

Università del Piemonte Orientale

Corso di Perfezionamento in
EBM e metodologia delle revisioni sistematiche di studi di efficacia

Il funzionamento del sistema editoriale

Fabrizio Faggiano



Obiettivo

- Presentare e discutere alcuni aspetti del sistema della editoria scientifica
- lasciando alla discussione il chiarimento di alcuni meccanismi complessi, quale ad esempio:
 - la relazione fra autori/referee/editors/editori
- tralasciando altri aspetti fondamentali che verranno affrontati in altre occasioni, quali ad esempio
 - il conflitto di interessi

Il sistema editoriale biomedico

- Sistema editoriale è l'insieme delle risorse (riviste cartacee, online, basi dati, siti web etc) deputato a diffondere i risultati della ricerca scientifica
- Obiettivo del sistema editoriale:
 - Trasferire le evidenze prodotte dalla ricerca nella pratica
 - Formare i professionisti
 - Favorire lo scambio di esperienze
 - Contribuire alla definizione delle priorità di ricerca
 - ...

Medical research should advance scientific knowledge and – directly or indirectly – lead to improvements in treatment or prevention of Disease [D. Altman]

- Requisiti ideali:
 - affidabilità
 - indipendenza
 - rilevanza
 - trasparenza
 - completezza

Generalità

If research is not published it might as well
not have been done

A research report is the only tangible
evidence that the study was done
[Doug Altman]

Attualità

- Ma stiamo assistendo alla concentrazione su pochi grandi editori, che agiscono in modo monopolistico
- Il maggiore editore è Elsevier (US)
 - 40% business armi
 - 3° per distribuzione utili (x il 60% da editoria scientifica)

Rapporto Commissione EU 2007

- Tra il 2001 e il 2005 la crescita dei prezzi è stata superiore all'inflazione ... del 29% in Europa. L'innovazione tecnologica ha permesso di scaricare una parte dei costi sugli autori (invio via web dei manoscritti, già impaginati e correzione delle bozze di stampa).
- L'innovazione tecnologica e la ... globalizzazione .. hanno determinato un **processo di concentrazione** nel settore dell'editoria scientifica, dove operano oggi poche multinazionali di grandissime dimensioni.
- La quota di citazioni detenuta dai primi tre editori è superiore al 50 per cento in ben sette aree scientifiche su ventidue.
- **Barriere all'entrata** difficilmente eliminabili, per l'importanza che la reputazione di una rivista può avere sulla carriera di chi vi pubblica
- Imposizione di contratti pluriennali per l'acquisto dell'**intero catalogo** (il *big deal*, in sostanza un gigantesco *bundling*), impedendo alle biblioteche di acquistare soltanto i titoli di effettivo interesse e fissando tassi di crescita dei prezzi vicini al 5 per cento all'anno

Open access

- Movimento che promuove l'apertura di riviste scientifiche online, le quali
 - Garantiscano lo stesso livello di qualità di quelle a pagamento
 - Liberamente accessibili dagli utenti finali
 - A bassi costi
 - scaricati sui ricercatori
 - Biomed Central www.biomedcentral.com
 - PLOS www.plos.org

<http://www.ec-petition.eu/>

RECOMMENDATION A1. GUARANTEE PUBLIC ACCESS TO PUBLICLY-FUNDED RESEARCH RESULTS SHORTLY AFTER PUBLICATION

- Research funding agencies have a central role... they should promote and support the archiving of publications in open repositories, after a time period (embargo). **This archiving could become a condition for funding.**
- Actions at the European level: (i) Establish a European policy mandating published articles arising from EC-funded research to be available after a given time period in open access archives, and (ii) Explore whether and how such policies and open repositories could be implemented.

La qualità della letteratura scientifica (1)

- Clinicians might read journals to learn how to treat their patients better
- “Editors, reviewers and authors are often tempted to pander to this group, by sexing up the results with unjustified clinical messages – sometimes augmented by an even more unbalanced press release.”

[Buckley, Emerg Med Australas 2005]

La qualità della letteratura scientifica (2)

- “In return for the altruism and trust that make clinical research possible, the research enterprise has an obligation to conduct research ethically and to report it honestly.”

[International Committee of Medical Journal Editors, 2004]

- “Failure to publish an adequate account of a well-designed clinical trial is a form of scientific misconduct which can lead to those caring for patients to make inappropriate treatment decisions

[Chalmers 1990]

