Avoidable waste in the production and reporting of research evidence

Iain Chalmers, Paul Glasziou

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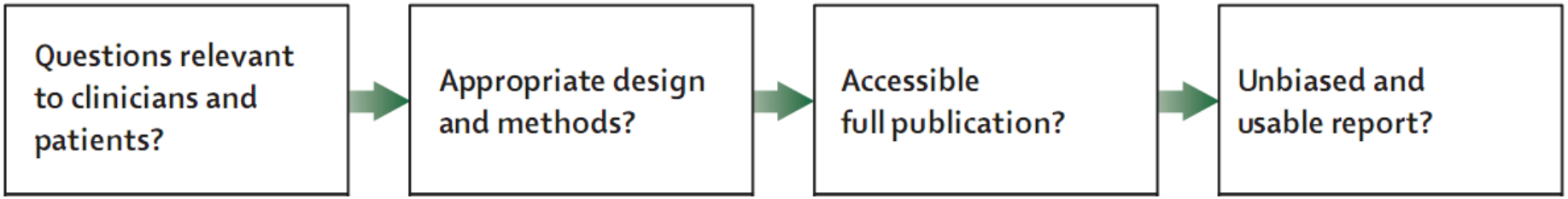


Overview

Waste occurs at 4 stages of research:
question; design; publication; the report

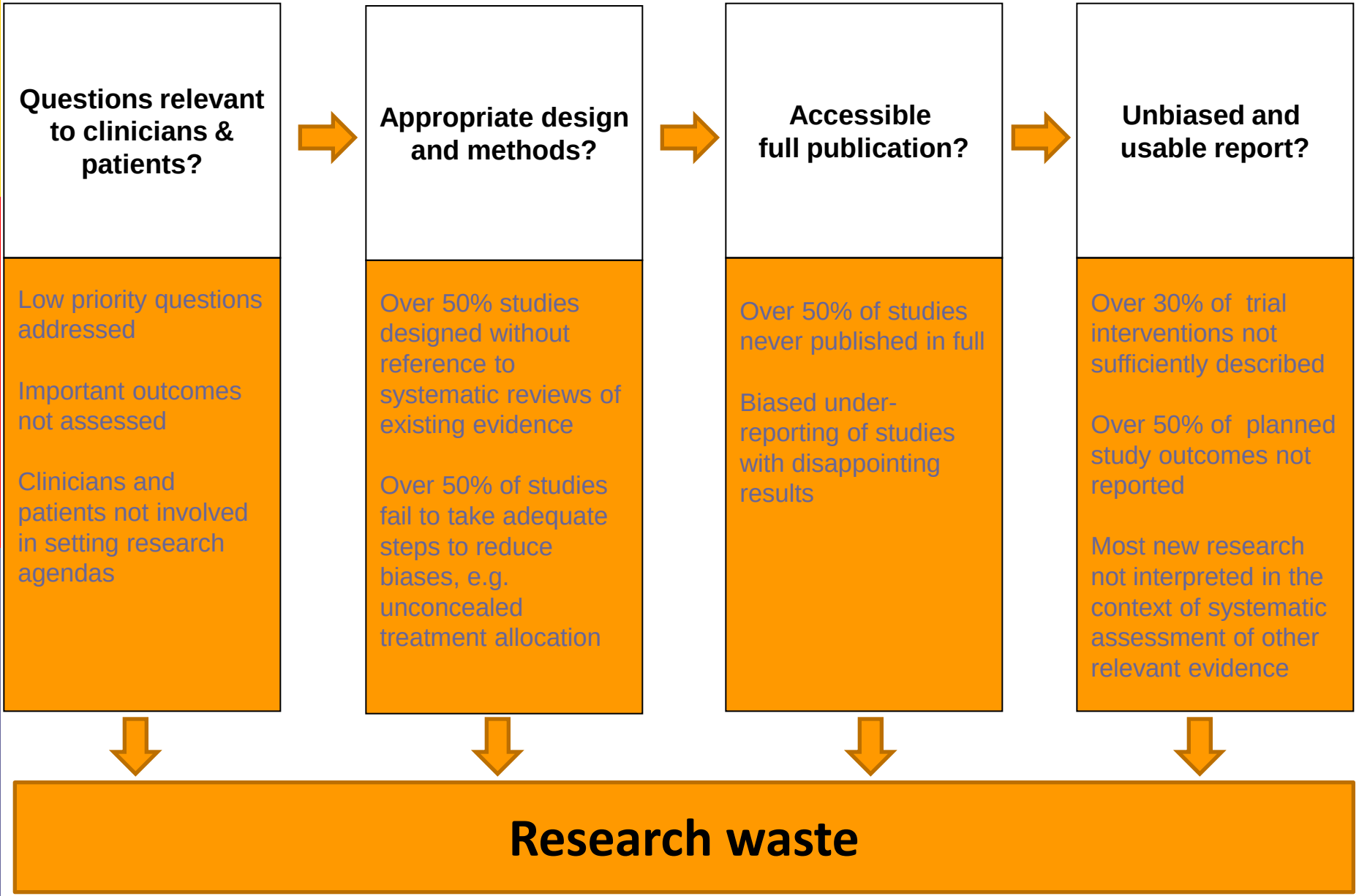
About 50% loss at last 3 stages

Implies 85% of $100Billion spent
on research each year is wasted

The personal impact of non-publication

"Research results should be easily accessible to people who need to make decisions about their own health... Why was I forced to make my decision knowing that information was somewhere but not available? Was the delay because the results were less exciting than expected? Or because in the evolving field of myeloma research there are now new exciting hypotheses (or drugs) to look at? How far can we tolerate the butterfly behaviour of researchers, moving on to the next flower well before the previous one has been fully exploited?"

The 4 stages: from question to report



Stage 1: study questions

Questions relevant to clinicians & patients?

Low priority questions studied

Important outcomes not assessed

Clinicians and patients not involved in setting research agendas

Research waste

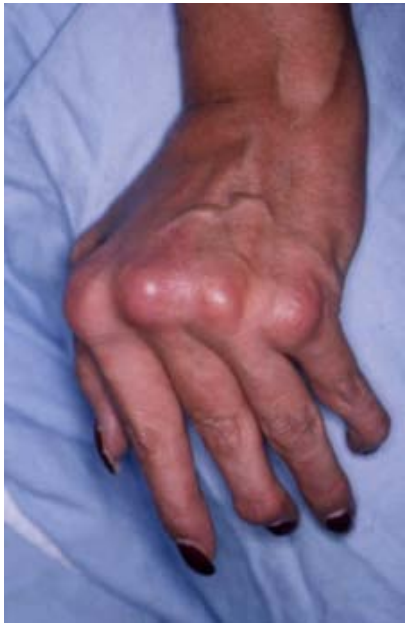
Research priorities among patients with osteoarthritis of the knee compared with researchers' priorities (Tallon et al. 2000).

