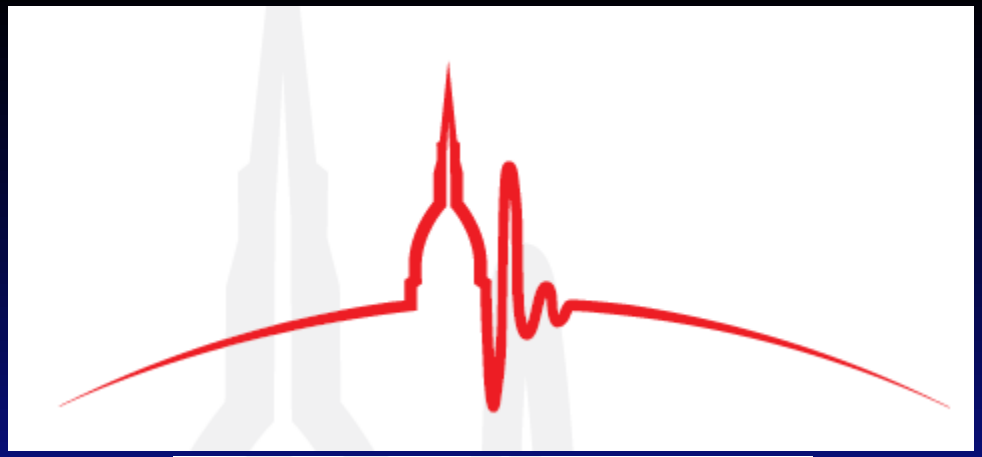


IX congresso nazionale
SIMEU
TORINO 6-8 NOVEMBRE 2014

8 novembre

Come leggere un articolo scientifico

Primiano Iannone
Direttore DEA
Ospedali del Tigullio, ASL4 Chiavarese (GE) Italy

PERCHÉ I MEDICI SENTONO IL BISOGNO DI AGGIORNARSI?

Nella metà dei casi perché cercano informazioni riguardanti la strategia terapeutica da seguire nei confronti di un paziente

Davies K. The information-seeking behaviour of doctors: a review of evidence. Health Info Libr J 2007; 24: 78-94

L'80 per cento delle domande che nascono nel corso di una giornata di lavoro è legato alla clinica .

Arroll B, et al. Use of information sources among New Zealand family physicians with high access to computers. J Fam Pract Online 2005; 51.

OPEN ACCESS Freely available online

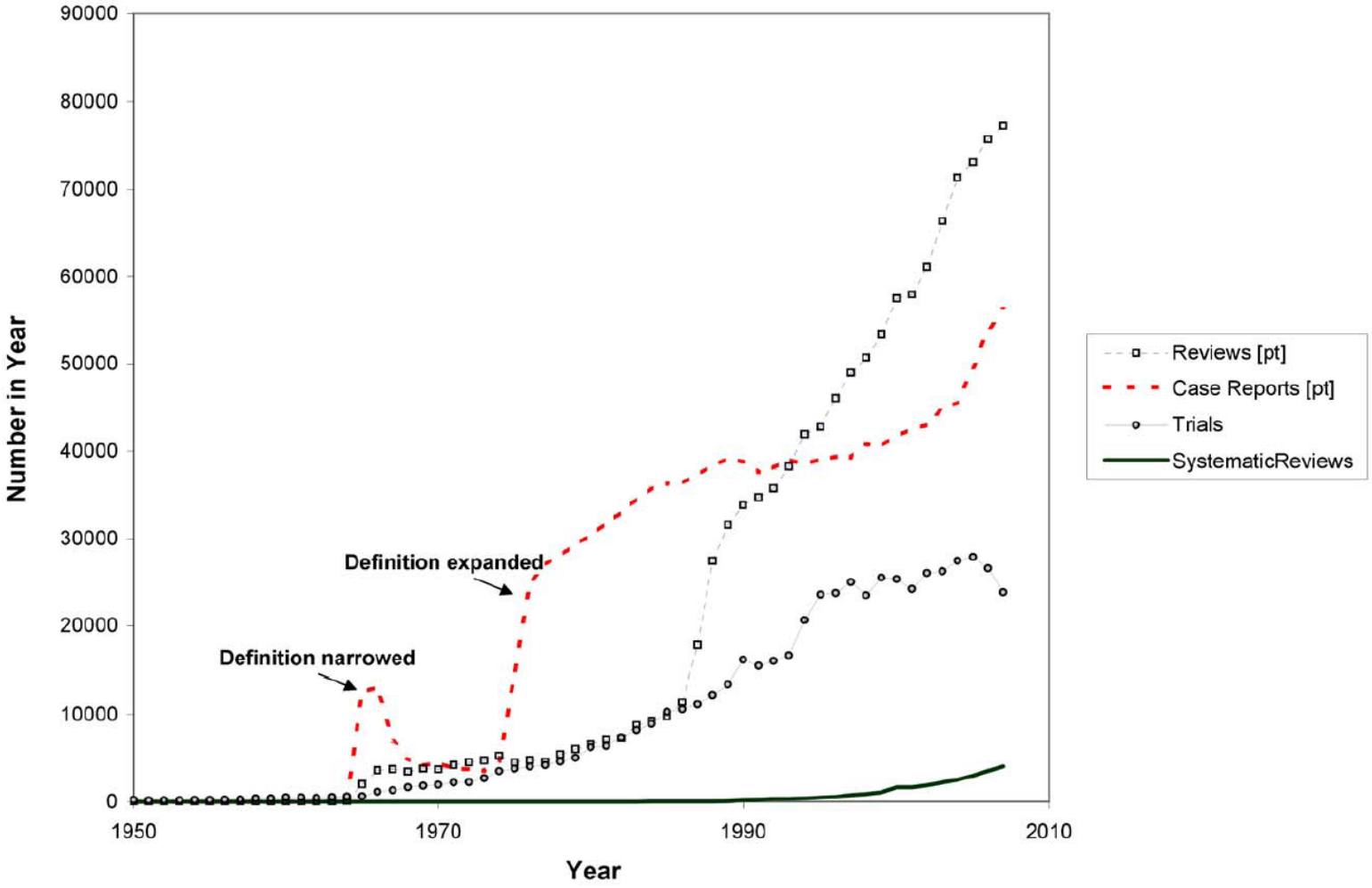
PLoS Med 7(9): e1000326. doi:10.1371/journal.pmed.1000326

Policy Forum

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

Hilda Bastian[1]*, **Paul Glasziou**[2], **Iain Chalmers**[3]

