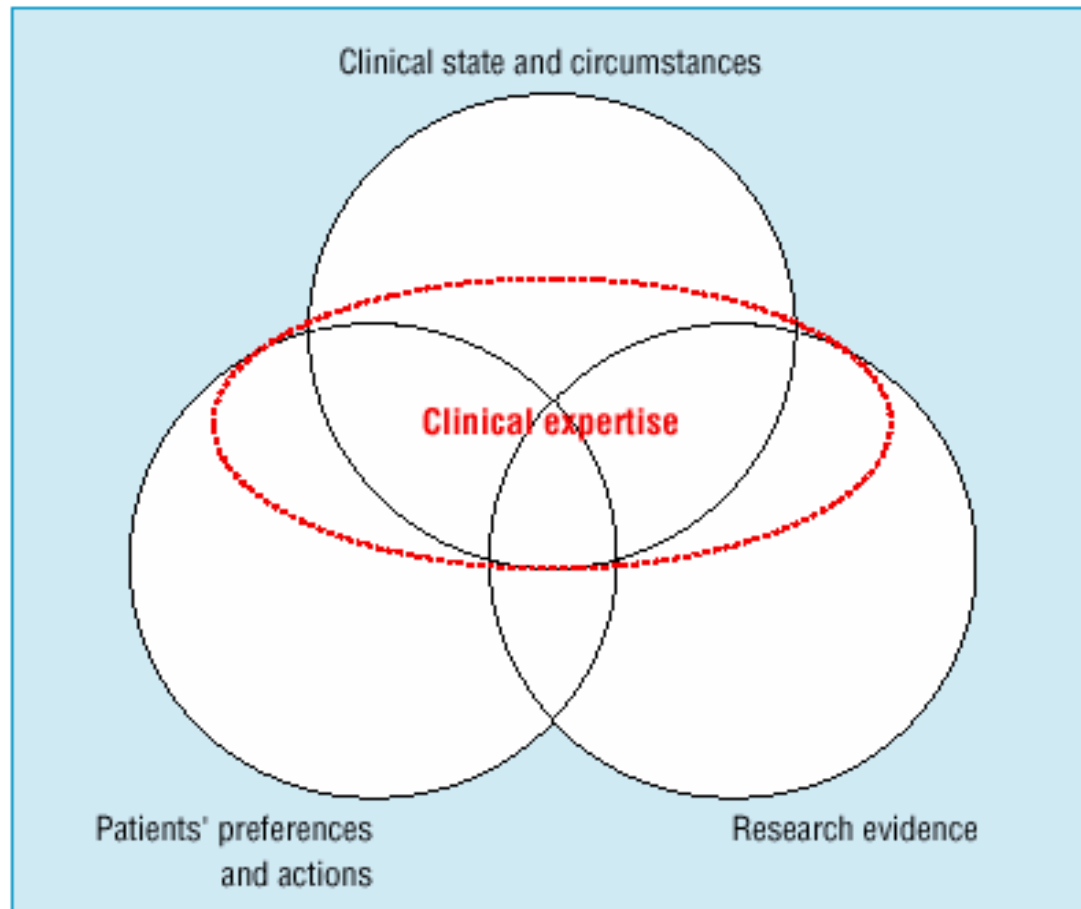


Introduzione metodologica

Trieste, 26 Febbraio 2009

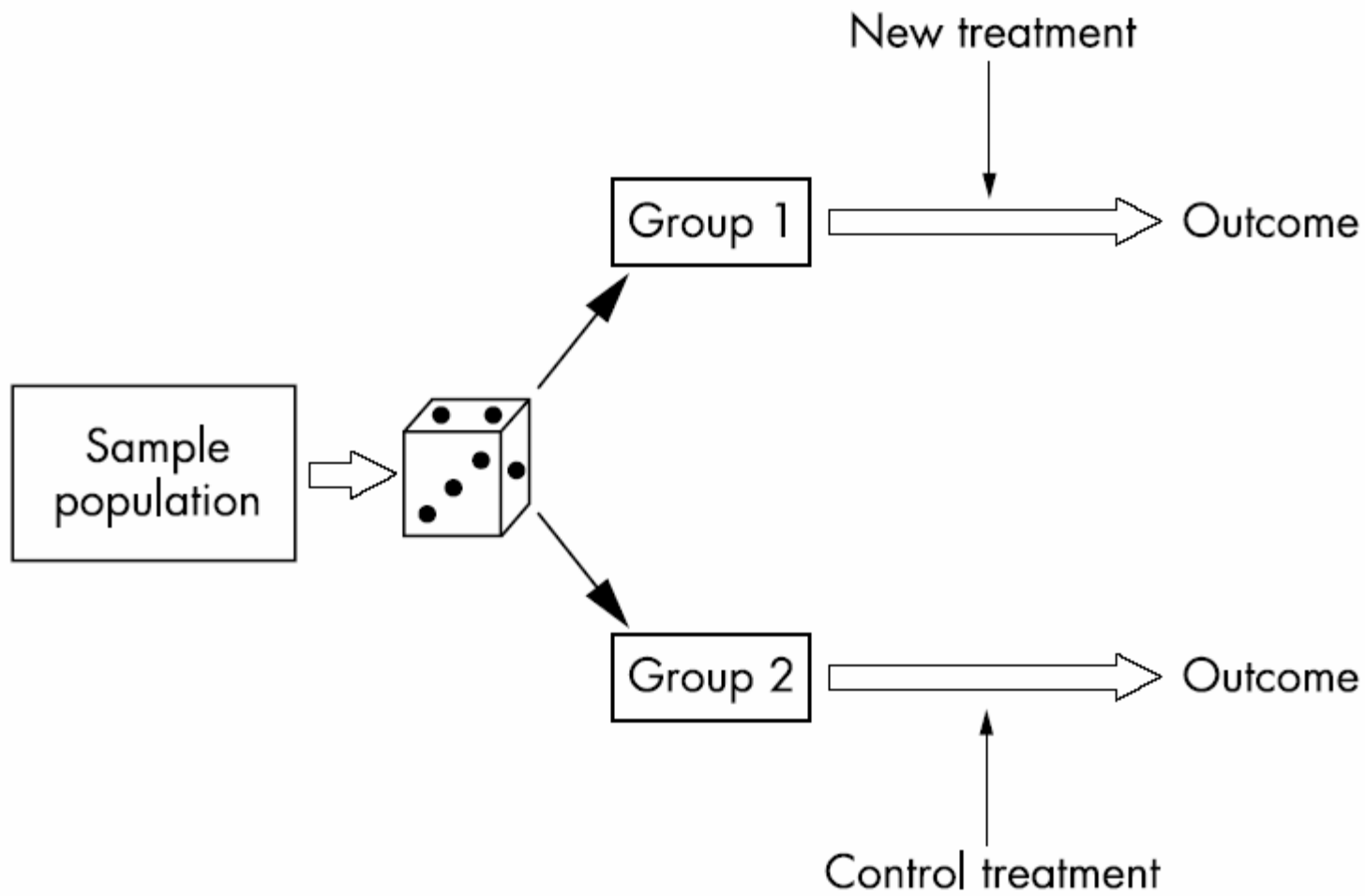


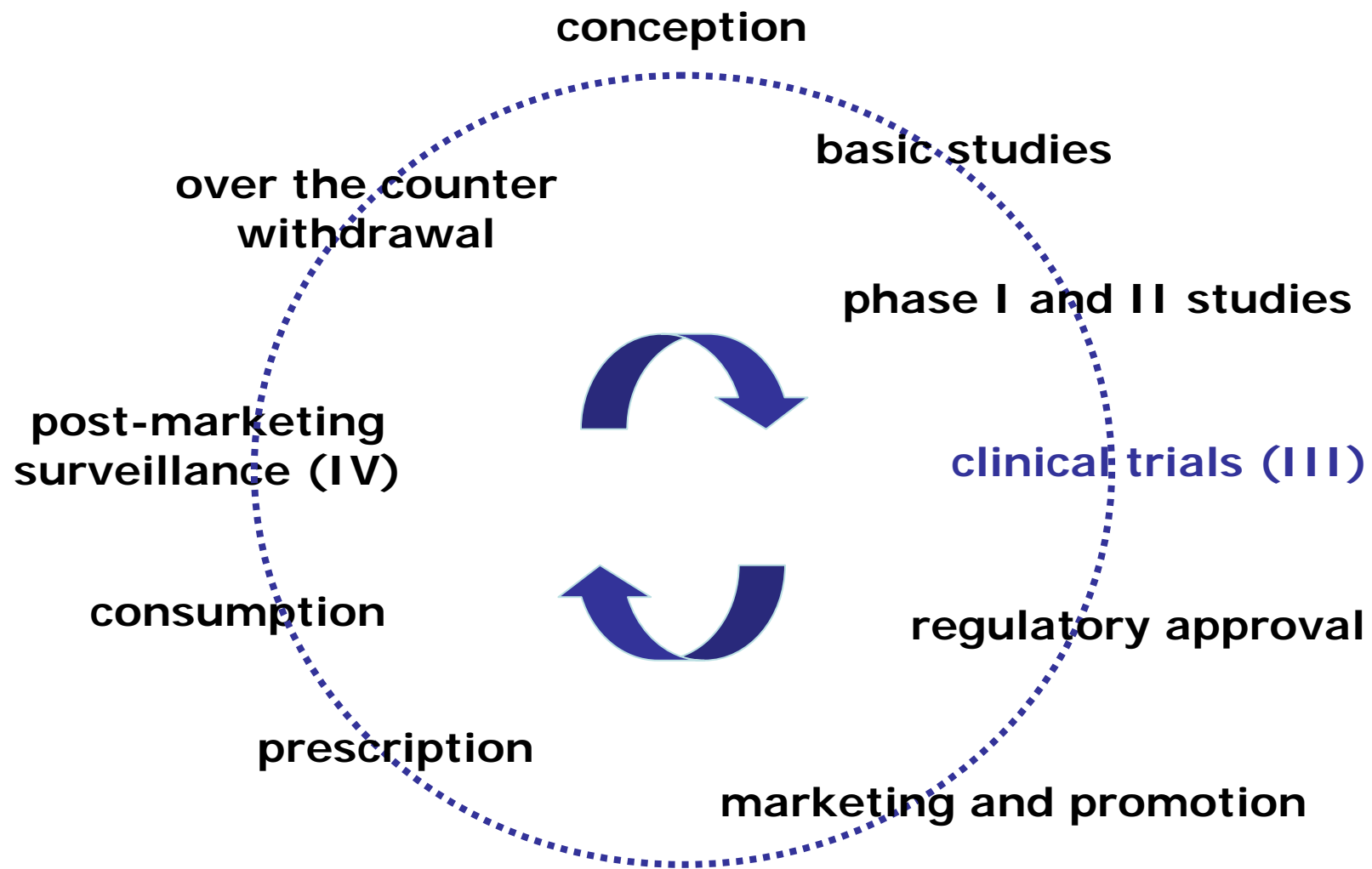
An updated model for evidence based clinical decisions¹

BMJ 2002;324:1350

Medicina basata sulle prove di efficacia

Le decisioni in medicina devono tenere in considerazione le evidenze scientifiche (= prove di efficacia) a nostra disposizione





*Cohen D, McCubbin M, Collin J, Perodeau G.
Medication as a social phenomena. Health 2001, 5, 461-489*

“Le sperimentazioni cliniche [...] non studiano i miei pazienti, non studiano i miei trattamenti, non valutano gli esiti che cerco di ottenere”

“... not my patients, not my treatments, not what I try to do”

[Keller MB, Lavori PW.](#)

The adequacy of treating depression.

J Nerv Ment Dis. 1988 Aug;176(8):471-4.

