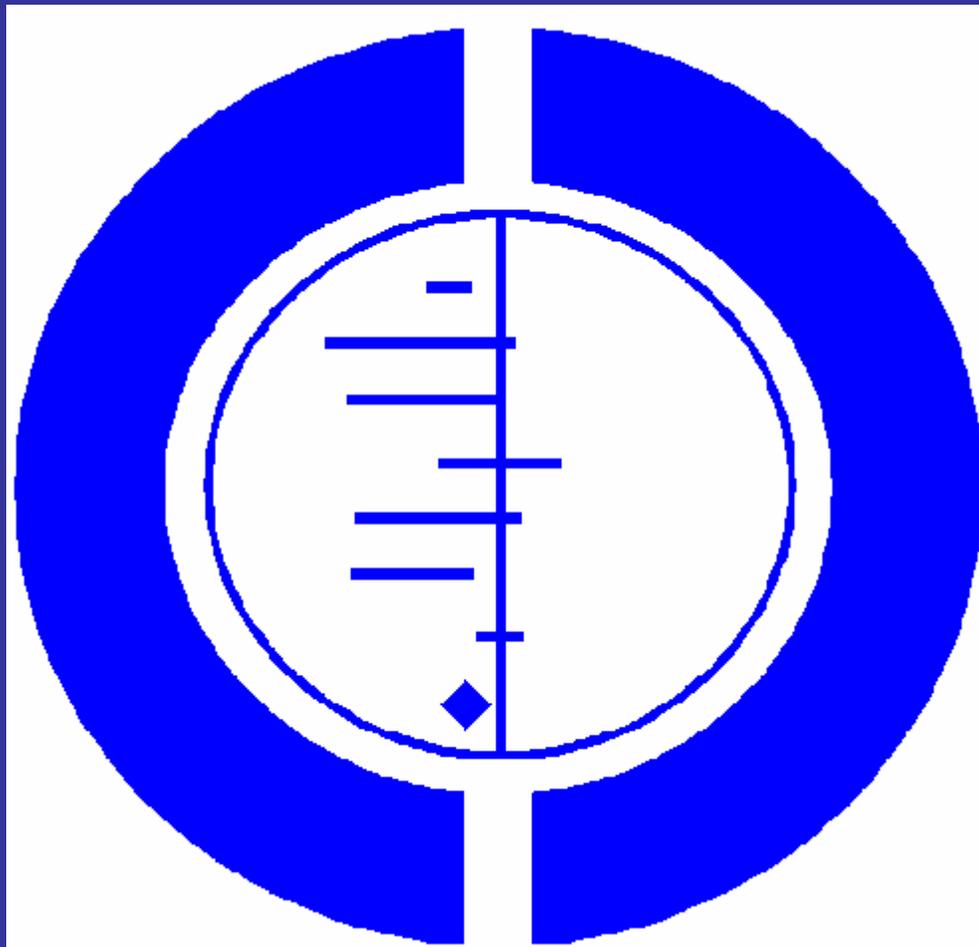
Can Med Assoc J 138:697-703.

**Electronic dissemination and
maintenance of systematic reviews of
controlled trials of perinatal care:**

1988-1992: *Oxford Database of Perinatal Trials* (ODPT)

1993-1995: *Cochrane Pregnancy and Childbirth Database* (CCPC)

1995- : *Cochrane Database of Systematic Reviews* (CDSR)



The Cochrane Collaboration

Preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions

[30 March 1994]

SECTION VI:

PREPARING AND MAINTAINING SYSTEMATIC REVIEWS

(‘The Cochrane Collaboration Tool Kit’)

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Associate Editors:

Iain Chalmers, Mike Clarke, Murray Enkin, Ken Schulz, Mark Starr

Citation frequency of *Cochrane Database of Systematic Reviews (CDSR)* (June 2008):

NEJM	186 000 citations
Lancet	136 000
JAMA	104 000
BMJ	62 000
Annals	41 000
Archives	30 000
Am J Med	22 000
Cochrane	15 000

First Impact Factor for *CDSR*: 4.654

[14th of 100 journals in Thomson ISI category for Medicine, General & Internal]

**What about relevant research
that isn't reported at all?**

Underreporting Research Is Scientific Misconduct

Iain Chalmers, FRCOG

JAMA, March 9, 1990—Vol 263, No. 10

“...failure to provide adequate, publicly available reports of the results of clinical trials does an injustice to the patients who have participated in them...”

