Il ruolo della EBM nel miglioramento della qualita della ricerca

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Centro Cochrane italiano

**XIII Riunione Annuale Network Cochrane italiano
Workshop**

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Contenuto della presentazione

- Perché è importante la ricerca

- Cosa ci ha insegnato la EBM?

- L'efficacia ed efficienza del sistema ricerca: gli *"sprechi evitabili"*

- Opportunità ed ostacoli

Perché è importante la ricerca

Perché è importante la ricerca

- **Per accrescere le conoscenze sugli interventi sanitari utili ai pazienti**

- **Per "completare" le conoscenze su molte tecnologie che arrivano nella pratica in uno stadio di "immaturità" conoscitiva**

- **Per aumentare la qualità del sistema**

- **Per garantire la sua sostenibilità**
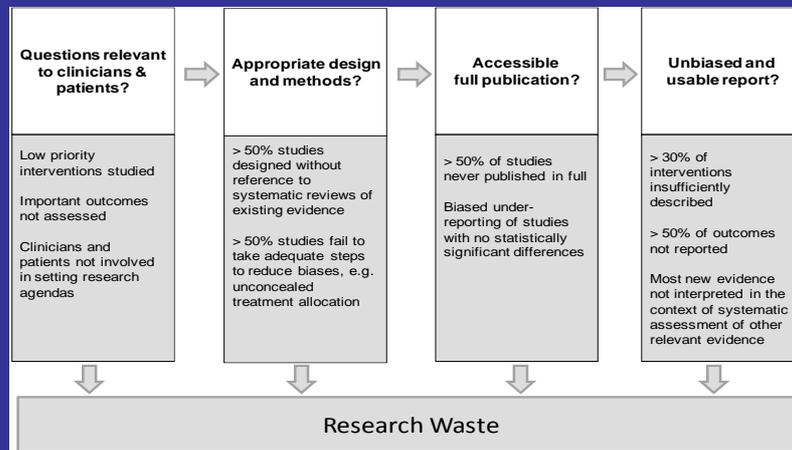
Cosa ci ha insegnato la EBM

- **Cattiva qualità metodologica**

- **Scarsa rilevanza clinica**

- **Sbilanciamento nella agenda della ricerca**

- **Conflitti di interesse e distorsioni sistematiche**

- **Inefficacia e inefficienza del sistema**

L'efficacia ed efficienza del sistema ricerca: gli *"sprechi evitabili"*

Le aree di *"spreco evitabile"* nel processo di ideazione, produzione, presentazione e disseminazione dei risultati della ricerca

Questions relevant to clinicians & patients?	Appropriate design and methods?	Accessible full publication?	Unbiased and usable report?
Low priority interventions studied Important outcomes not assessed Clinicians and patients not involved in setting research agendas	> 50% studies designed without reference to systematic reviews of existing evidence > 50% studies fail to take adequate steps to reduce biases, e.g. unconcealed treatment allocation	> 50% of studies never published in full Biased under-reporting of studies with no statistically significant differences	> 30% of interventions insufficiently described > 50% of outcomes not reported Most new evidence not interpreted in the context of systematic assessment of other relevant evidence

Research Waste

THE COCHRANE COLLABORATION®

A quali condizioni la ricerca può essere utile al sistema sanitario ed al paziente?

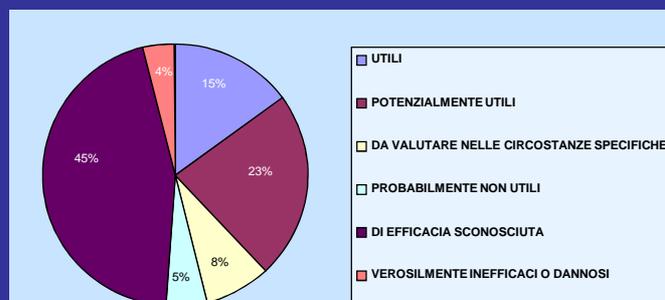THE COCHRANE COLLABORATION®

A quali condizioni può...?