Interventions	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		

Survey of patients with rheumatoid arthritis priority treatment outcome

What is patients' most important problem?

- It was not pain
- It was fatigue!



OMERACT

Outcome Measures in Rheumatology

Home | What is? | Next meeting | Docs | Bibliography | OMERACT List | Virtual Community

Welcome

This is the website for the **OMERACT** initiative, which stands for Outcome Measures in Rheumatology.

The OMERACT initiative is an informal international network, working groups and gatherings interested in outcome measurement across the spectrum of rheumatology intervention studies.

OMERACT strives to improve outcome measurement through a data driven, interactive consensus process. An Organizing Committee with members from 3 continents, Scientific & Business Advisory Committees, international opinion leaders and hard working participants, strive towards consensus on guidelines and recommendations.

OMERACT meetings are held every 2 years to develop new consensus and guidelines for outcomes in rheumatic diseases.

Review OMERACT 8's Proceedings

Program & Content

OMERACT 9

27 May - 31 May 2008

We are pleased to announce that OMERACT 9 conference on Outcome Measures in Rheumatology is going to be held in the spring of 2008 in Kananaskis in Canada.

For more information on OMERACT, please contact the OMERACT Secretariat, Leanne Idzerda, at omeract@uottawa.ca

News

REGISTRATION FOR OMERACT 9 CLOSED

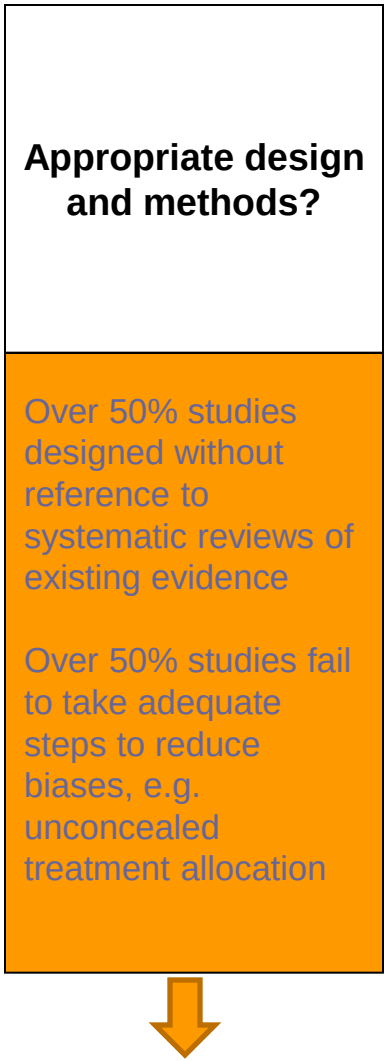
We would like to thank you for your support, which has helped make OMERACT such a great success. Due to this success there has been an immense interest in attending OMERACT 9 and all participant places have now been filled.

If you would like to place your name on a waiting list, please contact omeract9@q2q.co.uk

We would like to remind you that you are always welcome to partake in any of the OMERACT Working Groups and look forward to seeing you at OMERACT 10 in 2010!

DOWNLOAD PREREADING MATERIALS HERE

Stage 2: study design



New studies:

1. Ignore previous studies
2. Have avoidable design flaws

Research waste

The use of systematic reviews when designing studies

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

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

Clinical Trials 2005; **2**: 218–232

Dean Fergusson[a,b], Kathleen Cranley Glass[b,c], Brian Hutton[a] and Stan Shapiro[b,c,d]

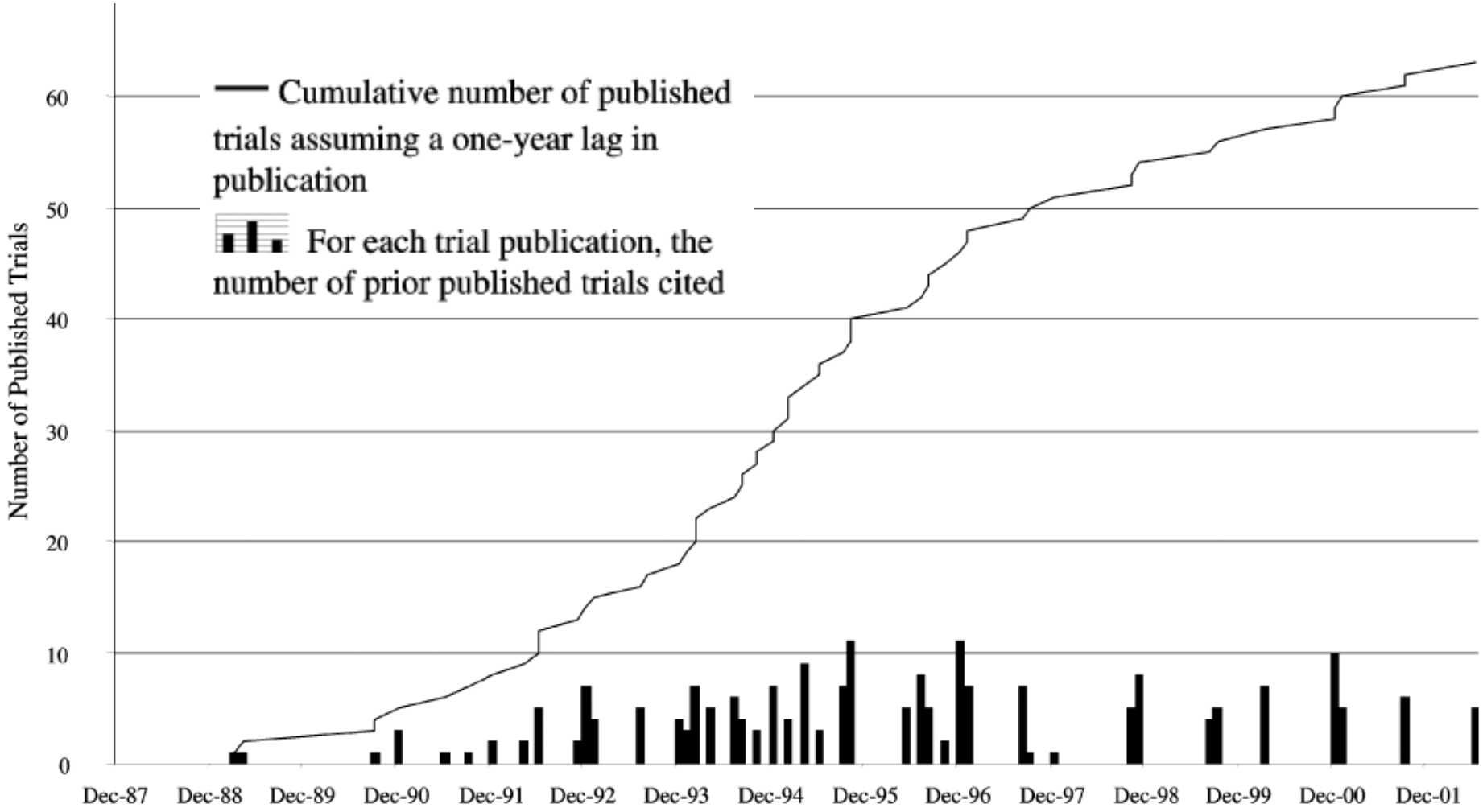
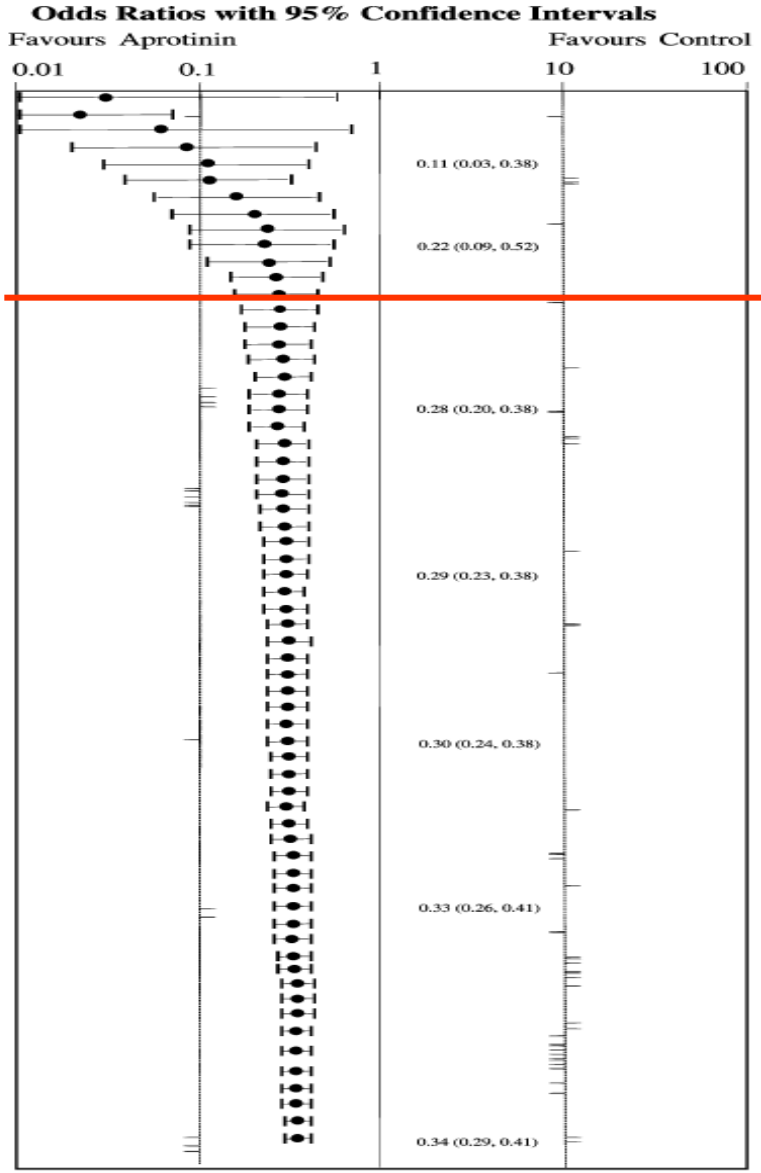