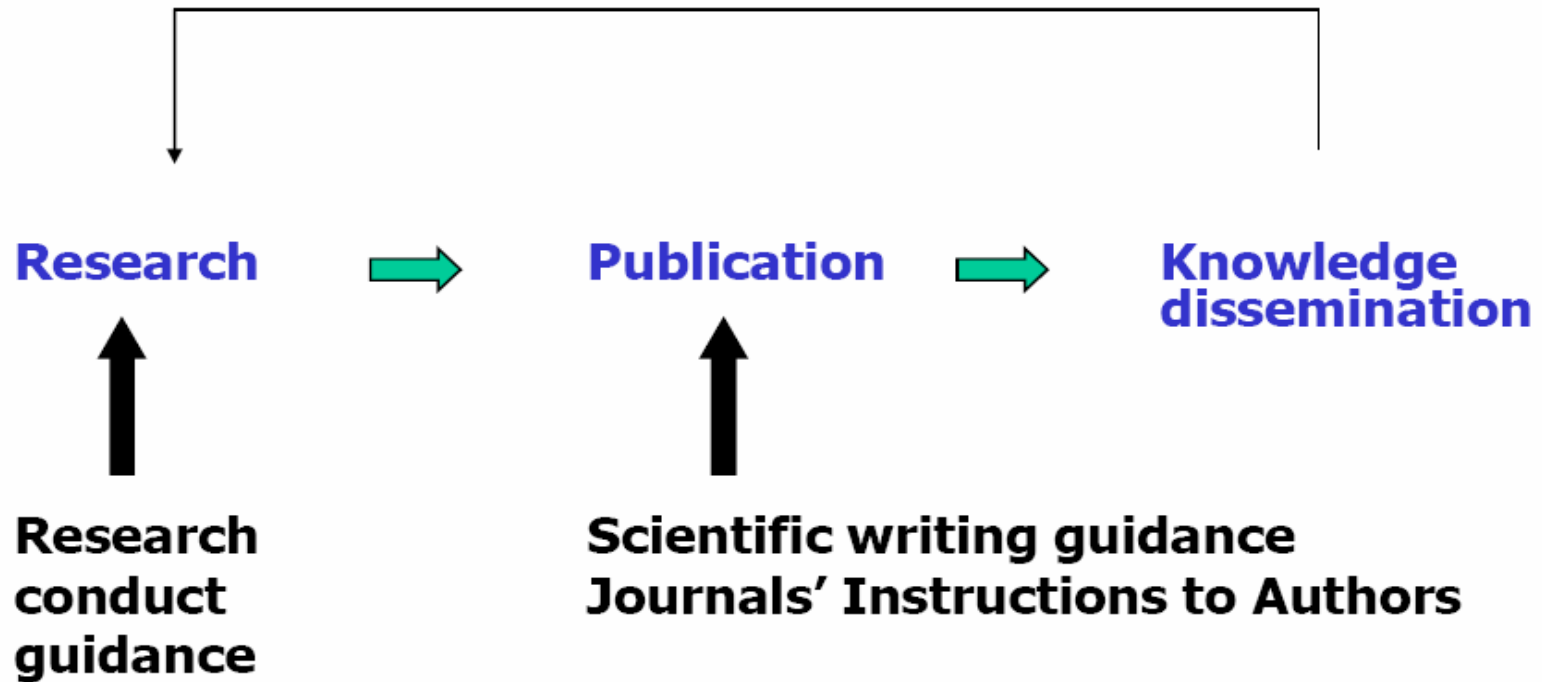
La qualità della letteratura scientifica (3)

- Scientific manuscripts should present sufficient data so that the reader can fully evaluate the information and reach his or her own conclusions about results
- Assessment of reliability of published articles is seriously impeded by inadequate reporting

Il processo di disseminazione



Cosa si può fare?

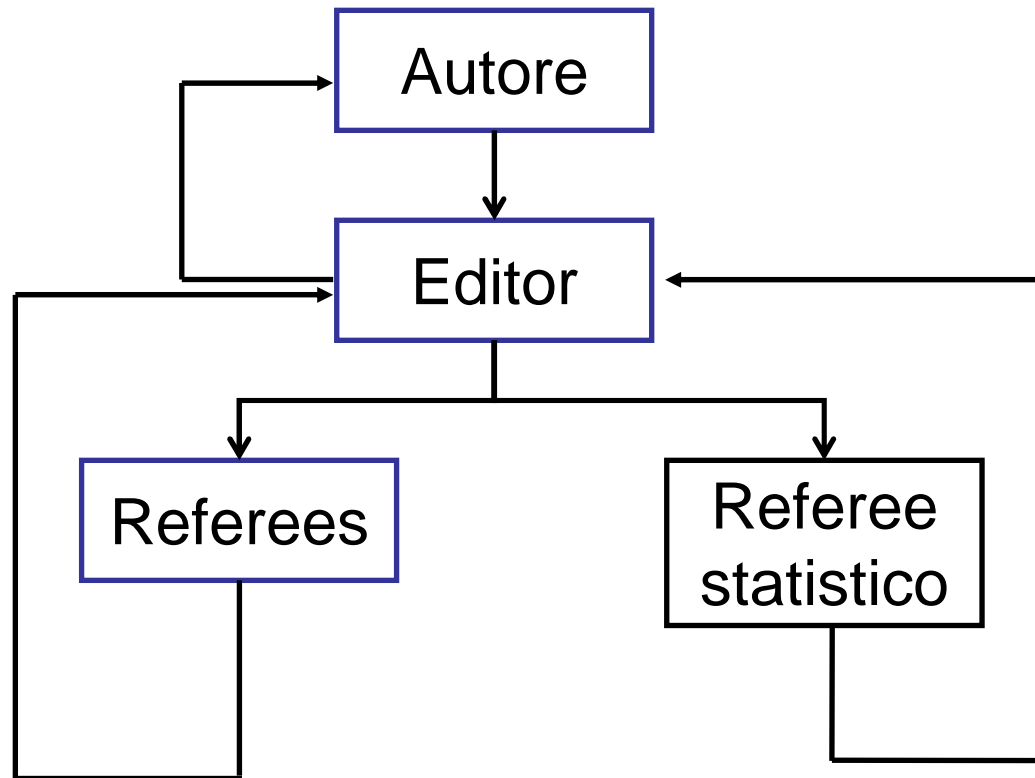


Il sistema di assicurazione di qualità della ricerca

La peer review:

- **Peer review** (also known as **refereeing**) is the process of subjecting an author's scholarly work, research, or ideas to the scrutiny of others who are experts in the same field. [Wikipedia Peer review 09/2009]

Processo della peer review



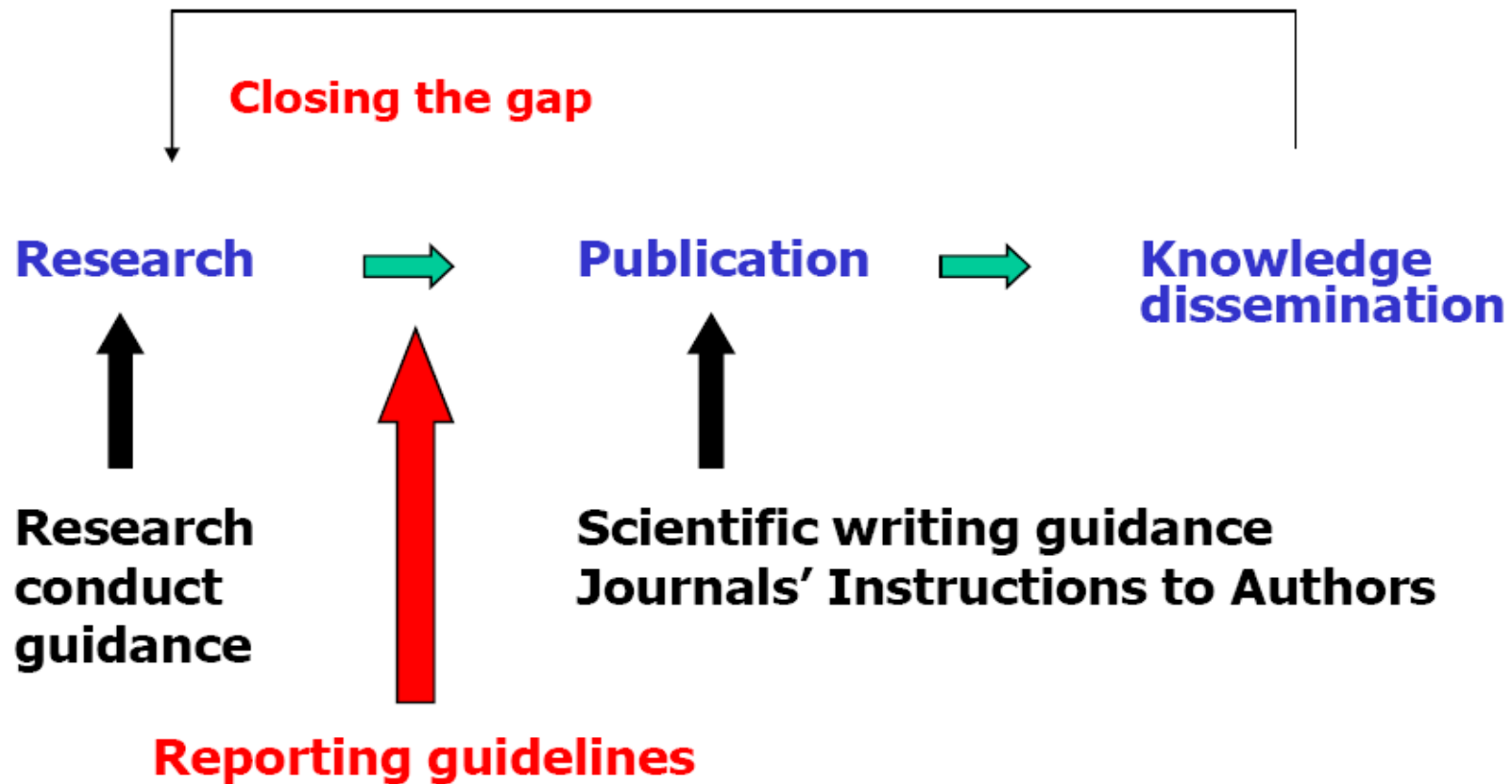
Il sistema di assicurazione di qualità della ricerca


- La peer review deve assicurare:
 - affidabilità dei risultati presentati
 - indipendenza dagli interessi
 - rilevanza
 - trasparenza
 - completezza
 - attinenza al focus della rivista

Il sistema di assicurazione di qualità della ricerca

- La peer review può essere praticata e interpretata in modi diversi
 - anonima vs nominativa
 - pedagogica vs autoritaria
 - ...

Le reporting guidelines



- 
- Good reporting is an essential part of good research Authors (and journals) have an obligation to ensure that research is reported adequately

La qualità del reporting

- Failure to report key aspects of trial conduct:
 - 73% Sample size calculation
 - 55% Defined primary outcome(s)
 - 60% Whether blinded
 - 79% Method of random sequence generation
 - 82% Method of allocation concealment

[Chan & Altman Lancet 2005]

La qualità del reporting

- “Data reporting was poor. 15 trials met the inclusion criteria for this review but only 4 could be included as data were impossible to use in the other 11.”

[Cochrane Library, accessed on 18 Sept 07]

La qualità del reporting

- “Despite quality guidelines, the average quality of published [systematic reviews] of antidepressants is barely acceptable. A need exists for adherence to standardized reporting and quality guidelines.”