Publication bias can kill!

Cowley et al. 1993: *“When we carried out our study in 1980 we thought that the increased death rate that occurred in the drug group was an effect of chance...The development of the drug was abandoned for commercial reasons, and this study was therefore never published; it is now a good example of ‘publication bias’. The results described here...might have provided an early warning of trouble ahead.”*

At the peak of their use in the late 1980s, it has been estimated that these drugs killed as many Americans **every year** as were killed during the whole of the Vietnam war.

Moore 1995.

Welcome to the WHO International Clinical Trials Registry Platform

The mission of the WHO Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.

The registration of all interventional trials is a scientific, ethical and moral responsibility.

**An illustration of the way that
clinical researchers and 'the
system' are failing patients**

**What is the best treatment
for vitiligo?**



Cochrane Review

**Whitton ME, Ashcroft DM, Barrett C W,
Gonzalez U.**

Interventions for vitiligo.

*The Cochrane Database of Systematic
Reviews 2006, Issue 1.*

Findings (1)

- 19 RCTs, generally short-term, poorly designed, and poorly reported
- No two trials compared the same interventions
- No trials on cosmetic camouflage or depigmentation
- Only one study examined the psychological effects of treatments

Findings (2)

- Large variations in methods for scoring re-pigmentation.
- No reliable data on patient-important outcomes or quality of life measures.
- Many trials too short-term to indicate any relevant longer term effects, whether beneficial or unwanted.

Findings (3)

Limited evidence, from single randomised trials, that there may be short-term benefits from:

- corticosteroids

- topical tacrolimus

- various forms of ultraviolet light

- gingko biloba

- skin grafting

Are there any potentially relevant unpublished trials?

Are there any potentially relevant unpublished trials?

Yes, there's an unpublished controlled trial of **pseudocatalase**



Before pseudocatalase



After pseudocatalase

- A 12-month RCT of pseudocatalase was done in 1997.
- The trial has still not been reported publicly in 2008.
- The research participants have not been told anything about the study findings.
- The responsible NHS Research Governance Department has so far been unable to account for this.

In summary

Over a period of more than 40 years, clinical researchers have:

- failed to do randomised trials of good quality
- failed to report all of the trials to which patients have contributed; and
- are only now beginning to show signs of collaborating in clinical research to meet the information needs of patients with vitiligo.



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network

Promoting improvements in the
quality of reports of research
should help to improve the
quality and relevance of research

**Some ways to improve the
relevance of research to
patients and clinicians**

1. Find out which unanswered questions are of importance to patients, carers and clinicians

Research priorities among patients with osteoarthritis of the knee compared with researchers' priorities (Tallon et al. 2000).

Interventions for osteoarthritis of the knee	Research priorities among 67 patients		Interventions evaluated in 460 RCTs	
	Number	Per cent	Number	Per cent
Knee replacement	24	35.8	13	2.8
Education and advice	14	20.9	14	3.0
Drugs	6	9.0	380	82.6
Complementary therapy	4	6.0	29	6.3
Physical therapies	2	3.0	24	5.2
Miscellaneous others	16	23.9		
No intervention	1	1.5		

**2. Find out which outcomes
are important to patients**

Commentary

Open Access

OMERACT: An international initiative to improve outcome measurement in rheumatology

Peter Tugwell*¹, Maarten Boers², Peter Brooks³, Lee Simon⁴, Vibeke Strand⁵ and Leanne Idzerda⁶

Abstract

OMERACT is the acronym for an international, informally organized network initiated in 1992 aimed at improving outcome measurement in rheumatology. Chaired by an executive committee, it organizes consensus conferences in a 2-yearly cycle that circles the globe. Data driven recommendations are prepared and updated by expert working groups. Recommendations include core sets of measures for most of the major rheumatologic conditions. Since 2002 patients have been actively engaged in the process.