“... not my patients”

Box 1 Some of the differences between routine clinical practice and traditional randomised controlled trial (RCT) design

Events in a typical RCT

Patients are recruited from specialist centres, or by advertising
Patients with comorbid medical or psychiatric disorders are excluded
Patients are carefully selected to generate homogeneous diagnostic groups according to DSM and ICD
Patients are allocated the treatment at random
Patients are given detailed information (which may be overinclusive) for informed consent
Patients are given a 1-week placebo run-in period to remove placebo responders

Events in the real world

Patients are mainly treated in primary care
Patients are probably treated whatever comorbid disorders are present
Patients with heterogeneous diagnoses according to DSM or ICD are ‘lumped’ together
Treatment is allocated via a complex process of explanation and negotiation
Patients provided brief information (which may be underinclusive) for informed consent
All patients are given active treatment from the start

“... not my treatments”

Placebo is used to compare active treatment
Patients are followed at frequent intervals and given detailed checklists of side-effects
Assessment end-point is typically 4–6 weeks after treatment begins

No placebo is used: choice is between active treatment and no treatment
Patients are followed at very varying intervals according to haphazard practice
Patients continue on treatment for 6 months, and patient and clinician are interested in much longer end-points

“... not what I try to do”

Assessment of outcome is based on depressive symptoms and side-effects
Patient and clinician are blind to treatment group

To patient and doctor, functional outcomes (e.g. return to work) may be more important
Both (usually) are aware of the drug the patient is given

Today's Random Medical News

from the New England
Journal of
Panic-Inducing
Gobbledygook

JIM BRAMAN



Cartoon deriding chronic disease epidemiology, for randomly generating fears by investigating seemingly unrelated risk factors and diseases

This cartoon contains a grain of truth: observational research is at its methodological best in discovering unexpected adverse effects.

Advances in Psychiatric Treatment (2002), vol. 8, pp. 326–333

The pragmatic randomised controlled trial

Matthew Hotopf

"... my patients"

Box 2 The design of pragmatic RCTs

Pragmatic RCTs:

- reflect the heterogeneity of patients in general practice
- minimise exclusion criteria
- focus on groups with a wide range of diagnoses
- define patient groups by presentation rather than diagnosis

"... my treatments"

- may not employ placebos
- may not be blinded
- must carefully conceal allocation during randomisation

“ ... what I try to do”

Box 3 Outcomes in a pragmatic randomised controlled trials

Outcome measures should reflect ‘real world’ concerns:

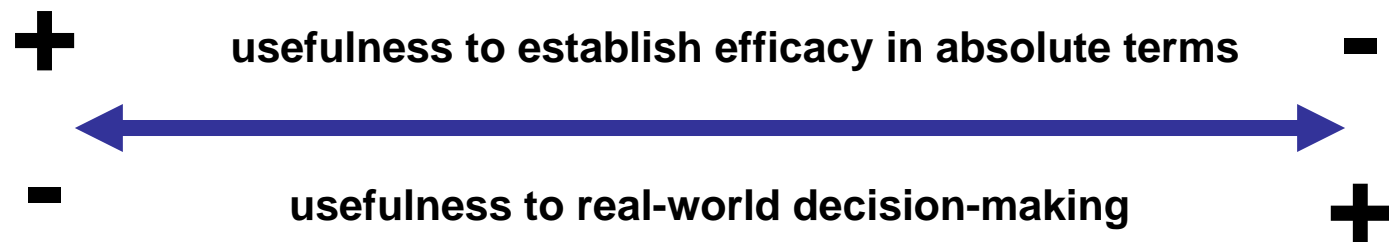
- return to work
- readmission to hospital
- reduction in visits to the GP
- cost-effectiveness
- suicide attempts
- death from suicide
- acts of violence

Functional outcomes should be emphasised
Outcomes must be measured over a sufficient time period

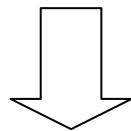
- ❑ **Pazienti non selezionati in setting rappresentativi**
 - ❑ **Trattamenti simili a quelli erogati in pratica**
 - ❑ **Indicatori di esito clinicamente rilevanti**
 - ❑ **Campioni numerosi**
 - ❑ **Durata adeguata**
 - ❑ **Indipendenza da interessi commerciali**
-