[Hemels et al. Curr Med Res Opin 2004. Systematic reviews of pharmaco-therapy in major depressive disorder]

Selective reporting

- In addition, there is accumulating evidence of two major threats to the medical literature **Study publication bias** – studies with less interesting findings are less likely to be published
- **Outcome reporting bias** – results included within published reports are selected to favour those with statistically significant results

II CONSORT statement

- Consolidated Standards of Reporting Trials – Proposto negli anni '90 dal International Committee of Medical Journal Editors (ICMJE, The Vancouver Group)
- Main objective:
 - To facilitate critical appraisal and interpretation of RCTs by providing guidance to authors about how to improve the reporting of their trials
- Secondary objective:
 - To encourage and provide incentives for researchers to conduct high-quality, unbiased randomized trials

Fattori di successo

- Collaborative, open, ongoing process
- Membership of group
 - Methodologists
 - Trialists
 - Editors
- Focus on reporting rather than conduct
Evidence-based
- High profile publications

Altri statements

- Other study types – CONSORT as a model
- – QUOROM (meta-analyses of RCTs)
- – STARD (diagnostic studies)
- – STROBE (observational studies)
- – REMARK (tumour marker prognostic studies)

EQUATOR

- Enhancing the QUALity and Transparency Of health Research
 1. Provide resources enabling the improvement of health research reporting
 - Website
 - Courses
 2. Monitor progress in the improvement of health research reporting

Welcome to the EQUATOR Network website



Too often, good research evidence is undermined by poor quality reporting.

The EQUATOR Network is a new initiative that seeks to improve the quality of health care by promoting transparent and accurate reporting of health research.

[Find out how that goal will be achieved.](#)

If you share this goal, why not [join our Network?](#)

On this site:

Resource centre

Find [up-to-date information](#) about the reporting of health research.

Training Courses

We are also developing [educational materials and training modules](#) for editors, peer reviewers and researchers.

Support for reporting guidelines developers

Find out how to [join the EQUATOR Network.](#)

Progress in health research reporting

Find out how we are monitoring progress in the improvement of health research reporting.

reporting guidelines



[Go straight to the reporting guidelines](#)

editors

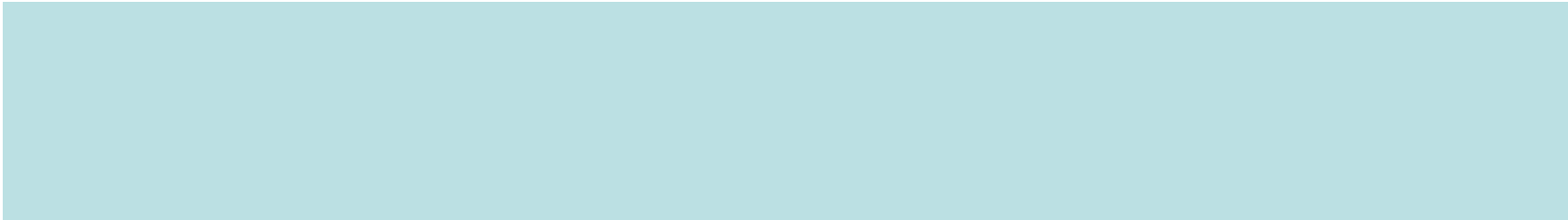


[Read editorials on reporting guidelines](#)

supporters



Funded by: [National Knowledge Service](#) and [National Institute for Health Research](#)

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- www.consort-statement.org
 - www.strobe-statement.org
 - www.equator-network.org

Tipologie di articolo scientifico

- Articoli originali (letteratura primaria):
 - presentano risultati di una ricerca
 - di base, RCT, studi osservazionali etc
- Revisioni – reviews (l. secondaria):
 - effettuano una sintesi dei risultati delle ricerca precedenti
 - possono essere “narrative” o “sistematiche”
- Editoriali (l. secondaria):
 - scritti da editors di riviste,
 - scopo: commentare, sottolineare l'importanza, collegare ricerche diverse e spesso incentivare l'adozione dei risultati della ricerca nella pratica
- Lettere:
 - per commentare, criticare altri contributi pubblicati
 - oppure per presentare risultati di ricerca non ancora pubblicati
- News, commenti, *education and debates* etc

Nascita delle revisioni sistematiche

“È causa di grande preoccupazione constatare come la professione medica non abbia saputo organizzare un sistema in grado di rendere disponibili, e costantemente aggiornate, revisioni critiche sugli effetti dell’assistenza sanitaria”

*Cochrane A.
Effectiveness and efficiency.
Random reflections on health service.
London: Nuffield Provincial Hospital Trust,
1972.*

Accedere ai risultati della ricerca scientifica può essere:

- Complesso
- Pletorico (per il numero di studi pubblicati)
- Confusivo per l'eterogeneità dei risultati
 - Vd oltre
- Metodologicamente difficile

Three solutions

Clinical performance can keep up to date:

- 1 by learning how to practice evidence-based medicine ourselves.
- 2 by seeking and applying evidence-based medical summaries generated by others.
- 3 by accepting evidence-based practice protocols developed by our colleagues.