- **Capace di ridurre l'incertezza**

- Rilevante rispetto ai bisogni dei pazienti e dell'organizzazione sanitarie

- Svolta come parte integrante della pratica clinica

- Ben condotta

- Appropriatamente riportata e disseminata

Categorisation of treatment effects in *Clinical Evidence June 2008*

Utili	Interventions for which effectiveness has been demostrated by clear evidence from RCTs and for which expectation harms is small compared with the benefits.
Potenzialmente utili	Interventions for which effectiveness is less well established
Da valutare nelle specifiche circostanze	Interventions for which clinicians and patients should weigh up the beneficial and harmful effects according to individual circumstances and priorities.
Probabilmente non utili	Interventions for which lack of effectiveness is less well estabilished
Verosimilmente inefficaci o dannosi	Interventions for which inefectiveness or harmfulness is demonstrated by clear evidence.

- □ UTILI
- ■ POTENZIALMENTE UTILI
- □ DA VALUTARE NELLE CIRCOSTANZE SPECIFICHE
- □ PROBABILMENTE NON UTILI
- ■ DI EFFICACIA SCONOSCIUTA
- ■ VEROSILMENTE INEFFICACI O DANNOSI

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- Sistematicamente legata alla innovazione clinica ed organizzativa

La ricerca spesso non si occupa dei bisogni dei pazienti

Two examples

Relation between agendas of the research community and the research consumer

Deborah Tallon, Jiri Chard, Paul Dieppe

The Lancet, 2000

THE RELATION BETWEEN FUNDING BY THE NATIONAL INSTITUTES
OF HEALTH AND THE BURDEN OF DISEASE

CARY P. GROSS, M.D., GERARD F. ANDERSON, PH.D., AND NEIL R. POWE, M.D., M.P.H., M.B.A.

N Engl J Med, 1999

Treatment	Have not tried	Not helpful	Slightly helpful	Moderately/ extremely helpful	Total responses
Knee replacement	73 (92%)	0	1 (1%)	5 (6%)	79
Tablets*	8 (9%)	6 (7%)	16 (18%)	59 (66%)	89
Injections in the knee	42 (51%)	7 (9%)	10 (12%)	23 (28%)	82
Aids and adaptions	37 (44%)	1 (1%)	22 (26%)	25 (29%)	85
Removal of fluid/debris	50 (63%)	6 (8%)	8 (10%)	15 (19%)	79
Other treatment	14 (58%)	1 (4%)	4 (17%)	5 (21%)	24
Physical therapy	36 (44%)	7 (9%)	19 (23%)	20 (24%)	82
Complementary therapy	57 (72%)	5 (6%)	8 (10%)	9 (11%)	79
Education and advice	40 (49%)	5 (6%)	20 (24%)	17 (21%)	82
No treatment at all	35 (76%)	6 (13%)	4 (9%)	1 (2%)	46

*We used the word tablets in the questionnaire, rather than NSAIDs or analgesics, since focus group discussion suggested some patients do not differentiate between these drug types.

Table 2: **Summary of patients' responses to the question: how helpful do you find these treatments for reducing pain and disability?**