Priority treatment outcome
from a survey of patients
with rheumatoid arthritis
was not pain

Priority treatment outcome
from a survey of patients
with rheumatoid arthritis
was not pain

It was fatigue!



THE JAMES LIND ALLIANCE
Tackling treatment uncertainties together
Research priorities in Asthma

**Description of a workshop to set priorities for
treatment uncertainty research in Asthma, March 2007**

1 (a) What are the adverse effects associated with long-term use of short and long-acting bronchodilators; inhaled and oral steroids; and combination and additive therapies in adults?

(N.B this includes children aged 12 years old and over)

1 (b) What are the adverse effects associated with long-term use of short and long-acting bronchodilators; inhaled and oral steroids; and combination and additive therapies in children?

STROBE and MOOSE

STROBE Statement

STrengthening the Reporting of OBservational studies in
Epidemiology

STROBE checklist, version 4 (as published in Oct / Nov 2007)

STROBE checklist for cohort, case-control, and cross-sectional studies (combined)

[pdf download](#) [Word download](#)

Checklist for cohort studies

[pdf download](#) [Word download](#)

Checklist for case-control studies

[pdf download](#) [Word download](#)

Checklist for cross-sectional studies

[pdf download](#) [Word download](#)

Meta-analysis of Observational Studies in Epidemiology

A Proposal for Reporting

3. Make uncertainties explicit

One creditworthy contribution to posterity (based on the Johari Window)



“As we know, there are **known knowns**. There are things we know we know.

“We also know there are **known unknowns**. That is to say we know there are some things we do not know.

“But there are also **unknown unknowns**, the ones we don't know we don't know.”

Donald Rumsfeld

Database of
Uncertainties about the
Effects of
Treatments

DUETS: www.duets.nhs.uk

An initiative of the **National
Therapeutic Ignorance Service**

Uncertainties in DUETs

[June 2008]

- ⊕ Cancer (23)
- ⊕ Cardiovascular diseases (27)
- ⊕ Ear nose and throat disorders (118)
 - Eyes and vision (1)
 - Gastroenterological and liver diseases (15)
 - Haematological disorders (7)
 - Infection (9)
- ⊕ Mental health (172)
 - Musculoskeletal diseases (10)
 - Neonatal diseases (8)
- ⊕ Neurological conditions (12)
- ⊕ Nutritional metabolic and endocrine disorders (55)
 - Oral and dental conditions (2)
- ⊕ Respiratory diseases (315)
- ⊕ Skin disorders (64)
 - Symptoms (4)
 - Trauma (6)
- ⊕ Urological and genital disorders (4)
- ⊕ Women's health conditions (71)