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



la Repubblica
SABATO 1 GIUGNO 2013

L'allarme arriva da una ricerca curata da due professori dell'Università di Cardiff

Il numero delle pubblicazioni, è ormai fuori controllo Non basta una vita per aggiornarsi

LA SOLITUDINE DELL'ESPERTO

COSÌ LA BOLLA INFORMATIVA ANNULLA LA CONOSCENZA

MASSIMIANO BUCCHI

Le cifre

28.100

RIVISTE
E' il numero di pubblicazioni scientifiche esistenti

1milione 800

ARTICOLI
Sono quelli di scienza che vengono pubblicati ogni anno

3%

AUMENTO
E' la percentuale di crescita annuale degli articoli pubblicati

In questo caos di dati e studi diventa più facile poter dubitare di pareri e competenze

$$\text{Usefulness of medical information} = \frac{\text{relevance x validity}}{\text{work to access}}$$

Shaughnessy A F, Slawson D C, Bennett J H. Becoming an information master: a guidebook to the medical information jungle. **J Fam Pract** 1994;**39**:489-99

Le quattro cose su cui un articolo scientifico deve essere chiaro

Why did You start the study ?	Introduction
What did You do ?	**methods**
What did You find ?	Results . analysis
What does it mean ?	Discussion

imrad

definizione precisa del problema del paziente

P.I.C.O.

Population
Intervention (exposure)
Comparison
Outcome

Quesito ➔ studio

1. **Terapia:** **effetti di differenti trattamenti**
2. **Harm :** **effetti di potenziali agenti/interventi dannosi**
3. **Diagnosi:** **capacità di un test o intervento nell'identificare una condizione o malattia**
4. **Prognosi:** **stimare il decorso futuro della malattia del paziente**
5. **Valutazione di tecnologie sanitarie**
6. **Costi vs benefici/efficacia/utilità di interventi sanitari**

(Editoriali, commenti e lettere non rispondono a quesiti in modo strutturato ma esprimono opinioni)

FIGURE 1A–2

Randomized Controlled Trial

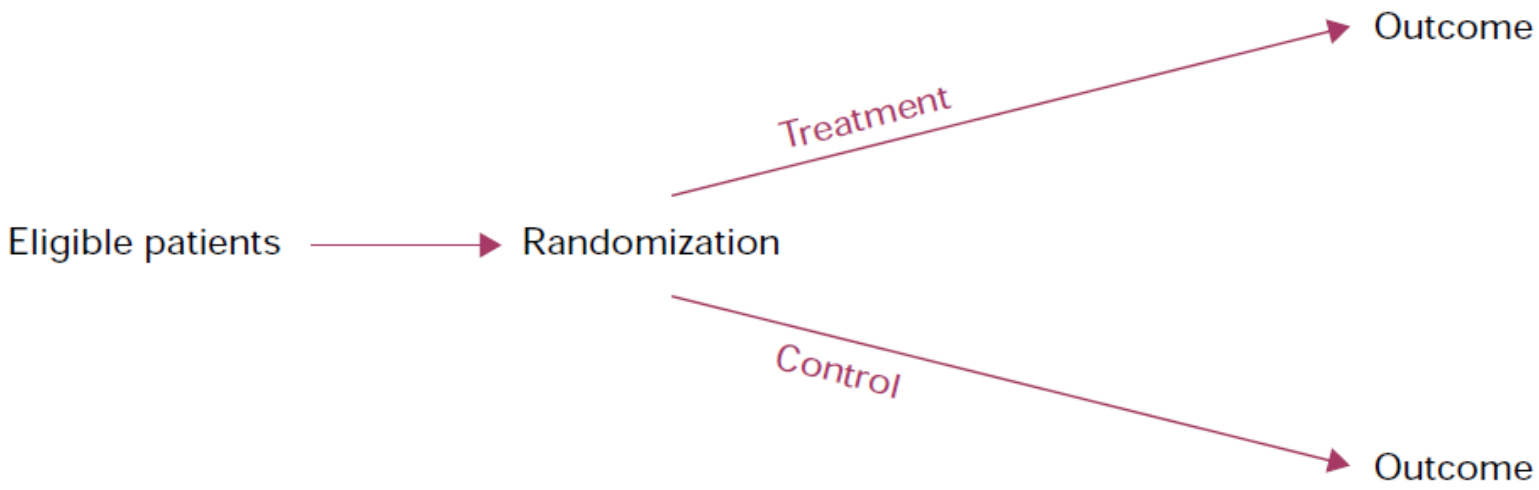
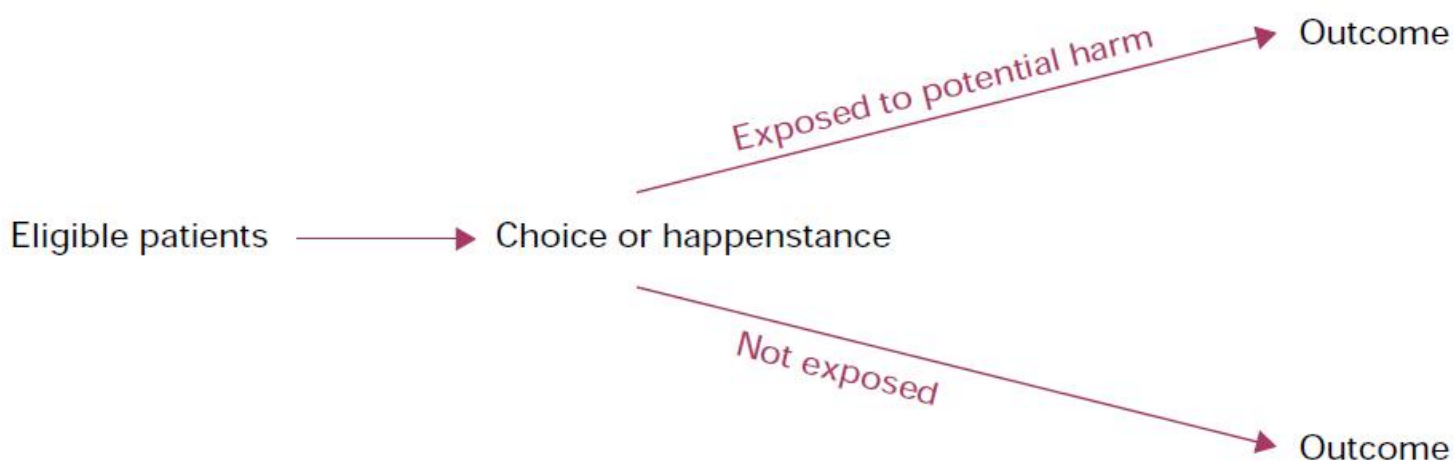