THE RELATION BETWEEN FUNDING BY THE NATIONAL INSTITUTES OF HEALTH AND THE BURDEN OF DISEASE

Cary P. Gross, M.D., Gerard F. Anderson, Ph.D., and Neil R. Powe, M.D., M.P.H., M.B.A.
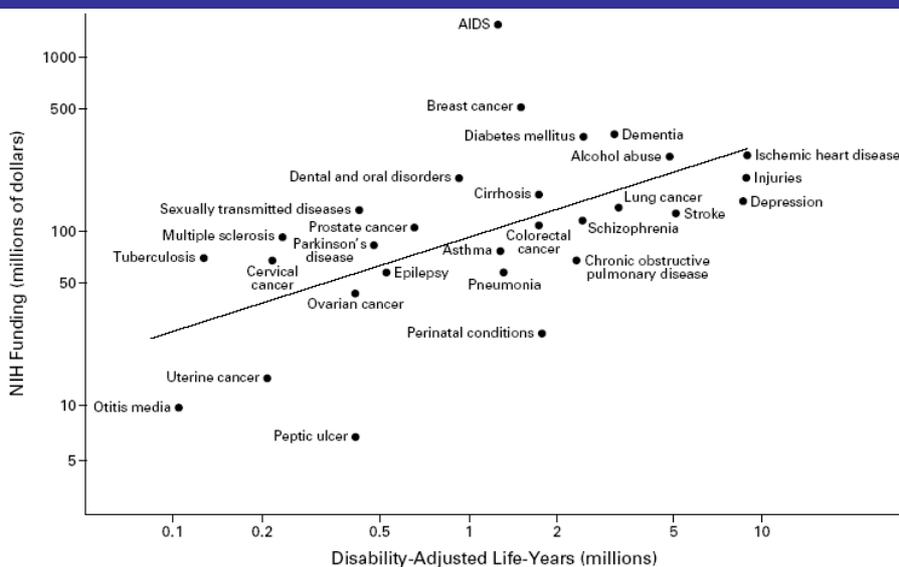
N Engl J Med, 1999

Figure 1. Relation between NIH Disease-Specific Research Funding in 1996 and Disability-Adjusted Life-Years for 29 Conditions in 1990.

The axes are drawn to logarithmic scale. The line represents funding predicted on the basis of a linear regression with disability-adjusted life-years as the explanatory variable. One disability-adjusted life-year is defined as the loss of one year of healthy life to disease.

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Essay

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

There is increasing concern that most current published research findings are false. The probability that a research claim is true may depend on study power and bias, the number of other studies on the same question, and importantly, the ratio of true to no relationships among the relationships probed in each scientific field. In this framework, a research finding is less likely to be true when the studies conducted in a field are smaller; when effect sizes are smaller; when there is a greater number and lesser preselection of tested relationships; where there is greater flexibility in designs, definitions

factors that influence this problem and some corollaries thereof.

Modeling the Framework for False Positive Findings

Several methodologists have pointed out [9–11] that the high rate of nonreplication (lack of confirmation) of research discoveries is a consequence of the convenient, yet ill-founded strategy of claiming conclusive research findings solely on the basis of a single study assessed by formal statistical significance, typically for a p-value less than 0.05. Research is not most appropriately represented and summarized by p-values, but,

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships or searches for only one or a few true relationships among thousands and millions of hypotheses that may be postulated. Let us also consider, for computational simplicity, circumscribed fields where either there is only one true relationship (among many that can be hypothesized) or the power is similar to find any of the several existing true relationships. The pre-study probability of a relationship being true is $R/(R + 1)$. The probability of a study finding a true relationship reflects the power $1 - \beta$ (one minus

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Publication bias

is the tendency on the parts of investigators, reviewers, and editors to submit or accept manuscripts for publication based on the direction or strength of the study findings

- Kay Dickersin
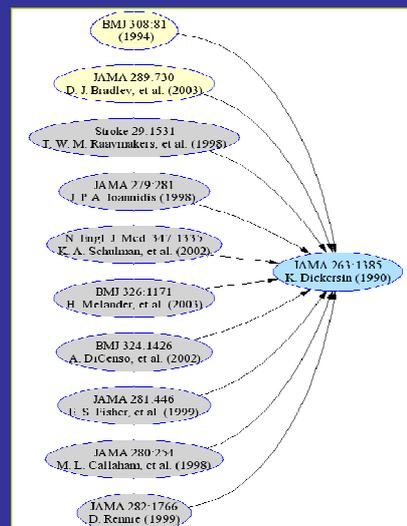
Dickersin K. JAMA 1990;263:1385-9

Outcome reporting bias

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

Context Selective reporting of outcomes within published studies based on the nature or direction of their results has been widely suspected, but direct evidence of such bias is currently limited to case reports.