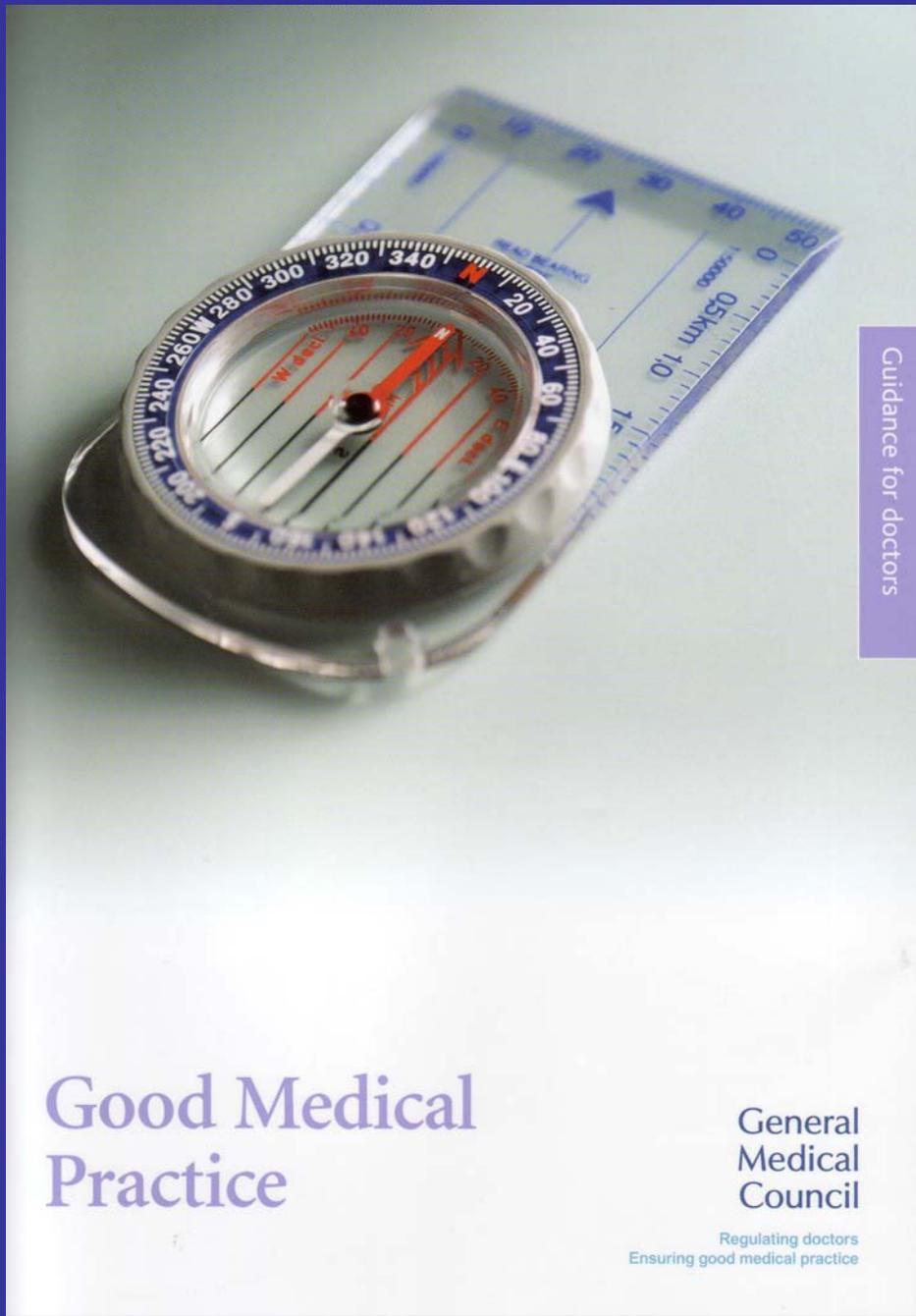
Sources of uncertainties about the effects of treatments

From patients (241)	From carers (67)	From clinicians (79)	Research recommendations (408)	Ongoing research (88)
-------------------------------	---------------------	-------------------------	-----------------------------------	--------------------------

What is the best way of dealing with allergies to cats & dogs to prevent asthma?