FIGURE 1A–3

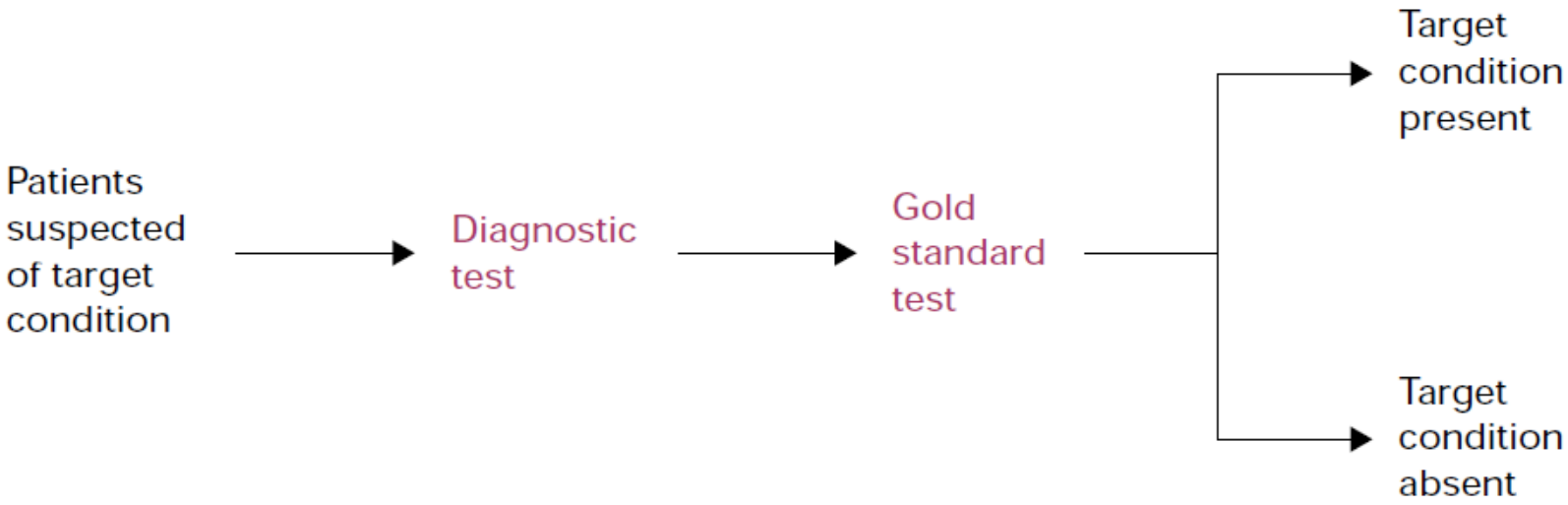
Observational Study: Assessing Exposure



coorte

FIGURE 1A–4

Study Design to Assess a Diagnostic Test



Cross sectional study

1747

James Lind

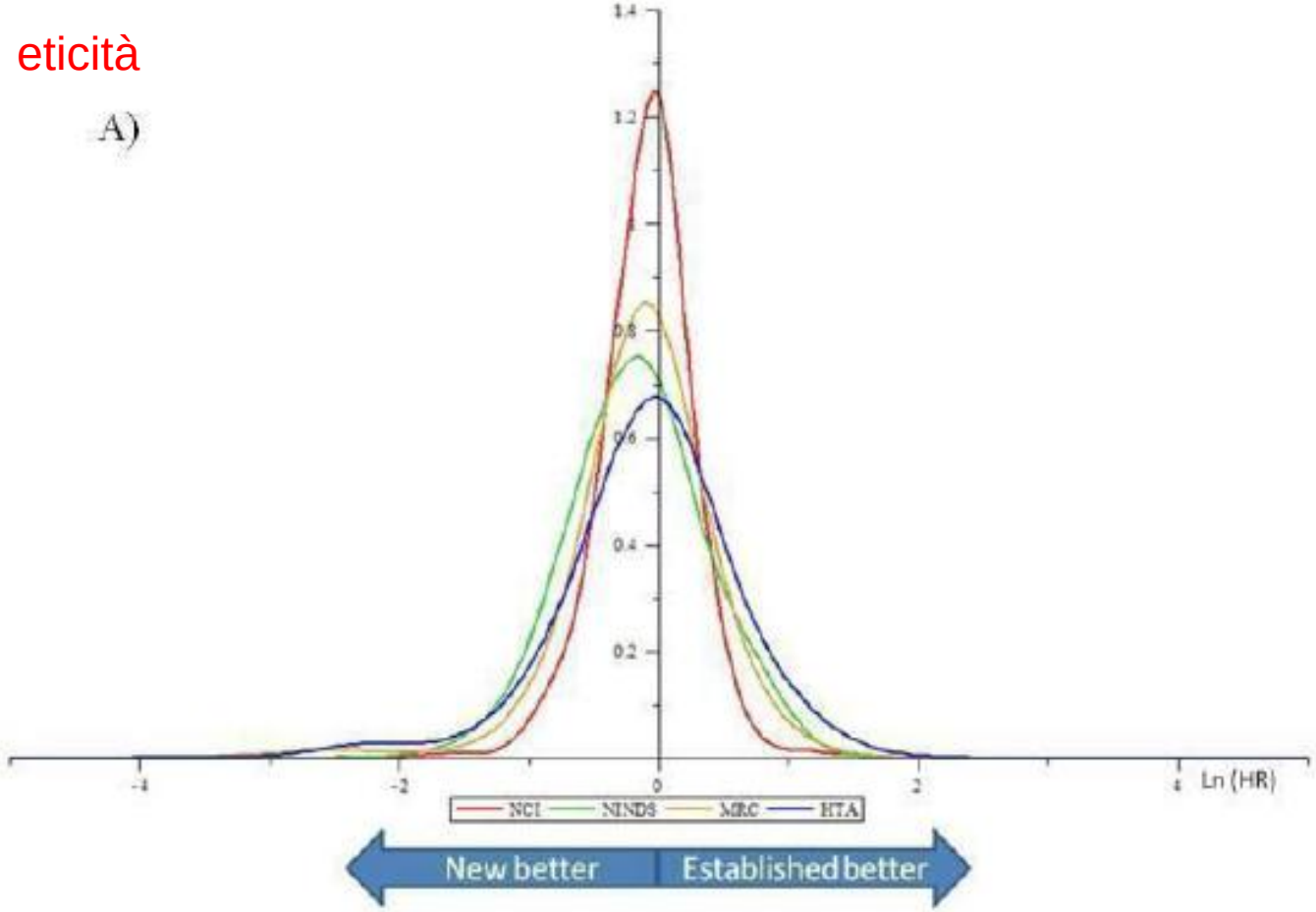
Medico di Bordo

Vascello
Salisbury
IV Flotta di SMR

Questioni importanti nella valutazione di un RCT

Eticità	equipoise ?	Best standard treatment ?
Rilevanza	POEMS vs DOE	Endpoints Surrogati vs hard
Validità	•Randomizzazione ? •Concealement ? •Intention to treat ? •Bilanciamento fattori prognostici ? •Cecità (pazienti, medici, valutatori) ? •Lost to follow up ? •Violazioni protocollo ?	
Risultati	•Entità effetti •Precisione delle stime	•Misurazioni (RRR, ARR,NNT ?) •P value •Limiti di confidenza
Applicabilità	• validità esterna •Rischi •Costi	

eticità



New treatments compared to established treatments in randomized trials (Review)