TRIAL PRAGMATICI DI EFFECTIVENESS

SPECTRUM FROM EXPLANATORY TO PRAGMATIC TRIALS

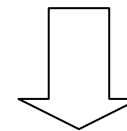


**EXPLANATORY
(efficacy) trials**

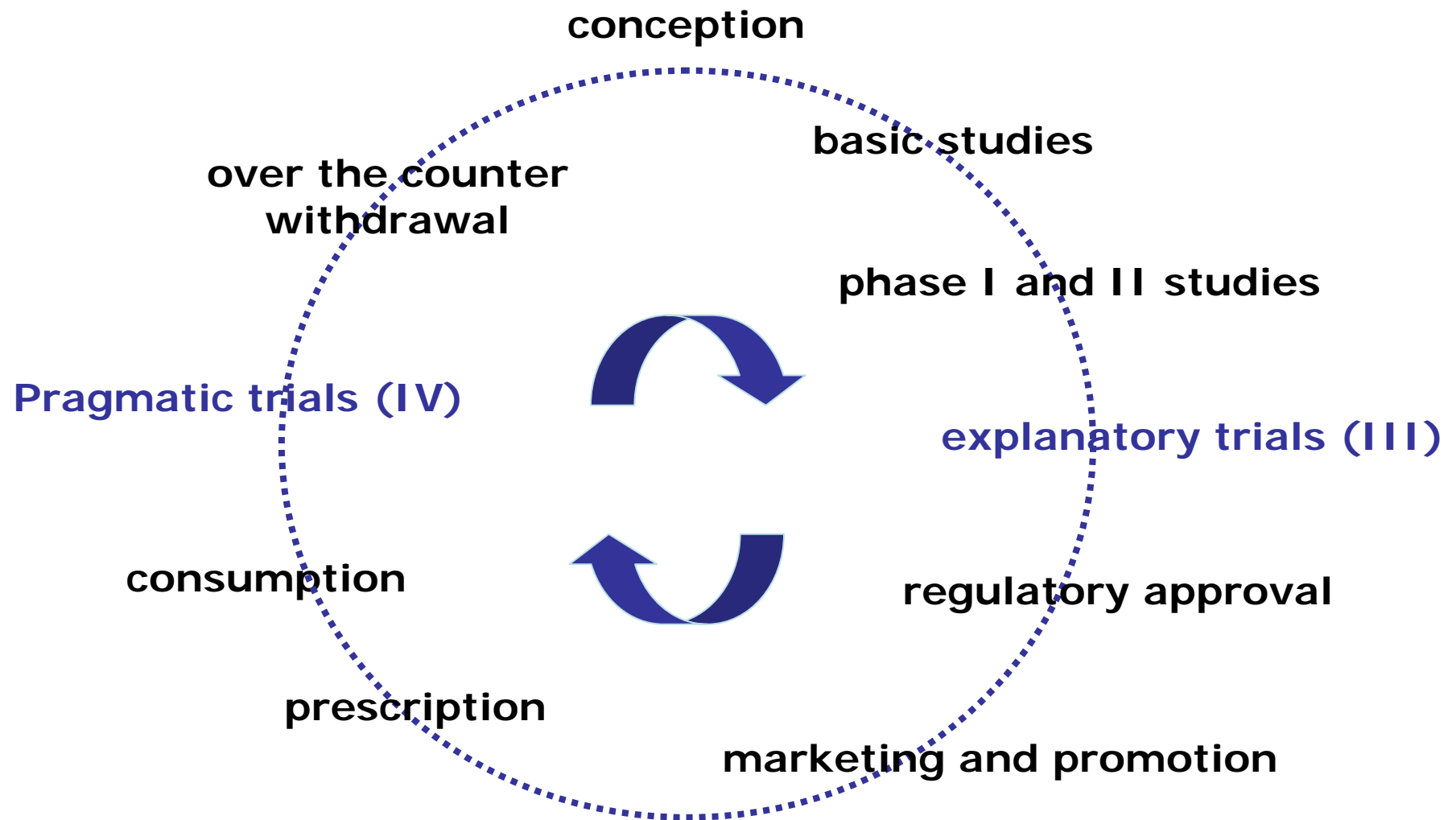


**Phase III
studies**

**PRAGMATIC
(effectiveness) trials**



**Phase IV
studies**



*Cohen D, McCubbin M, Collin J, Perodeau G.
Medication as a social phenomena. Health 2001, 5, 461-489*