DUETs module	Asthma
Record type	Uncertainties identified from patients' questions
Source	Asthma UK Adviceline
Why is there uncertainty?	Reliable up-to-date systematic reviews have revealed important continuing uncertainties about treatment effects
References to reliable up-to-date systematic reviews:	Kilburn S, Lasserson TJ, McKean M. Pet allergen control measures for allergic asthma in children and adults. Cochrane Database of Systematic Reviews 2001, Issue 1. Art. No.: CD002989. DOI: 10.1002/14651858.CD002989 .
What is needed?	Further research
Systematic reviews that need updating or extending	Abramson MJ, Puy RM, Weiner JM. Allergen immunotherapy for asthma. Cochrane Database of Systematic Reviews 2003, Issue 4. Art. No.: CD001186. DOI: 10.1002/14651858.CD001186 .
Systematic reviews in preparation	<i>None identified</i>
Ongoing controlled trials	Manchester Asthma and Allergy Study - Primary prevention of asthma and allergy by allergen avoidance in high risk infants ISRCTN63558189 Prevention of asthma in children at high risk of developing asthma ISRCTN ISRCTN66748327 Air cleaners for children and adolescents with asthma and dog allergy NCT00220753

4. Do research to address uncertainties



Guidance for doctors

Good Medical Practice

General Medical Council

Regulating doctors
Ensuring good medical practice

Maintaining and improving your performance

14 You must work with colleagues and patients to maintain and improve the quality of your work and promote patient safety. In particular, you must:

(f) help to resolve uncertainties about the effects of treatments

For over 30 years there was uncertainty about whether to use caffeine in newborn infants to reduce apnoeic episodes.

Failure to address this uncertainty has had terrible, enduring consequences for children and adults.

Long-Term Effects of Caffeine Therapy for Apnea of Prematurity

Barbara Schmidt, M.D., Robin S. Roberts, M.Sc., Peter Davis, M.D., Lex W. Doyle, M.D., Keith J. Barrington, M.D., Arne Ohlsson, M.D., Alfonso Solimano, M.D., Win Tin, M.D., for the Caffeine for Apnea of Prematurity Trial Group

Conclusions Caffeine therapy for apnea of prematurity improves the rate of survival without neurodevelopmental disability at 18 to 21 months in infants with very low birth weight.

New Eng J Med 2007; 357:1893-1902

An exemplar of what is
needed

Assessing the effects of
administration of systemic
corticosteroids in acute
traumatic brain injury

A systematic review of existing knowledge

Corticosteroids in acute traumatic brain injury: systematic review of randomised controlled trials

Philip Alderson, Ian Roberts

Alderson P, Roberts I (1997). *BMJ* 314:1855-9;
and *Cochrane Database of Systematic Reviews*.

The review revealed important uncertainty about whether systemic steroids did more good than harm.