Objective To study empirically the extent and nature of outcome reporting bias in a cohort of randomized trials.

Design Cohort study using protocols and published reports of randomized trials approved by the Scientific-Ethical Committees for Copenhagen and Frederiksberg, Denmark, in 1994-1995.

Chan A-W et al. JAMA 2004;291:2457-65

Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials
Comparison of Protocols to Published Articles

An-Wen Chan, MD, DPhil

Results One hundred two trials with 122 published journal articles and 3736 outcomes were identified. Overall, 50% of efficacy and 65% of harm outcomes per trial were incompletely reported. Statistically significant outcomes had a higher odds of being fully reported compared with nonsignificant outcomes for both efficacy (pooled odds ratio, 2.4; 95% confidence interval [CI], 1.4-4.0) and harm (pooled odds ratio, 4.7; 95% CI, 1.8-12.0) data. In comparing published articles with protocols, 62% of trials had at least 1 primary outcome that was changed, introduced, or omitted. Eighty-six percent of survey responders (42/49) denied the existence of unreported outcomes despite clear evidence to the contrary.

Chan A-W et al. JAMA 2004;291:2457-65

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LA RICERCA
INDIPENDENTE SUI FARMACI
PROMOSSA DALL'AIFA

*Convegno Nazionale
Roma, 30 settembre 2008 - Centro Congressi "Frentani"
Via dei Frentani, 4*

Rapporto
sull'organizzazione
della ricerca
indipendente
sui farmaci
promossa dall'AIFA
nel triennio 2005 - 2007

A cura dell'Ufficio Ricerca e Sviluppo e della
Commissione Ricerca e Sviluppo dell'AIFA