Studio clinico controllato (RCT) = evidenze sulla efficacia e tollerabilità degli interventi

Per ogni argomento vi sono molti RCT:

- piccoli numeri di pazienti
- bassa qualità
- risultati spesso discordanti



**RACCOGLIERE IN MODO SISTEMATICO
LE INFORMAZIONI CONTENUTE NEI RCT**



Gruppi di ricerca con la missione di raccogliere in modo sistematico le evidenze scientifiche (*Cochrane Association*) e di presentarle sotto forma di revisioni sistematiche della letteratura (*systematic reviews*, SR)



Nuove analisi statistiche (aumentano il potere statistico, permettono di stratificare gli studi, forniscono misure che sintetizzano dati provenienti da molti trial)
= *meta-analisi*



DMSP-PSY

Cochrane
Association

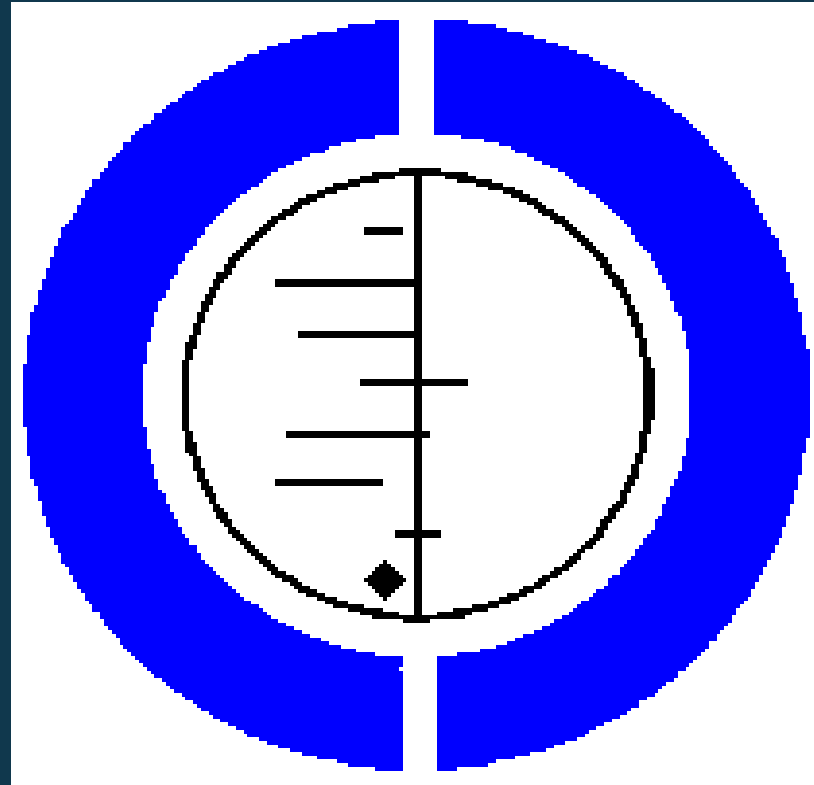


letteratura
scientifica



Cochrane
library

<http://www.cochrane.org/>



Levels of evidence:

- 1A systematic review of RCTs;
- 1B individual RCT;
- 2A systematic review of cohort studies;
- 2B individual cohort study, low-quality RCT;
- 2C ecological studies;
- 3A systematic review of case-control studies;
- 3B individual case-control study;
- 4 case series, poor-quality cohort and case-control studies.