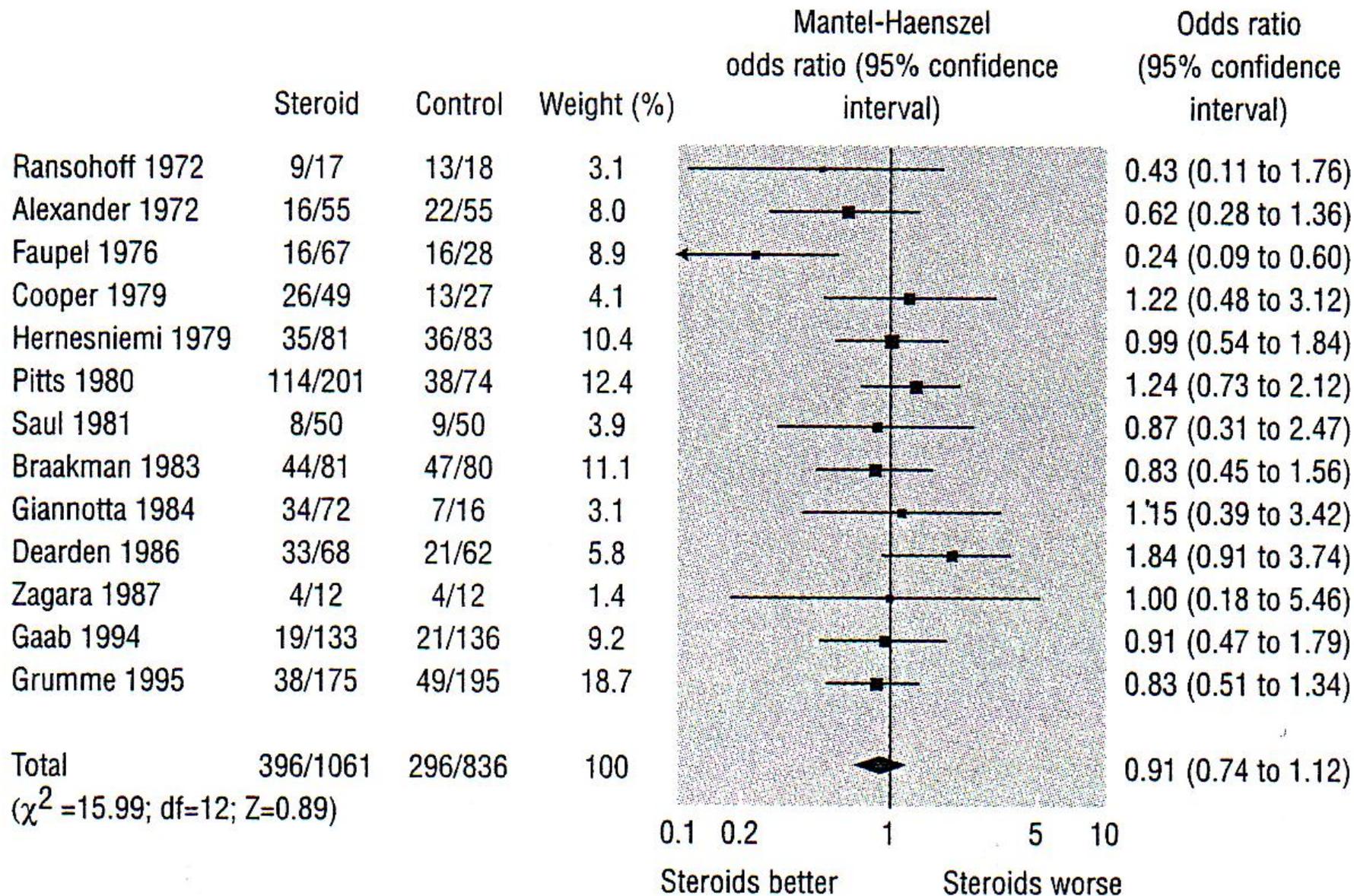


Fig 1 Summary odds ratio for death at end of study

Addressing an important uncertainty

Because the systematic review and a survey of clinical practice had revealed important uncertainty, **a large, publicly-funded, multicentre randomized trial was organised to address the uncertainty.**

The trial was registered prospectively on the ISRCTN register,

The protocol for the trial was published in BioMed Central.

Effect of intravenous corticosteroids on death within 14 days in 10 008 adults with clinically significant head injury (MRC CRASH trial): randomised placebo-controlled trial

