Risk of bias, Heterogeneity

BIAS

- ERRORI
- Sistematici

1. Agiscono sempre nella stessa direzione,
2. spostano la stima sempre dalla stessa parte

VALIDITA' INTERNA

La misura in cui uno studio riesce a cogliere la relazione «**vera**» fra due variabili:

ERRORE CASUALE:

..si verifica per effetto del caso

Replicazioni multiple della stessa misurazione producono differenti risultati in tutte le direzioni per variazioni casuali ma la media dà il risultato corretto

ERRORE SISTEMATICO (BIAS)

..si verifica per la presenza di un fattore che distorce sistematicamente le osservazioni nella stessa direzione

Replicazioni multiple della stessa misurazione producono risultati sempre nella stessa direzione e "sbagliati"

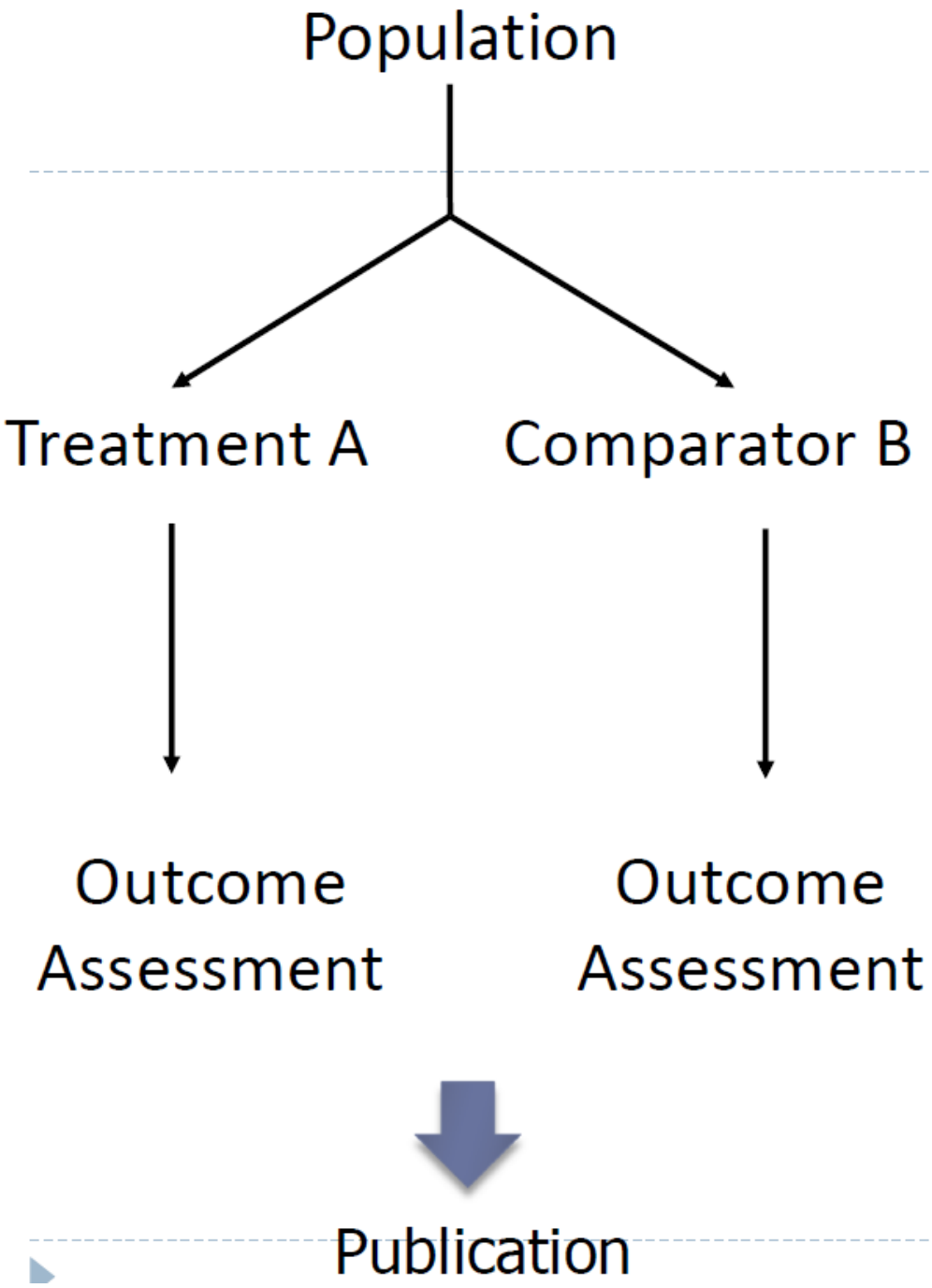
Errore sistematico e validità interna di uno studio

- **Gli errori sistematici**
- vanno previsti ed
- evitati o ridotti in fase di **disegno** dello studio

Bias

- **Systematic distortion** of the estimated intervention effect away **from the truth**, caused by **inadequacies** in the **design**, **conduct**, or **analysis** of a trial , or in the **publication of its results**.
- In other words, **in a biased** trial, the results observed **reflect other factors** in addition to (or, **in extreme cases, instead of**) the effect of the tested therapeutic procedure alone.