Djulbegovic B, Kumar A, Glasziou PP, Perera R, Reljic T, Dent L, Raftery J, Johansen M, Di Tanna GL, Miladinovic B, Soares HP, Vist GE, Chalmers I

DOI: 10.1002/14651858.MR000024.pub3.

eticità

Table 2. Proportion of Trials Significantly Favoring Newer Treatments Over Standard of Care

Trials	No./Total %			*P* for Trend
	Not-for-Profit (n = 104)	Not-for-Profit and For-Profit (n = 62)	For-Profit (n = 137)	
All	51/104 (49.0)	35/62 (56.5)	92/137 (67.2)	.005
Clinical end points	19/55 (34.6)	24/44 (54.6)	64/96 (66.7)	<.001
Drug	17/43 (39.5)	24/46 (54.4)	74/113 (65.5)	.002
Device	4/8 (50.0)	9/13 (69.2)	14/17 (82.4)	.07

Ridker et Al, JAMA 2006

Tipologie di RCT

"archetipo" ⟶ Superiorità : A è meglio di B ?

Ipotesi nulla (H0) da confutare: A non differisce da B

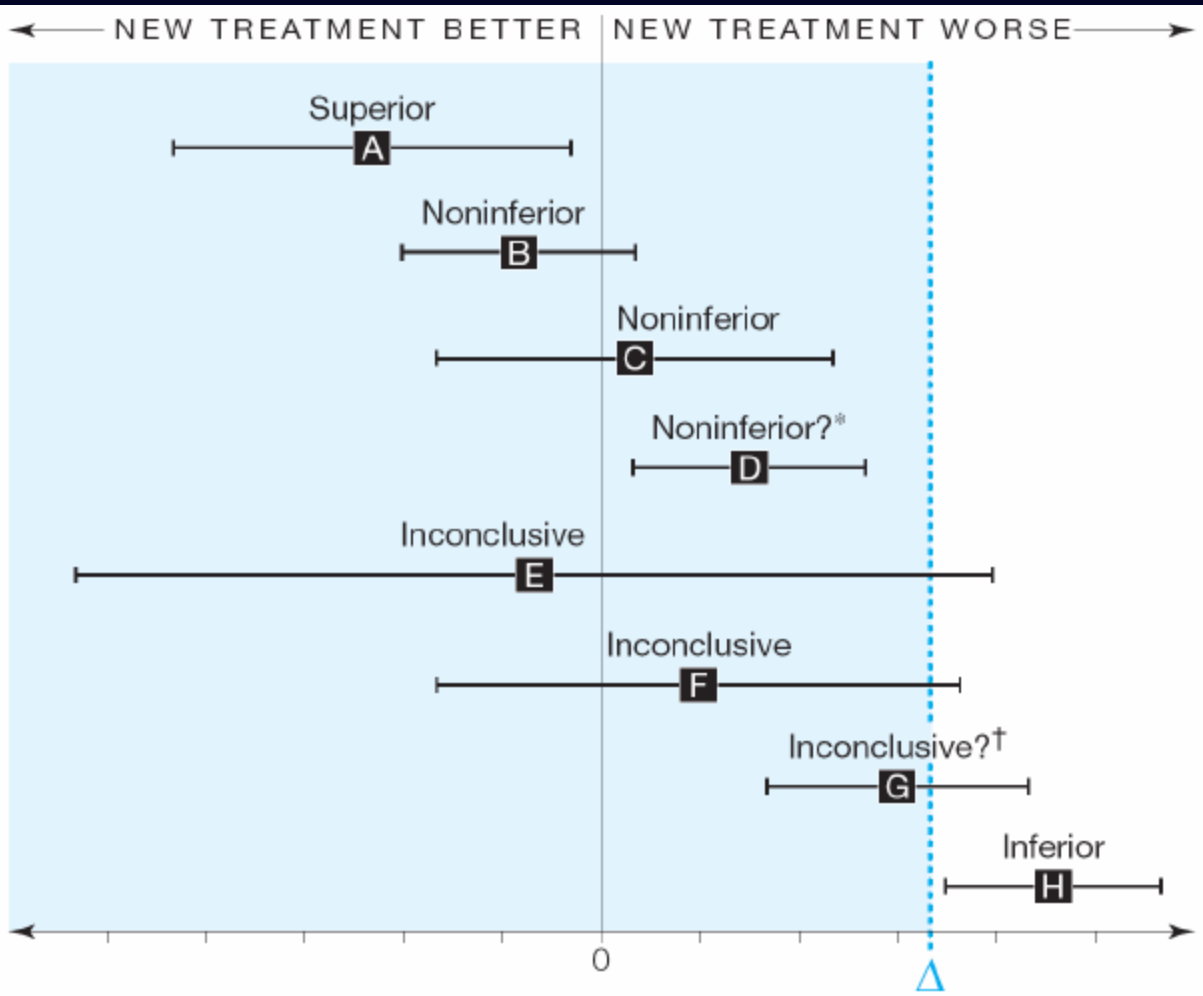
"nuovi disegni"

Equivalenza : A non differisce da B più di un certo margine (delta) ?