Figure 6 Citations of prior publications.

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

Ref #	Year of Publication	# Pts
6	Dec-87	22
7	Mar-89	99
8	Apr-89	175
9	Sep-90	219
10	Oct-90	257
11	Dec-90	296
12	Jun-91	376
13	Sep-91	396
14	Dec-91	455
15	Apr-92	486
16	Jun-92	601
17	Jun-92	2385
18	Jun-92	2445
19	Nov-92	2495
20	Dec-92	2664
21	Jan-93	2754
22	Jul-93	2795
23	Aug-93	3005
24	Dec-93	3044
25	Jan-94	3146
26a	Feb-94	3201
26b	Feb-94	3342
27	Feb-94	3396
28	Apr-94	3475
29	Jul-94	3575
30	Aug-94	3668
31	Aug-94	3724
32	Oct-94	3822
33	Oct-94	3854
34	Dec-94	3882
35	Dec-94	4047
36	Feb-95	4147
37	Feb-95	4210
38	Feb-95	4240
39	Apr-95	4338
40	Jun-95	4382
41	Jun-95	4420
42	Sep-95	4450
43	Oct-95	4548
44	Oct-95	4578
45	Oct-95	4832
46	May-96	4882
47	Jul-96	4975
48	Aug-96	5023
49	Aug-96	5135
50	Oct-96	5326
51	Dec-96	5970
52	Jan-97	6008
53	Jan-97	6060
54	Aug-97	6227
55	Sep-97	6333
56	Dec-97	6376
57a	Oct-98	6442
57b	Oct-98	6507
58	Nov-98	7303
59	Aug-99	7360
60	Sep-99	7510
61	Mar-00	7593
62	Dec-00	7677
63	Dec-00	7697
64	Jan-01	7897
65	Sep-01	7952
66	Sep-01	8011
67	Jun-02	8040



Enough in 1992?

Avoidable design flaws are common

Adequacy and reporting of allocation concealment: review of recent trials published in four general medical journals

Catherine Hewitt, Seokyung Hahn, David J Torgerson, Judith Watson, J Martin Bland

What is already known on this topic

The effect of adequacy of allocation concealment in randomised controlled trials may influence the degree of effect

What this study adds

Despite researchers' acceptance that adequate allocation concealment is important, almost a fifth of trials recently published in major medical journals used inadequate concealment and a quarter failed to describe how the allocation was concealed

BMJ 2005;330: 1057-8.

Stage 3: publication

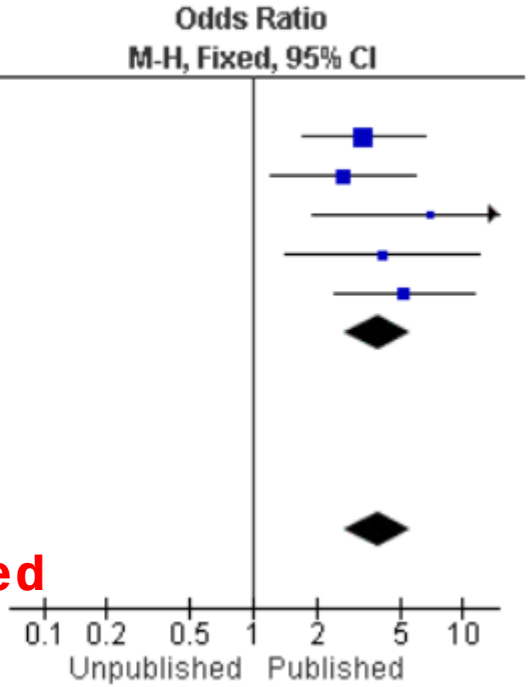
Research waste

Publication bias and rates

Figure 1. Forest plot of comparison: 1 Rate of publication and significance of trial result (pooled), outcome: 1.1 Total number of trials published.