AIFA

Le opportunità

- **Parte integrante della pratica clinica**

- **Costi contenuti**

- **Risultati più vicini a quanto si può ottenere nella pratica clinica "reale"**
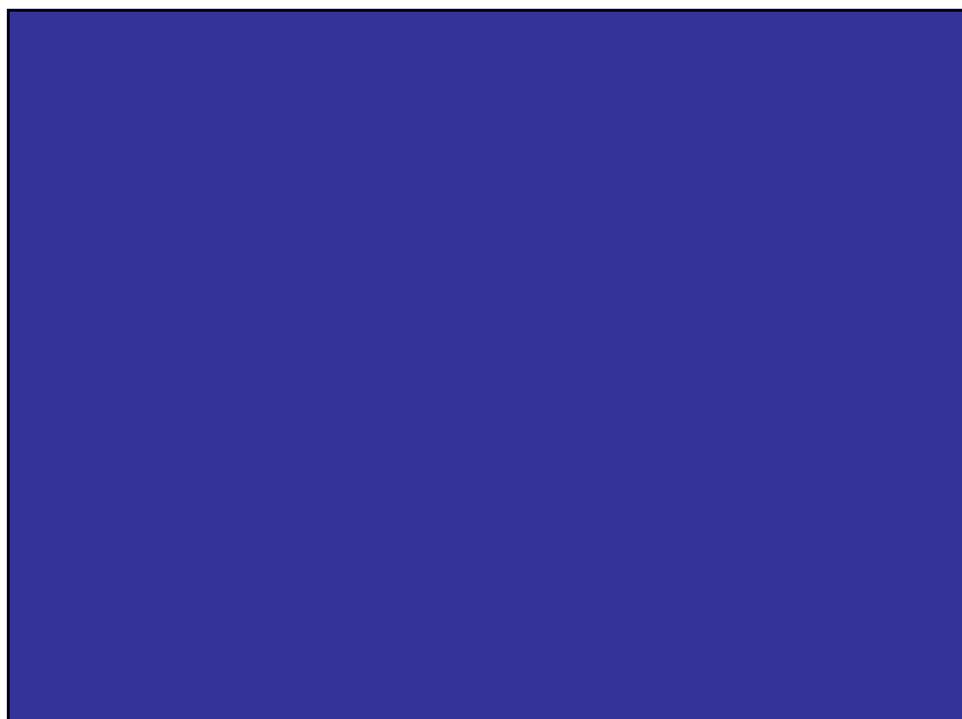
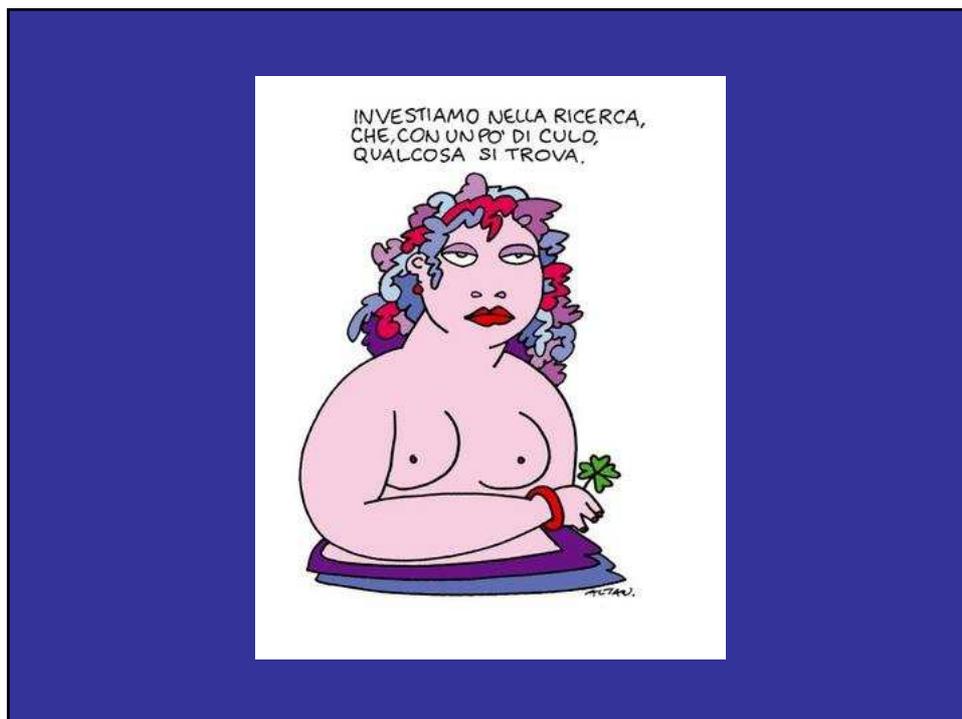- **Possibilità di un rapido trasferimento dei risultati**

Gli ostacoli

14

Gli ostacoli

- **Ambiente culturale non favorevole**

- **Doppio standard etico tra ricerca e pratica clinica**

- **Mancanza della infrastruttura necessaria**

- **Mancanza di adeguati incentivi**

- **Conflitti/mancanza di interesse**

A field guide to experts

Andrew D Oxman, Iain Chalmers, Alessandro Liberati on behalf of the World Artifexology Group

Experts are common but not well understood. This guide introduces novice expert spotters to the essentials of artifexology—the study of experts

British Medical Journal, 2004

Species of experts

Crow
Type: Large and noisy expert. Often wrong, hence the expression "eat crow" (although crows have never been known to do this)
Plumage: Boring, conservative ties. Chunky around the belly, glossy hair
Voice: Boasting and bragging
Habitat: Everywhere
Mating habits: Multiple encounters (whenever possible) at conferences
Migration patterns: Generally insists on flying first class and staying in suites

Vulture
Type: A large, bald headed expert of prey
Plumage: Nondescript. All types of regular ties
Voice: Grunting
Habitat: Academic institutions
Mating habits: Takes advantage of students
Migration patterns: Soars at high altitudes, seeking carrion
Feeding habits: Feeds on junior colleagues, unsuspecting associates, honorariums, and stock options

Any resemblance to persons, living or dead, is purely coincidental