Ipotesi nulla (H0) da confutare: A differisce da B

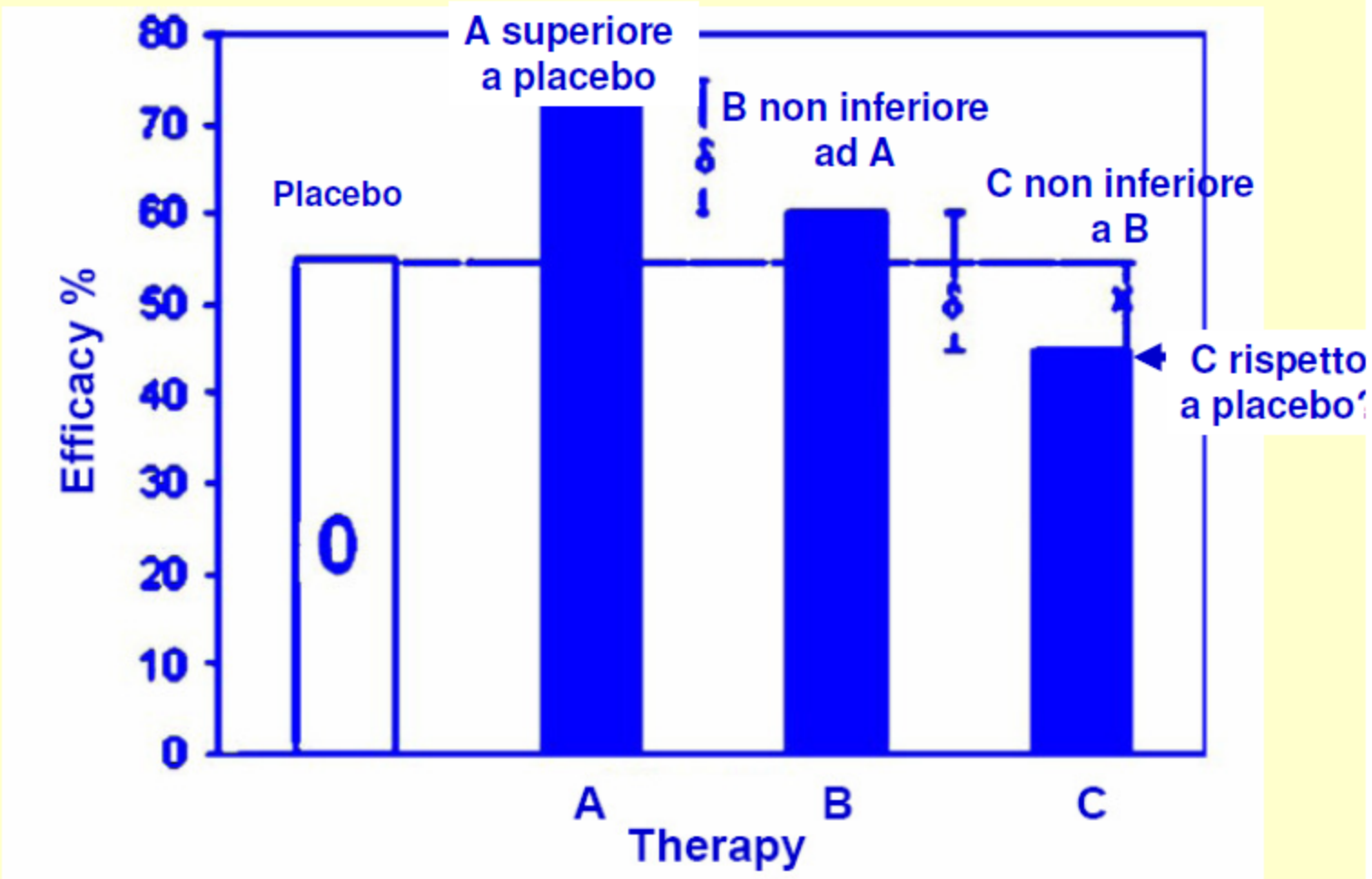
Non inferiorità : A non è peggio di B Più di un certo margine (delta) ?

Ipotesi nulla (H0) da confutare: A è peggio di B



Treatment Difference for Adverse Outcome
(New Treatment Minus Reference Treatment)

Modificato da presentazione Prof. Garattini (Non inferiority trials) Cochrane Colloquium 2008 - Friburgo



rilevanza

Hard vs surrogate outcomes : es: mortalità all causes vs riduzione PA

Patients' centeredness : es escalation tp diabetica vs Hb glicata

Composite vs single : IMA + hospitalisation + mortality vs mortality alone

Validità

All'inizio dello studio il gruppo sperimentale e di controllo hanno una prognosi simile ?

Randomisation

concealement

Intention to treat

Durante lo studio il gruppo sperimentale e quello di controllo sono trattati allo stesso modo,
tranne che per il trattamento oggetto di indagine ?

Cecità

Completezza follow up

Validità

Bilanciamento iniziale dei fattori prognostici

L'RCT deve riportare i fattori prognostici noti nei due gruppi all'ingresso dello studio

Randomizzazione tanto più efficace quanto più grande è il trial

Validità

completezza follow-up

TABLE 1B-2

When Does Loss to Follow-up Seriously Threaten Validity?

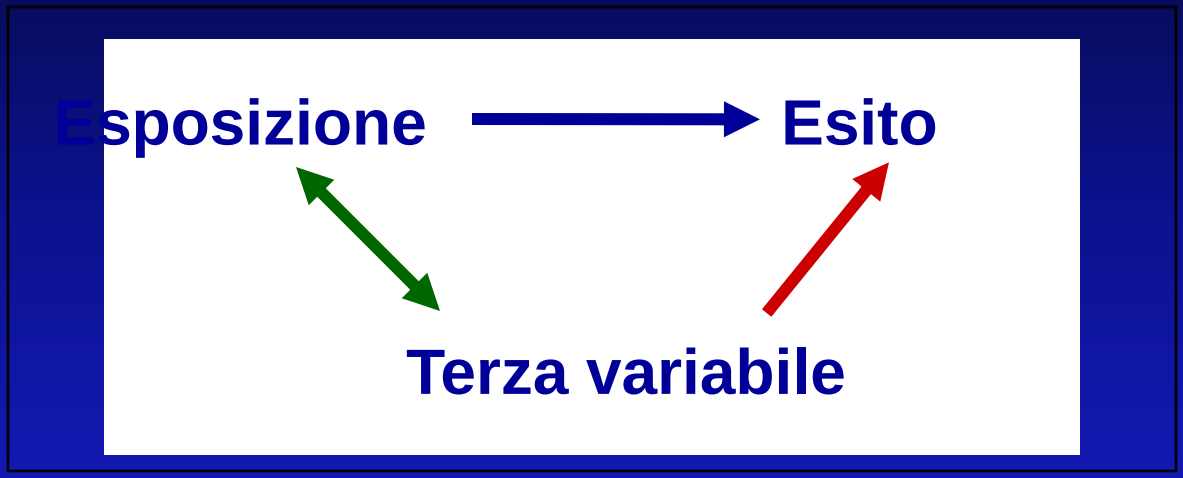
	Trial A		Trial B	
	Treatment	Control	Treatment	Control
Number of patients randomized	1000	1000	1000	1000
Number (%) lost to follow-up	30 (3%)	30 (3%)	30 (3%)	30 (3%)
Number (%) of deaths	200 (20%)	400 (40%)	30 (3%)	60 (6%)
RRR not counting patients lost to follow-up	0.2/0.4 = 0.50		0.03/0.06 = 0.50	
RRR for worst-case scenario*	0.17/0.4 = 0.43		0.00/0.06 = 0	

* The worst-case scenario assumes that all patients allocated to the treatment group and lost to follow-up died and all patients allocated to the control group and lost to follow-up survived.