Study or Subgroup	Positive Events	Positive Total	Negative Events	Negative Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.1.1 Positive versus negative or null						
Bardy 1998	52	111	16	77	35.1%	3.36 [1.73, 6.53]
Dickersin 1992	84	96	52	72	26.0%	2.69 [1.22, 5.96]
Dickersin 1993	121	124	63	74	6.7%	7.04 [1.90, 26.16]
Ioannidis 1998	20	27	16	39	11.9%	4.11 [1.41, 11.99]
Stern 1997	55	76	18	54	20.3%	5.24 [2.46, 11.17]
Subtotal (95% CI)		**434**		**316**	**100.0%**	**3.90 [2.68, 5.68]**
Total events	332		165			
Heterogeneity: Chi² = 2.40, df = 4 (P = 0.66); I² = 0%						
Test for overall effect: Z = 7.12 (P < 0.00001)						
Total (95% CI)		**434**		**316**	**100.0%**	**3.90 [2.68, 5.68]**
Total events	332		165			
Heterogeneity: Chi² = 2.40, df = 4 (P = 0.66); I² = 0%						
Test for overall effect: Z = 7.12 (P < 0.00001)						

66% published



Hopewell S, et al. CDSR 2009

About half of trials are unpublished

"Less than half of all studies, and about **60%** of randomized or controlled clinical trials, initially **presented as summaries or abstracts at professional meetings** are subsequently published as peer-reviewed journal articles."

Scherer RW, Langenberg P, von Elm E.
Full publication of results initially presented in abstracts.
Cochrane Database of Systematic Reviews 2007, Issue 2.

Stage 4: Useable report

Unbiased and usable report?

Over 30% of interventions not sufficiently described

Over 50% of planned study outcomes not reported

Most new research not interpreted in the context of systematic reviews of other relevant evidence

Research waste

What is the treatment?

The paper's description of sodium reduction

- "Individual and weekly group counseling sessions were offered initially, with less intensive counseling and support thereafter, specific to sodium reduction."

TOHP Study BMJ, Apr 2007; 334: 885

What is sodium reduction?

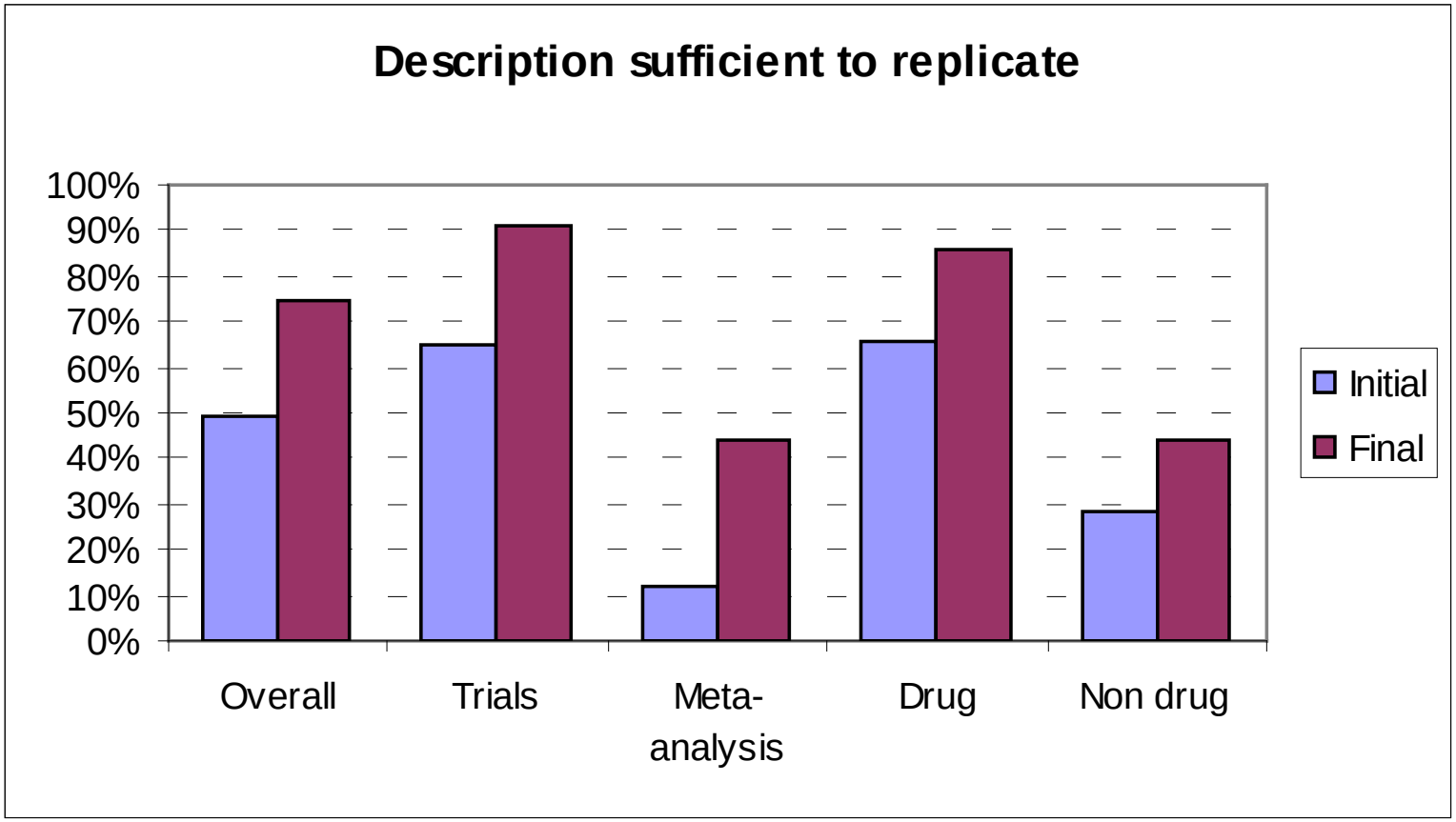
The paper's description

- "Individual and weekly group counseling sessions were offered initially, with less intensive counseling and support thereafter, specific to sodium reduction."

Previous reference

- (i) an individual session followed by 10 weekly group 90 minute sessions with a nutritionist, followed by a transitional stage of some additional sessions
- (ii) Topics in the weekly sessions included Getting Started, sodium basics, the morning meal, midday sources of sodium, the main meal, planning ahead, creative cooking, eating out, food cues, and social support,
- (iii) the sessions included sampling of foods, discussion of articles on sodium reduction, and problem-solving,
- (iv) patients kept diaries at least 6 days per week, and urine sodiums were measured.