(EBM center - Oxford, 1998)



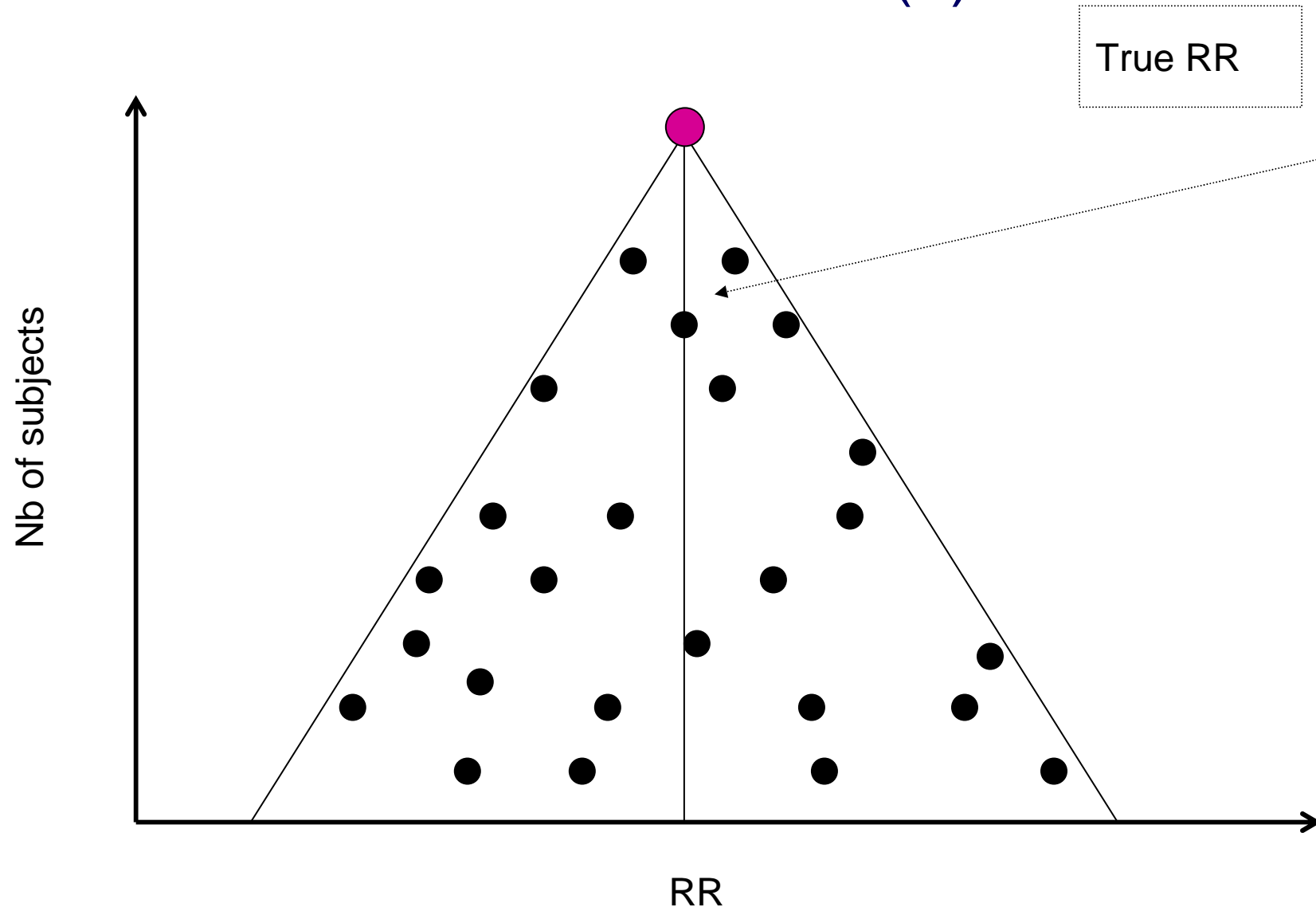
Come sintetizzare i risultati di più studi?

- Rassegna narrativa tradizionale
 - assenza regole esplicite e condivise di:
 - strategia di ricerca degli studi
 - criteri di selezione degli studi sulla base della qualità
 - estrazione dei dati
 - sintesi dei dati (di solito qualitativa)
 - Quindi non riproducibilità

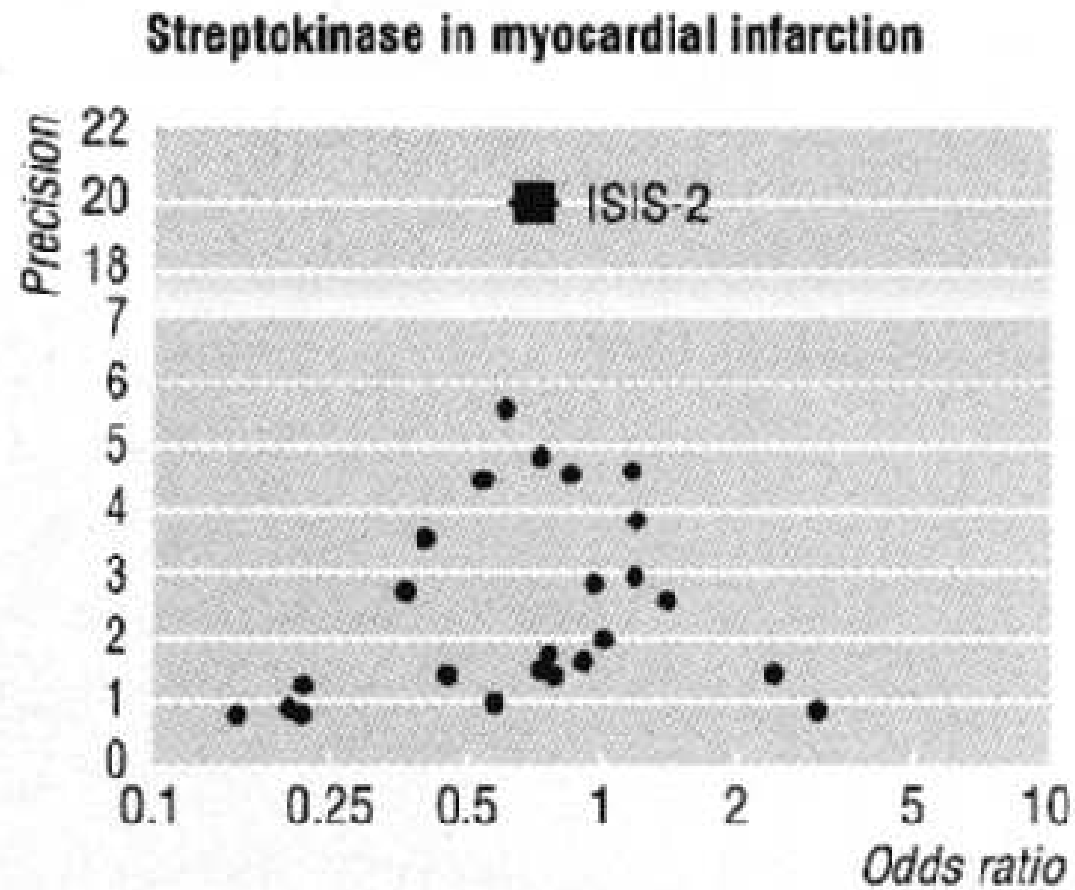
Publication bias (I)