RRR indicates relative risk reduction.

Fattore di confondimento

Due condizioni:



Essere associato con l'esposizione senza esserne una conseguenza

Essere associato all'esito indipendentemente dall'esposizione

Table 1| **Cochrane Collaboration's tool for assessing risk of bias (adapted from Higgins and Altman13)**

Bias domain	Source of bias	Support for judgment	Review authors' judgment (assess as low, unclear or high risk of bias)
Selection bias	Random sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence
	Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen before or during enrolment	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations before assignment
Performance bias	Blinding of participants and personnel*	Describe all measures used, if any, to blind trial participants and researchers from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Detection bias	Blinding of outcome assessment*	Describe all measures used, if any, to blind outcome assessment from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Detection bias due to knowledge of the allocated interventions by outcome assessment
Attrition bias	Incomplete outcome data*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition or exclusions where reported, and any reinclusions in analyses for the review	Attrition bias due to amount, nature, or handling of incomplete outcome data
Reporting bias	Selective reporting	State how selective outcome reporting was examined and what was found	Reporting bias due to selective outcome reporting
Other bias	Anything else, ideally prespecified	State any important concerns about bias not covered in the other domains in the tool	Bias due to problems not covered elsewhere

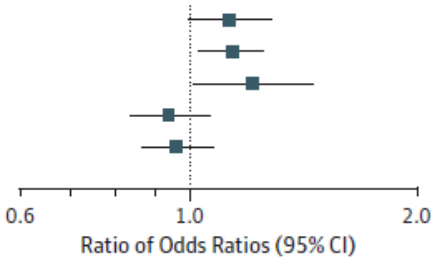
*Assessments should be made for each main outcome or class of outcomes.

BMJ 2011; 343: d5928

Figure. Difference in Treatment Outcomes Between Trials at High or Unclear Risk and Trials at Low Risk of Bias for Each Key Domain and Overall

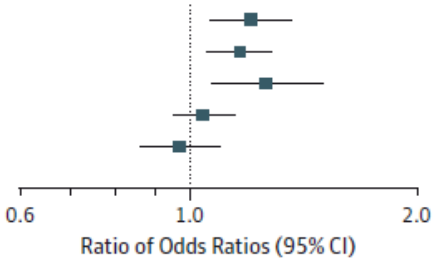
Subjective Outcomes

Domain	No. of Meta-analyses	Ratio of Odds Ratios (95% CI)	I^2, %
Sequence generation	69	1.13 (0.99-1.28)	28
Allocation concealment	69	1.14 (1.03-1.25)	0
Blinding	51	1.21 (1.01-1.46)	23
Incomplete outcome data	58	0.94 (0.84-1.07)	11
Overall	39	0.96 (0.87-1.08)	0



Objective Outcomes

Domain	No. of Meta-analyses	Ratio of Odds Ratios (95% CI)	I^2, %
Sequence generation	59	1.20 (1.06-1.36)	20
Allocation concealment	55	1.16 (1.05-1.28)	0
Blinding	25	1.26 (1.07-1.49)	0
Incomplete outcome data	46	1.04 (0.95-1.15)	6
Overall	36	0.97 (0.86-1.10)	0



A ratio of odds ratios greater than 1 indicates larger treatment outcomes for trials at high or unclear risk of bias than for trials at low risk.