Is the inadequate description fixable?



Glasziou P, et al. BMJ 2008;336:1472-74

Systematic review: what specific regimen?

- STUDY: meta-analysis of behavioural interventions for insomnia adults
  - ".. confirms the efficacy of behavioral interventions for person with chronic insomnia."
- PROBLEM: No regimens for 'behavioural intervention' described
  - Author asked: "what specific treatment regime (or regimes) would you recommend based on your review?"
  - Author response: "It was found that cognitive, behavioral and relaxation therapies all in general lead to similar improvements in sleep outcomes---although cognitive approaches might have been a bit better. The references for these studies are found in the article. "

Rx

"Behavioural Intervention"

So what can we do?

- Training
- Standards (CONSORT)
- Non-pharmacopeia

Panel: Stages of waste in the production and reporting of research evidence—barriers (in italics) and recommendations (bullet points)

Questions relevant to clinicians and patients

Poor engagement of end users of research in research questions and design

- Increase involvement of patients and clinicians in shaping research agendas and specific questions

Incentives in fellowships and career paths to do primary research even if of low relevance

- Emphasise initial training in critical appraisal and systematic reviews rather than the conduct of primary research

Appropriate design and methods

Poor training in research methods and research reporting

- Require training of all clinicians in methodological flaws and biases in research; improve training in research methods for those doing research apprenticeships

Lack of methodological input to research design and review of research

- Increase numbers of methodologists in health-care research

Incentives for primary research ignore the need to use and improve on existing research on the same question

- Research funding bodies should require—and support—grant proposals to build on systematic reviews of existing evidence

Published research fails to set the study in the context of all previous similar research

- Journal editors should require new studies to be set in the context of systematic assessments of related studies

Accessible full publication

Non-registration of trials

- Require—by incentives and regulation—registration and publication of protocols for all clinical trials at inception

Failure of sponsors and authors to submit full reports of completed research

- Support timely open access to full results on completion

Unbiased and usable report

Poor awareness and use by authors and editors of reporting guidelines

- Increase author and journal awareness of and training in reporting guidelines, such as CONSORT and STARD statements (http://www.equator-network.org)

Many journal reviews focus on expert judgments about contribution to knowledge, rather than methods and usability

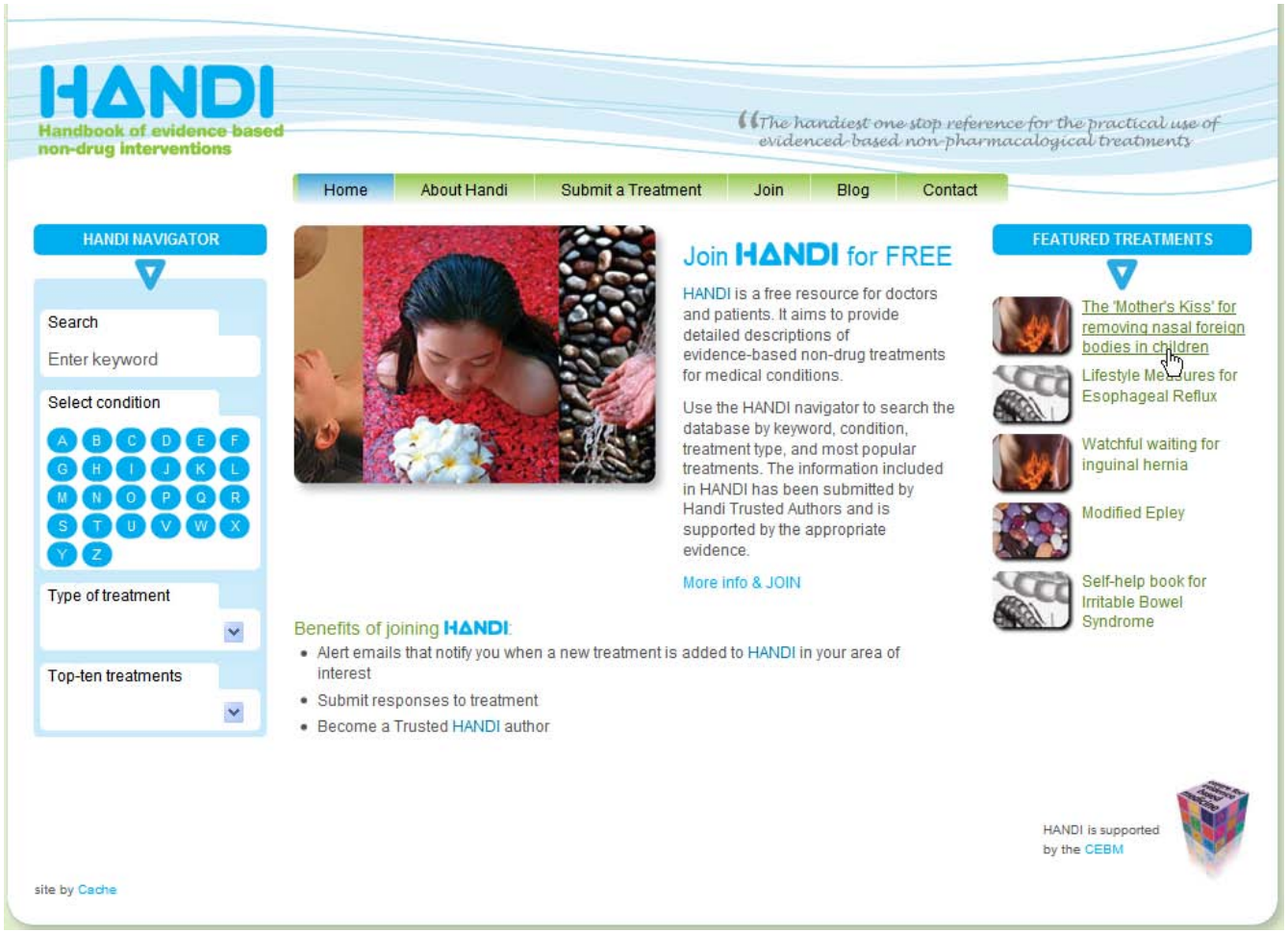
- Supplement peer review of studies with review by methodologists and end users

Space restrictions in journals prevent publication of details of interventions and tests