*CRASH trial collaborators**

Lancet 2004; 364: 1321-28

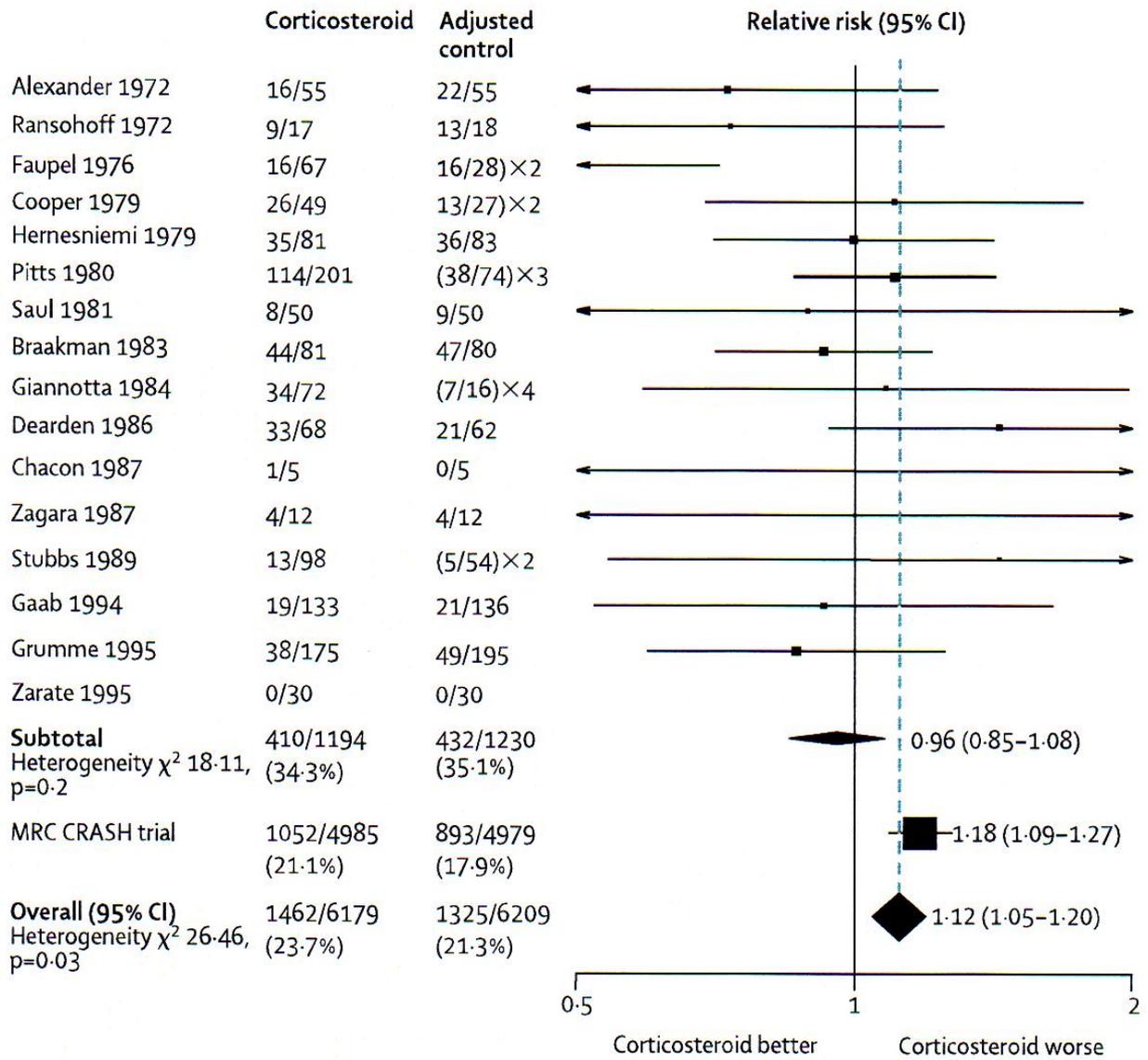


Figure 5: Updated meta-analysis of effect of corticosteroids on death after head injury

- **The report of the CRASH trial is exemplary because:**
- it refers to current uncertainty about the effects of a treatment, manifested in a **systematic review of all the existing evidence**, and in **variations in clinical practice**
- It notes that the **trial was registered** and the **protocol published** prospectively
- it sets the new results in the context of **an updated systematic review of all of the existing evidence**
- it provides readers with **all the evidence needed for action** to prevent thousands of iatrogenic deaths

How can medical journals help prevent poor medical research? Some opportunities presented by electronic publishing

Iain Chalmers, Douglas G Altman

*Lancet 1999; **353**: 490–93
See Commentary page 428*

**Review and electronic publication of
research protocols**

**Electronic publication and archiving of
medical research**

Editorial

Patient Safety Requires a New Way to Publish Clinical Trials

Richard Smith*, Ian Roberts



Box 2. Our Proposed New System

- A systematic review is posted on the Web
- If a new trial is needed, it is registered and a full protocol is devised in light of the systematic review and posted on the Web
- Anybody can comment online on the interpretation of the systematic review data, the importance of the trial question, or the reliability of its methods
- The statistical analysis would be pre-specified and pre-programmed
- When data collection is completed, the entire dataset would be uploaded and the analyses run
- There would be no investigator commentary on the trial data
- The systematic review would be updated to include the new trial
- Journals would not publish trials but rather commentaries and reports on systematic reviews