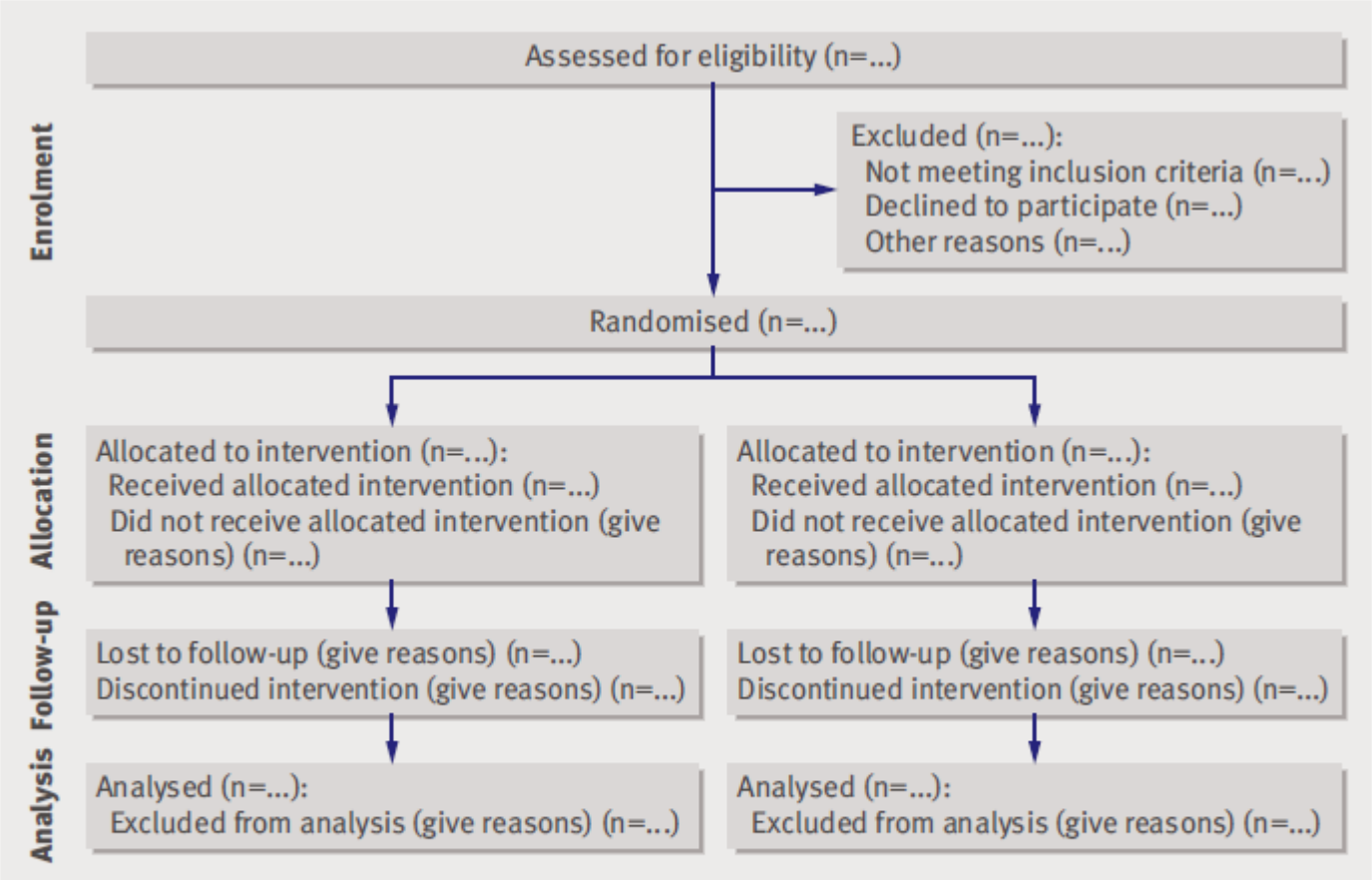
RESEARCH METHODS & REPORTING

BMJ | 27 MARCH 2010 | VOLUME 340

CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials

Kenneth F Schulz,[1] Douglas G Altman,[2] David Moher,[3] for the CONSORT Group

25 items



Flow diagram of the progress through the phases of a parallel randomised trial of two groups (that is, enrolment, intervention allocation, follow-up, and data analysis)

Magnitude of treatment effect

the lower the NNT (=1/ARR) , more effective the treatment is

TABLE 2B2-3

The 2 x 2 Table

		Outcome	
		Yes	No
Exposure	Yes	a	b
	No	c	d

$$\text{Absolute Risk Reduction (ARR)} = \frac{c}{c+d} - \frac{a}{a+b}$$

$$\text{Number Needed to Treat (NNT)} = \frac{1}{ARR}$$

TABLE 2B2-6

Relationship Between the Baseline Risk, the Relative Risk Reduction, and the Number Needed to Treat*

Control Event Rate	Intervention Event Rate	Relative Risk	Relative Risk Reduction	Risk Difference	NNT
0.02	0.01	50%	50%	0.01	100
0.4	0.2	50%	50%	0.2	5
0.04	0.02	50%	50%	0.02	50
0.04	0.03	75%	25%	0.01	100
0.4	0.3	75%	25%	0.1	10
0.01	0.005	50%	50%	0.005	200

* Relative risk is equal to the intervention event rate/control event rate; the relative risk reduction is equal to 1 – relative risk; the risk difference is equal to control event rate – intervention event rate; the NNT is equal to 1 / risk difference.

Consider baseline risk

Errori tipo I e tipo II

Errore tipo I

↓

Rischio di trovare una differenza che non esiste (FP)

↓

Chi-quadro

↓

5%

Errore tipo II

↓

Rischio di NON trovare una differenza che esiste (FN)

↓

10-20 %

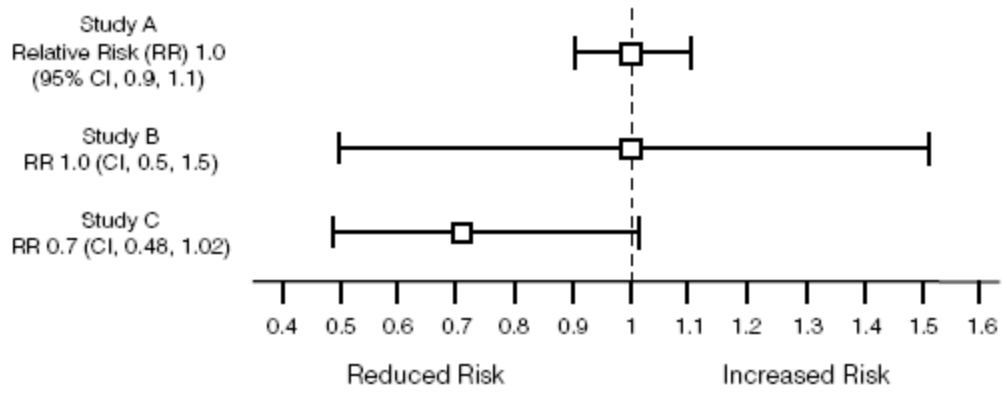


FIGURE. Role of 95% CIs in assessing type II errors.

Study A suggests that the intervention has no effect (i.e. the relative risk is 1) and is very precise (i.e., the confidence interval is narrow). You can be confident that it is not missing an important difference. In other words, you can be confident that there's no type II error.

Study B suggests that the intervention has no effect (i.e., the RR is 1) but is very imprecise (i.e., the confidence interval is wide). This study may be missing an important difference. In other words, you should be worried about type II error, but this study is just as likely to be missing an important harmful effect as an important beneficial one. A type II error is possible, and it could be in either direction.

Study C suggests that the intervention has a clinically important beneficial effect (i.e., the RR is much less than 1) and is also very imprecise. Most of the confidence interval includes clinically important beneficial effects. Consequently, a type II error is very likely. This is a study you would like to see repeated using a larger sample.