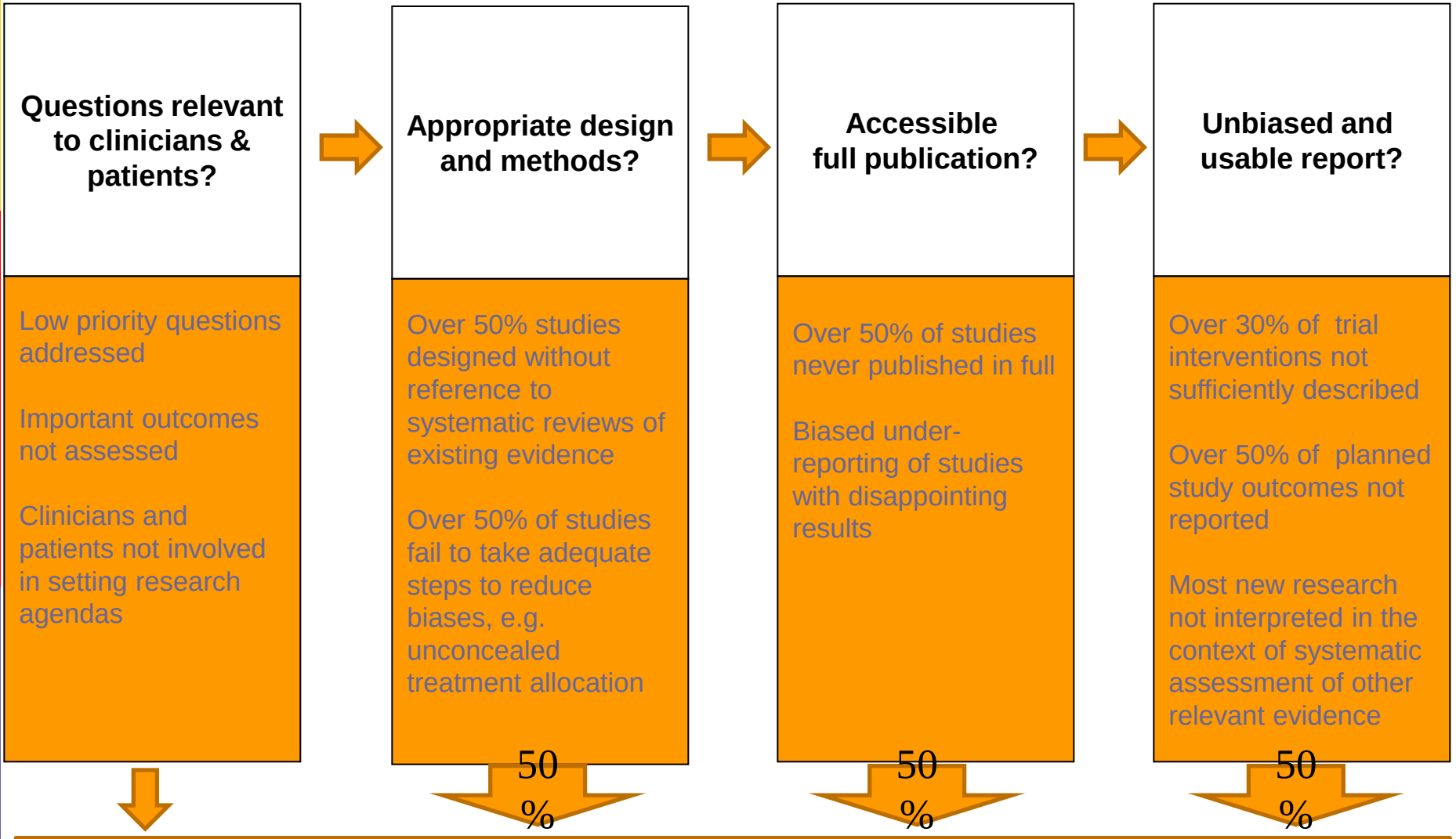
- Support free access repositories—separate from any publications—so that clinicians and researchers have details of the treatments, test, or instruments studied

Repository of intervention descriptions is needed

A “Handbook” of Non-Drug Interventions



The 4 stages: from question to report



85% Research waste = over $85 Billion / year

Summary

- Waste at 4 stages of research: question; design; publication; report
- About 50% loss at last 3 stages
- Implies 85% of $100Billion spent on research each year is wasted

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		

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	

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

Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials

Comparison of Protocols to Published Articles

An-Wen Chan, MD, DPhil
Asbjørn Hróbjartsson, MD, PhD
Mette T. Haahr, BSc
Peter C. Gøtzsche, MD, DrMedSci
Douglas G. Altman, DSc

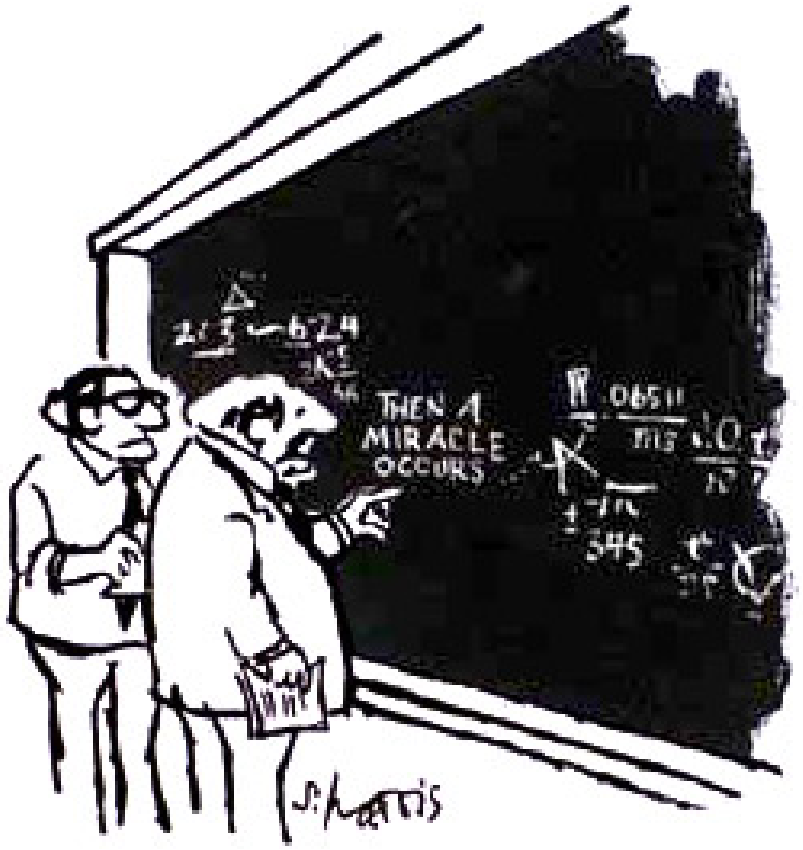
Conclusions The reporting of trial outcomes is not only frequently incomplete but also biased and inconsistent with protocols. Published articles, as well as reviews that incorporate them, may therefore be unreliable and overestimate the benefits of an intervention. To ensure transparency, planned trials should be registered and protocols should be made publicly available prior to trial completion.