- Def: differential probability of publication of *positive (expected)* results compared to *negative* ones
- It causes a bias (usually an increase in RR) in the estimated means of the results
 - *funnel-plot* can identify it
 - *systematic reviews* are able to manage it

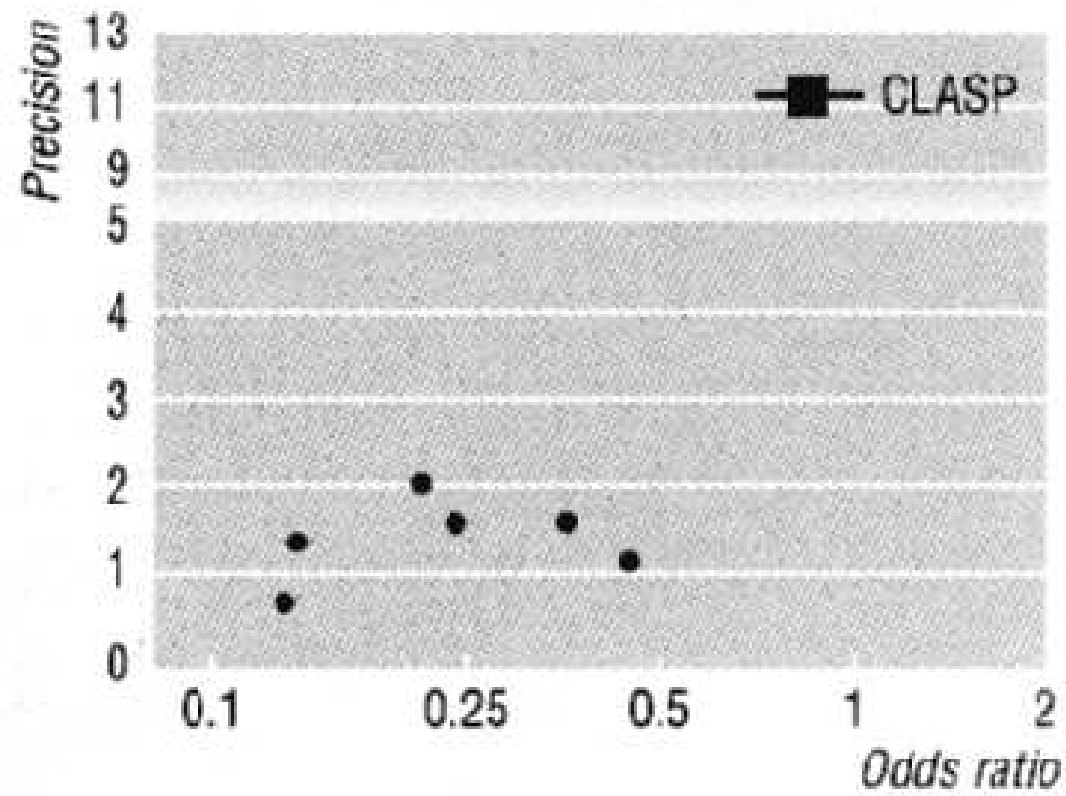
Publication bias (II)