Applicabilità

population

intervention

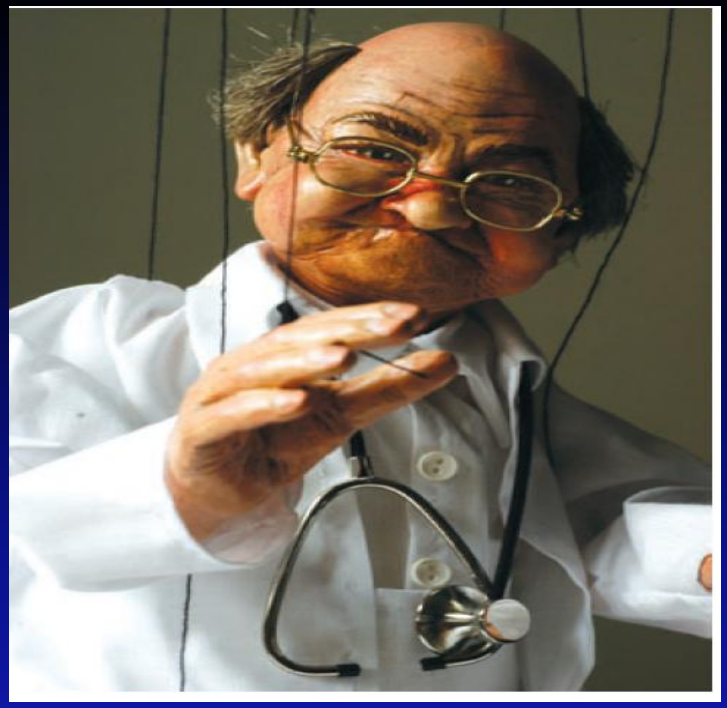
outcomes

Directeness o trasferibilità

Head to head comparison

Patients preferences and values

Costs & context



KEY OPINION LEADERS
Independent experts or drug representatives in disguise?

Ray Moynihan examines the role of the influential experts paid by industry to help "educate" the profession and the public

Key opinion leaders—what fees can they command?

Single lecture or scientific speech $3000
(source: Marketwire)

Hourly rate for influential physicians offering advice—up to $400
(source: Cutting Edge Information)

Work for drug companies on clinical trials—More than £200 an hour
(source: BMA)

BMJ | 21 JUNE 2008 | VOLUME 336

"Meglio leggere un articolo in meno che credere di sapere le cose senza averle capite", sostiene un anziano primario che frequenta la biblioteca di Giovanni. Ad un giovane che chiedeva un parere su un lavoro che, per l'appunto, conservava dei punti oscuri, il Professore affidò questo consiglio: "Se non capisci, chiedi aiuto; se un collega non riesce ad aiutarti, chiedi al tuo Maestro; se anche questo non basta, scrivi un articolo sul *Lancet* per smascherare l'imbroglio…".

Prendersi tutto il tempo per leggere, senza distrazioni, e con attenzione

Slow reading… please

"There seems to be no study too fragmented, no hypothesis too trivial, no literature citation too biased or too egotistical, no design too warped, no methodology too bungled, no presentation of results too inaccurate, too obscure, and too contradictory, no analysis too self-serving, no argument too circular, no conclusions too trifling or too unjustified, and no grammar and syntax too offensive for a paper to end up in print"

Rennie Drummond deputy editor JAMA

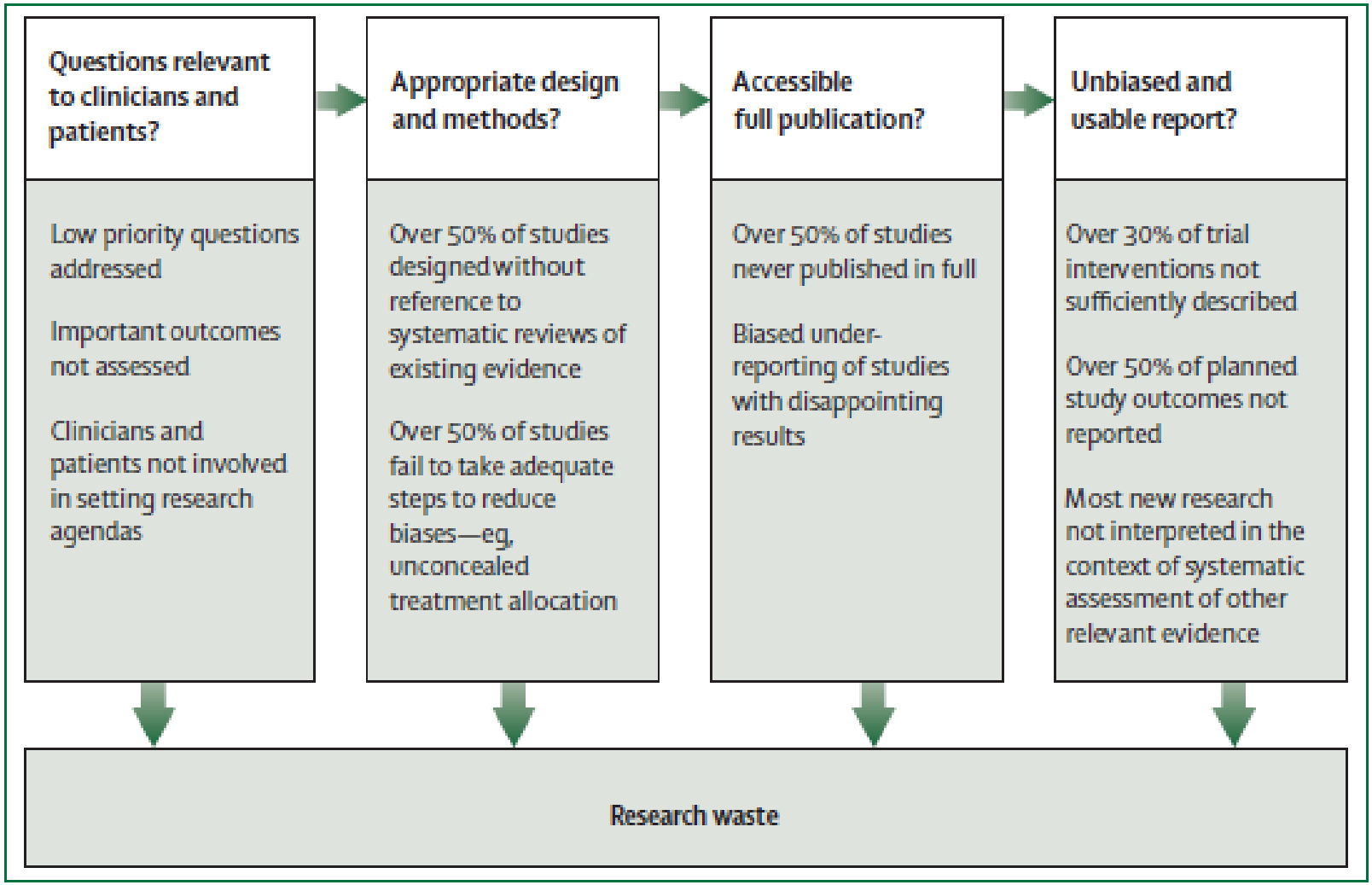


Figure: Stages of waste in the production and reporting of research evidence relevant to clinicians and patients

Chalmers, Lancet 2009

http://attentiallebufale.it/