JAMA. 2004;291:2457-2465 www.jama.com

Even though there is more to learn about the "epidemiology" and "treatment" of waste in the production and reporting of research evidence, we believe that all of our recommendations are justified on the basis of the evidence we have cited. Action to address this waste is needed now because it has human as well as economic consequences, as illustrated by the quotation with which this Viewpoint began.[1]

The problem

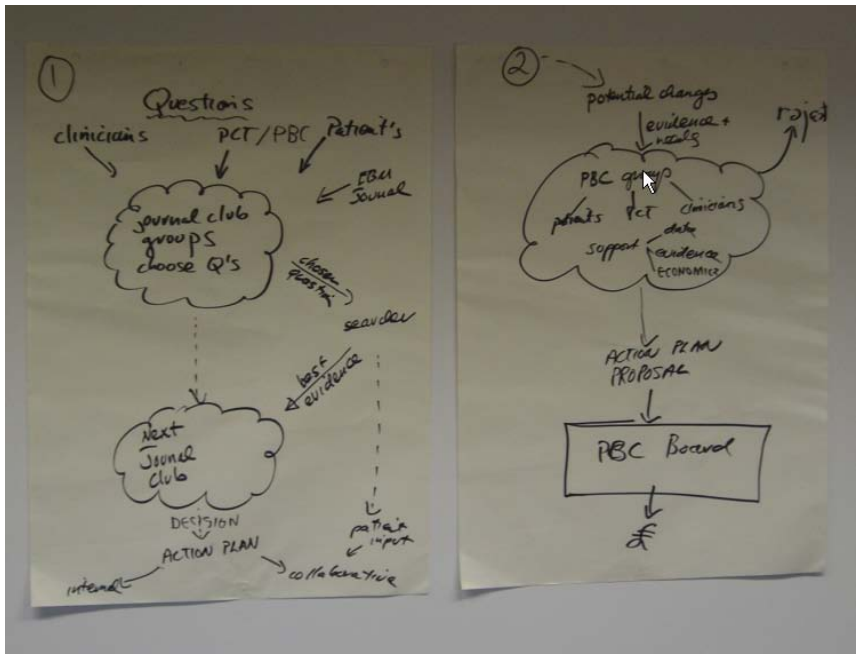
The real information needs of clinicians and patients



"I THINK YOU SHOULD BE MORE EXPLICIT HERE IN STEP TWO."