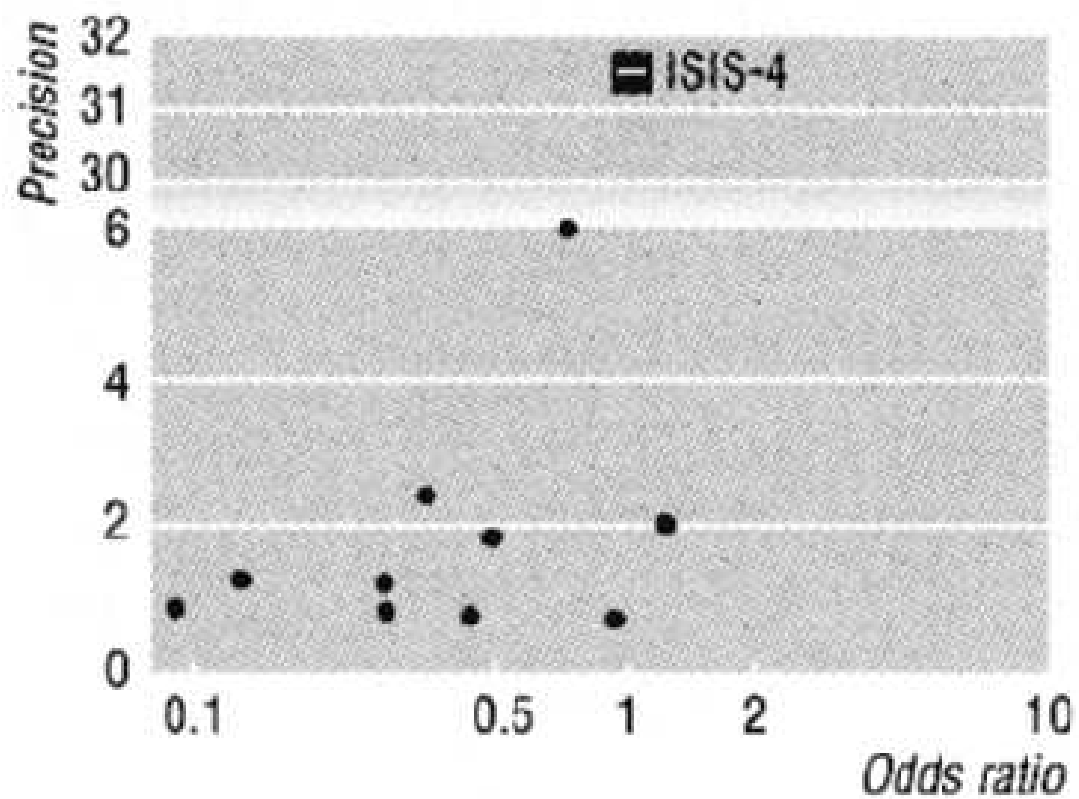
Funnel-plot for detection of publication bias



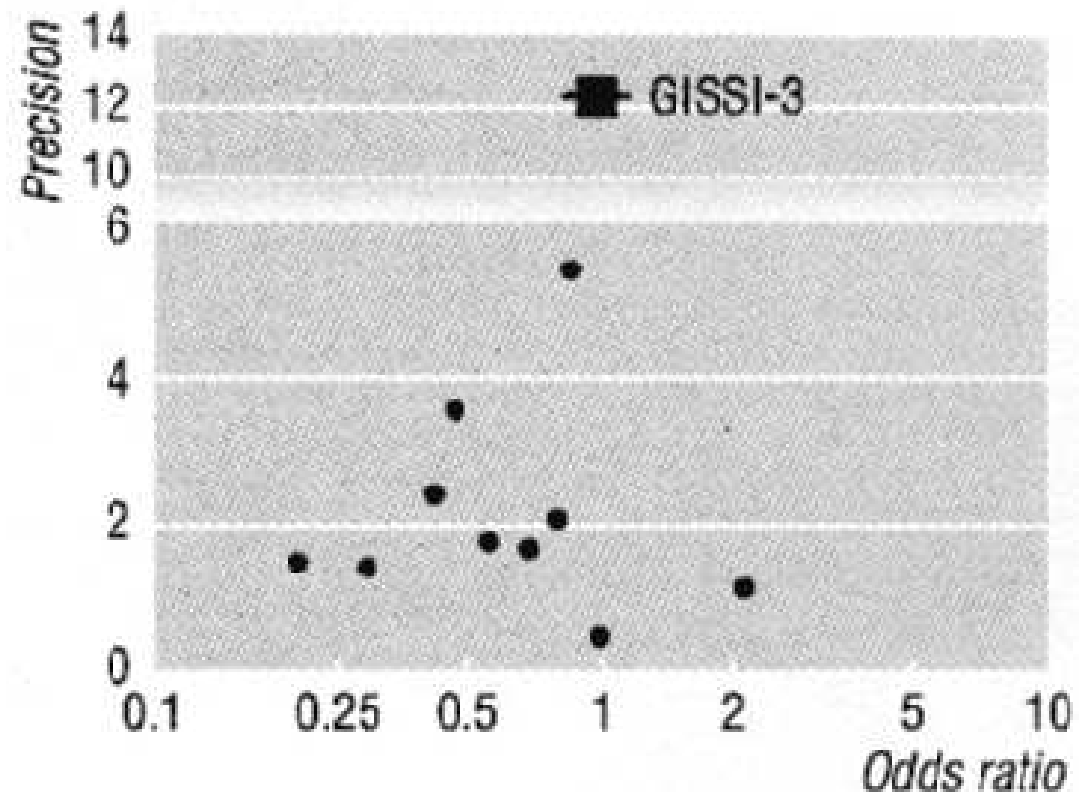
Aspirin for prevention of pre-eclampsia



Magnesium in myocardial infarction



Nitrates in myocardial infarction



Il controllo del Publication Bias

- Registri di trial
 - In cui ogni nuovo trial viene registrato
 - E può essere rintracciato anche se i suoi risultati non vengono pubblicati
- www.clinicaltrials.gov (per gli USA)
 - che contiene anche un guida metodologica agli RCT
 - nel 2004 11000 record in 50 paesi (50% non ancora pubblicati)
 - ma solo il 40% dei trial oncologici dell'industria vs il 90% di quelli finanziati dal pubblico
- eudract.emea.eu.it (European Clinical Trial Database)
 - nato dalla direttiva 2001/20/EC

Clinical Trial Registration

A Statement From the International Committee of Medical Journal Editors

a small proportion of trials. In this Editorial, published simultaneously in all member journals, the International Committee of Medical Journal Editors (ICMJE) proposes comprehensive trials registration as a solution to the problem of selective awareness and announces that all 11 ICMJE member journals will adopt a trials-registration policy to promote this goal.