Reprise

Clinicians and patients need readier access to:

- reports of up-to-date, valid, systematic reviews
- details sufficient to inform their decision making; and
- information about relevant unpublished and ongoing trials

Saturday 22-29 December 2001

BMJ

Britain's gift: a "Medline" of synthesised evidence

Worldwide free access to evidence based resources could transform health care

Richard Smith *editor, BMJ*

Iain Chalmers *director*

LK Cochrane Centre, Oxford OX2 7LG

For example, we still do not know which treatments are useful for acute stroke, but if every patient in the world experiencing a stroke were admitted to trials we would have enough patients within 24 hours to answer many of these questions. If there were no trials underway addressing the patient's question then the patient and doctor would send a signal to a central database that the question needed answering. This would allow trials to be designed to answer the questions that mattered most to patients.

Protocols for systematic reviews and consequent research,
eg in Cochrane Library and through UK Clinical Trials Gateway

Published systematic reviews and reports of other types of research,
eg Cochrane reviews, DARE, articles in Lancet, BMJ, JAMA

Summaries of evidence, including evidence of uncertainty
eg BMJ Clinical Evidence, CKS, BNF, DUETs, Q&A's

Reports of patient experiences eg DIPEX

Guidelines informed by systematic
reviews eg NICE, SIGN

Tools for diagnosis,
treatment & monitoring

Prompts & reminders
eg Map of Medicine

**BETTER INFORMED
CHOICES AND DECISIONS**

ourNHS
our future



NHS NEXT STAGE REVIEW

Interim report

October 2007

Improve the evidence base

“a national clinical evidence base will be created, housing what local, national and international clinicians believe to be the best available evidence about clinical practice, pathways and models of care and innovations.”

“This will be available to commissioners, practitioners, patients and the public alike.”

“We will work with the relevant bodies, such as **NICE**, the **National Library for Health**, the new **Health Innovation Council** and the **Independent Reconfiguration Panel** to take this forward.”

There is

shared responsibility

to meet the research information needs
of patients and clinicians more
effectively

What can you do?

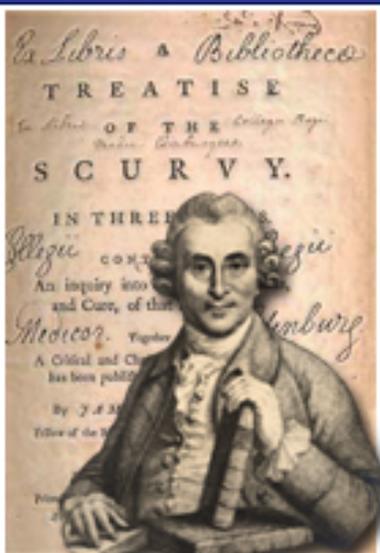
Address current system failures, in collaboration with others

Promulgate recognition of responsibilities to patients and clinicians among those who can improve access to relevant information

Promote effective coordination, to reduce inefficient use of existing resources

Lobby for relevant and transparent research and reporting practices

Exploit the possibilities offered by electronic publishing



The James Lind Library

Documenting the evolution of fair tests of medical treatments

The James Lind Library has been launched to mark the 250th anniversary of the publication of James Lind's *Treatise of the Scurvy*. Lind's 1753 book contains a systematic review of what had been written about scurvy, which was killing thousands of people every year, as well as one of the earliest accounts of a fair comparison of different medical treatments.

www.jameslindlibrary.org

Email: ichalmers@jameslindlibrary.org