“Working” on the Problem

Cognitive Style



Paul

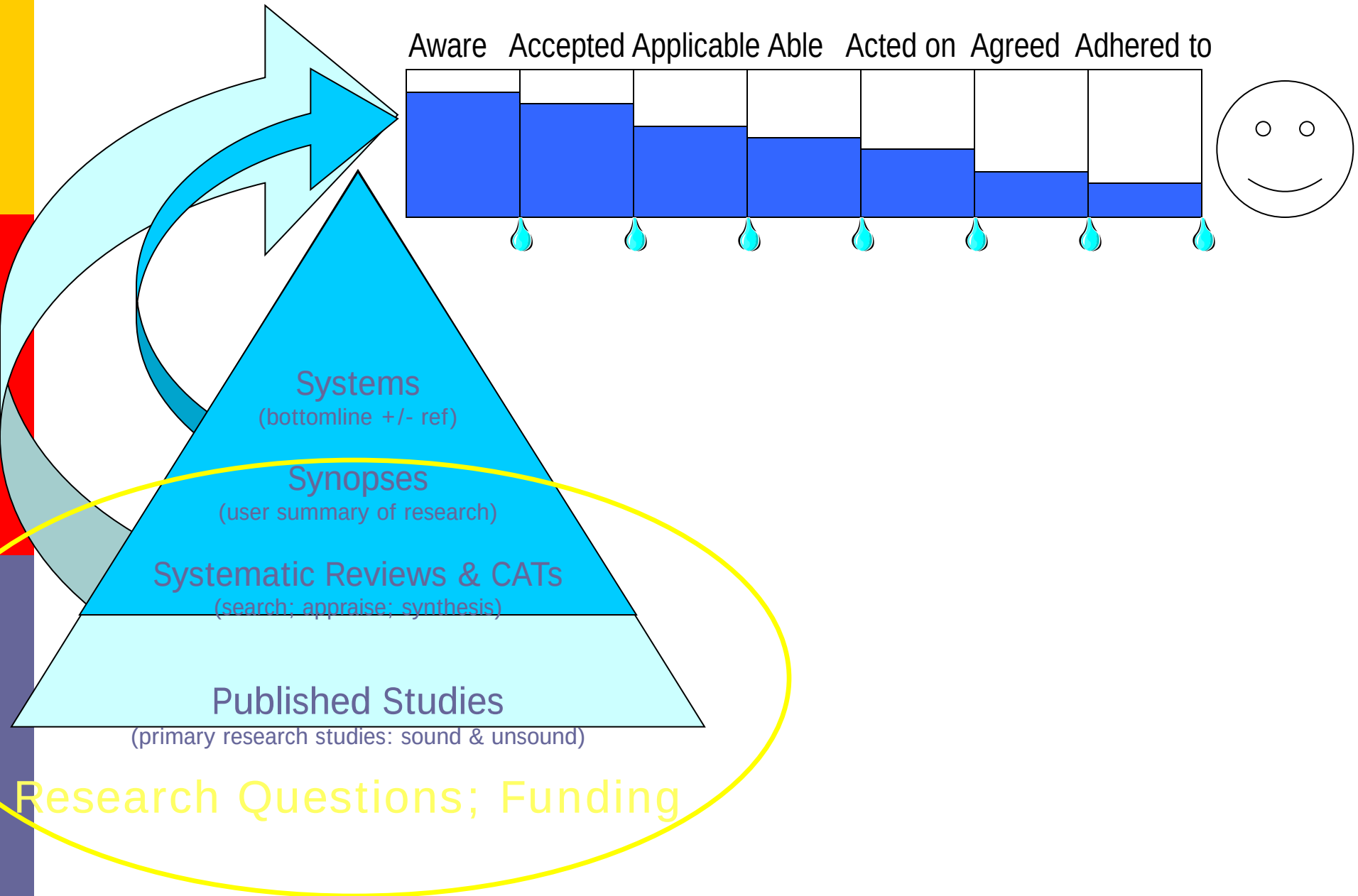
Biased or unusable reports of research

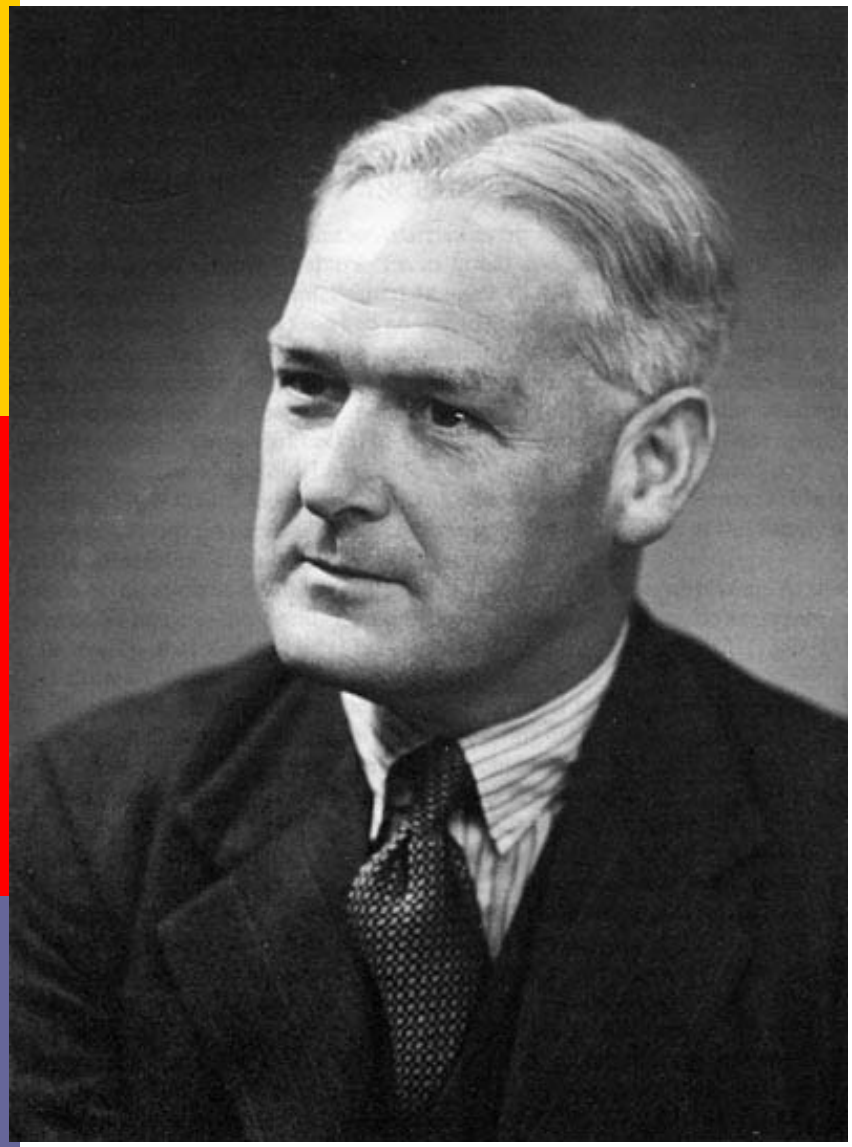
Although their quality has improved, reports of research remain much less useful than they should be. Sometimes this is because of frankly biased reporting—eg, adverse effects of treatments are suppressed, the choice of primary outcomes is changed between trial protocol and trial reports,[21] and the way data are presented does not allow comparisons with other, related studies. But even when trial reports are free of such biases, there are many respects in which reports could be made more useful to clinicians, patients, and researchers. We select here just two of these.

First, if clinicians are to be expected to implement treatments that have been shown in research to be useful, they need adequate descriptions of the interventions assessed, especially when these are non-drug interventions, such as setting up a stroke unit, offering a low fat diet, or giving smoking cessation advice. Adequate information on interventions is available in around 60% of reports of clinical trials;[22] yet, by checking references, contacting authors, and doing additional searches, it is possible to increase to 90% the proportion of trials for which adequate information could be made available.[22]

Iain

Mapping the research-practice gap

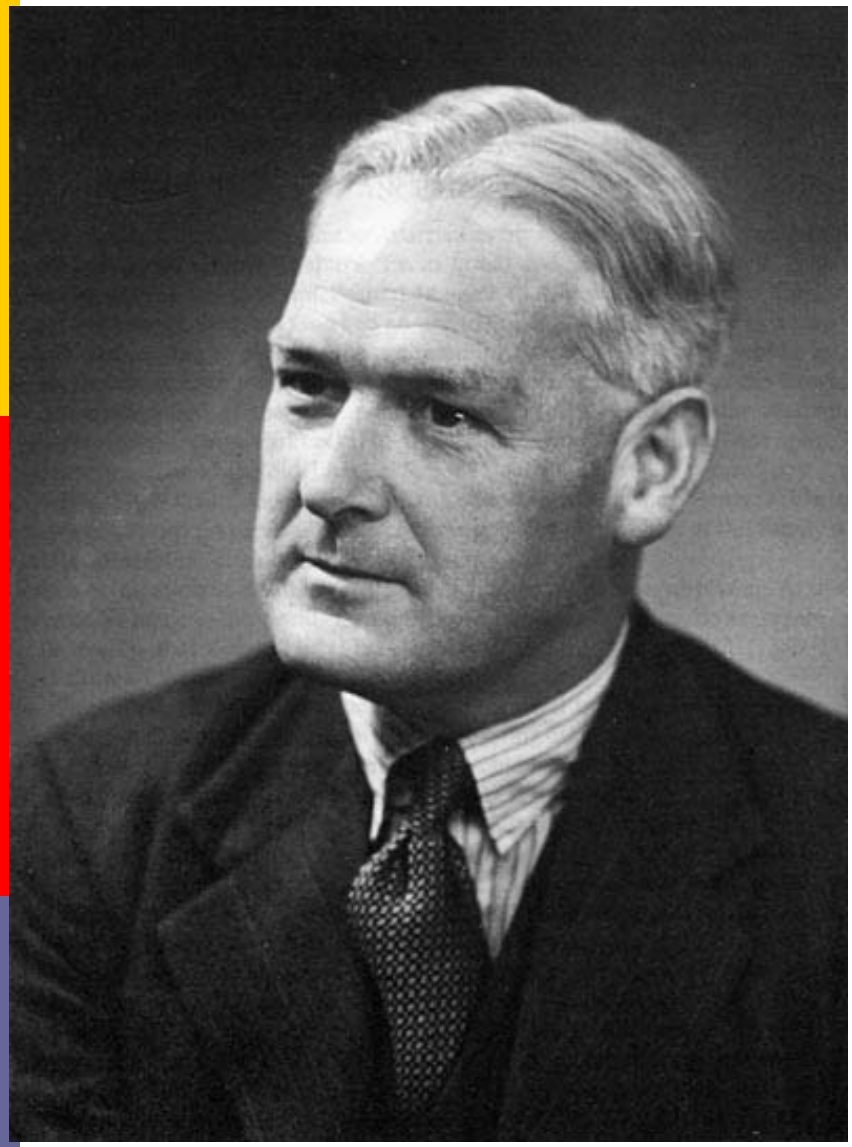




Austin Bradford Hill, 1965

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

1. Why did you start?



Austin Bradford Hill, 1965

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

4. And what does it mean anyway?

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

JOURNAL OF THE ROYAL SOCIETY OF MEDICINE Volume 100 April 2007

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

Mike Clarke[1] Sally Hopewell[1] Iain Chalmers[2]

J R Soc Med 2007;**100**:187–190