The ICMJE member journals will require, as a condition of consideration for publication, registration in a public trials registry. Trials must register at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005. For trials that began enrollment prior to this date, the ICMJE member journals will require registration by September 13, 2005, before considering the trial for publication. We speak only for ourselves, but we encourage editors of other biomedical journals to adopt similar policies. For this purpose, the ICMJE defines a clinical trial as any research project that prospectively assigns human subjects to intervention or comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Studies designed for other purposes, such as to study pharmacokinetics or major toxicity (eg, phase 1 trials), would be exempt.



Deangelis et al, JAMA 2004; 292:1363

Come sintetizzare i risultati di più studi?

- Rassegna 'classica'
 - assenza regole esplicite e condivise di:
 - strategia di ricerca degli studi
 - criteri di selezione degli studi sulla base della qualità
 - estrazione dei dati
 - sintesi dei dati (di solito qualitativa)
 - rischio di influenza dell'autore nella:
 - selezione degli studi
 - valutazione critica
 - sintesi dei risultati
 - interpretazione della sintesi

Qualità delle rassegne di letteratura

Rassegna di 106 rassegne sui rischi del fumo passivo
(Barnes, 1998)

Table 3.—Relationship Between Article Conclusions
and Author Affiliations

Article Conclusion	No. (%) of Reviews	
	Tobacco-Affiliated Authors (n = 31)	Non-Tobacco-Affiliated Authors (n = 75)
Passive smoking harmful	2 (6)	65 (87)
Passive smoking not harmful	29 (94)	10 (13)
Significance	$\chi^2_1 = 60.69; P < .001$	

Qualità delle rassegne di letteratura (II)

Table 4.—Factors Associated With Concluding That Passive Smoking Is Not Harmful to Health: Multiple Logistic Regression Analysis

Factors	Odds Ratio* (95% Confidence Interval)	P Value
Mean quality score (continuous)	1.5 (<0.1-67.5)	.83
Peer review status		
Non-peer reviewed vs peer reviewed	1.3 (0.3-5.4)	.70
Author affiliation		
Tobacco industry vs non-tobacco industry	88.4 (16.4-476.5)	<.001
Topic		
Lung cancer vs multiple health effects	1.6 (0.2-10.3)	.63
Heart disease vs multiple health effects	1.6 (0.2-14.7)	.67
Respiratory disorders vs multiple health effects	1.8 (0.3-11.9)	.56
Other health effects vs multiple health effects	4.6 (0.6-32.8)	.13
Year of publication (continuous)	1.1 (0.9-1.3)	.45

*Odds ratio corresponds to factors associated with concluding that passive smoking is not harmful.


Fumo passivo... continua

Papers

Environmental tobacco smoke and tobacco related
mortality in a prospective study of Californians, 1960-98

James E Enstrom, Geoffrey C Kabat

Enstrom BMJ 17 May 2003



Conclusions The results do not support a causal relation between environmental tobacco smoke and tobacco related mortality, although they do not rule out a small effect. The association between exposure to environmental tobacco smoke and coronary heart disease and lung cancer may be considerably weaker than generally believed.

Funding: The American Cancer Society initiated CPS I in 1959, conducted follow up until 1972, and has maintained the original database. Extended follow up until 1997 was conducted at the University of California at Los Angeles with initial support from the Tobacco-Related Disease Research Program, a University of California research organisation funded by the Proposition 99 cigarette surtax (www.ucop.edu/srphome/trdrp). After continuing support from the Tobacco-Related Disease Research Program was denied, follow up through 1999 and data analysis were conducted at University of California at Los Angeles with support from the Center for Indoor Air Research, a 1988-99 research organisation that received funding primarily from US tobacco companies.²⁴

Competing interests: In recent years JEE has received funds originating from the tobacco industry for his tobacco related epidemiological research because it has been impossible for him to obtain equivalent funds from other sources. GCK never received funds originating from the tobacco industry until last year, when he conducted an epidemiological review for a law firm which has several tobacco companies as clients. He has served as a consultant to the University of California at Los Angeles for this paper. JEE and GCK have no other competing interests. They are both lifelong non-smokers whose primary interest is an accurate determination of the health effects of tobacco.

Enstrom BMJ 17 May 2003

Commento # 1

- Le rassegne classiche non permettono di evitare:
 - il bias da conflitto di interessi
 - il publication bias

Come sintetizzare i risultati di più studi?

- Rassegna sistematica
 - presenta regole esplicite per evitare il **publication bias** e ridurre l'**eterogeneità** :
 - **esaustività della ricerca di studi**
 - sia temporale, che ricerca studi non pubblicati
 - valutazione e scelta degli studi (*critical appraisal*)
 - estrazione dei dati
 - sintesi quantitativa (**metanalisi**)
 - *peer reviewing*
 - la **Collaborazione Cochrane** come modello internazionale