Altman DG, Schulz KF, Moher D, et al. The revised CONSORT statement for reporting randomized trials: explanation and elaboration. Ann Intern Med 2001;134:663–94



Bias

Selection bias

Performance bias

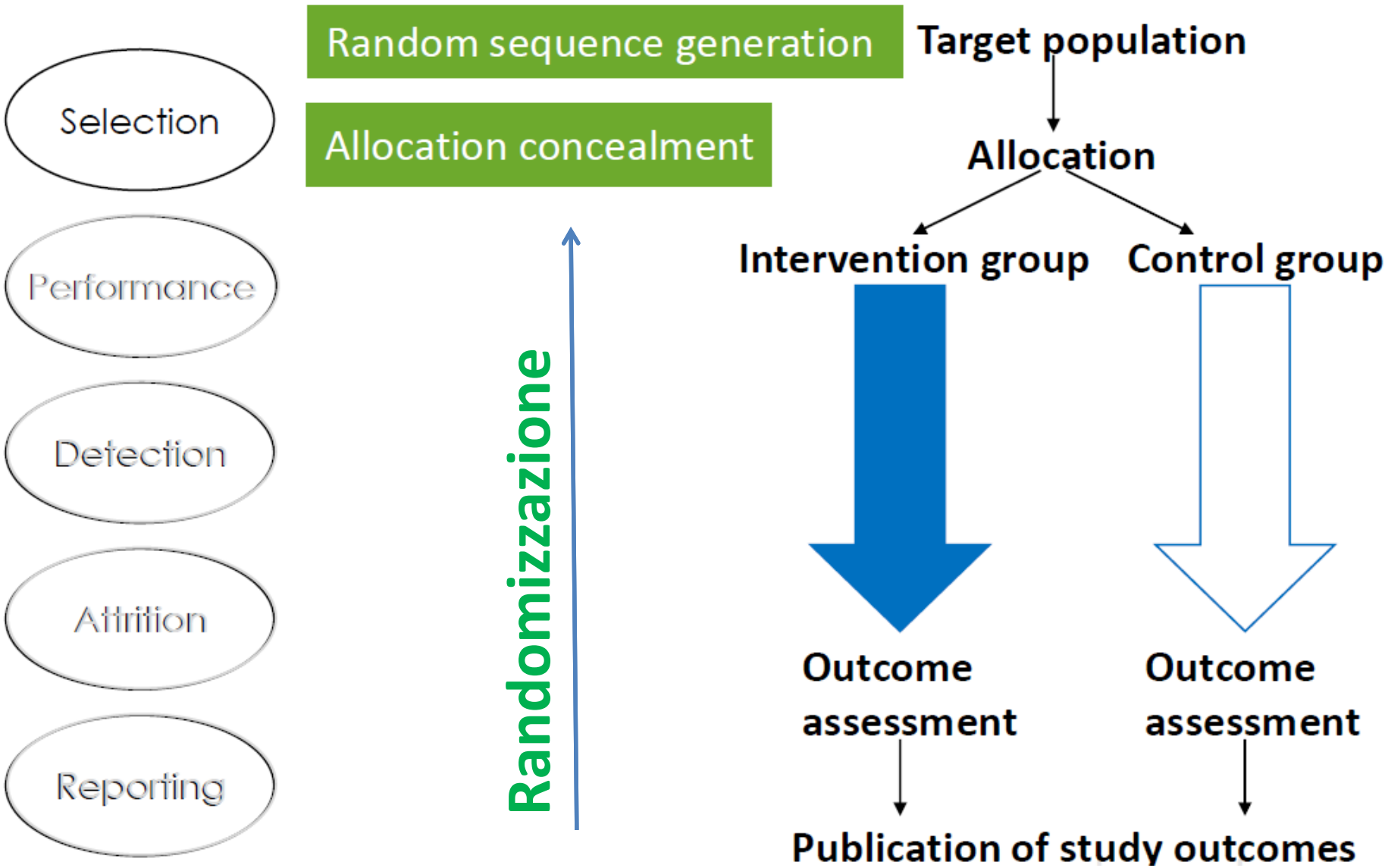
Detection bias

Attrition bias

Reporting bias

Critical apprisal RCT

Sources of bias



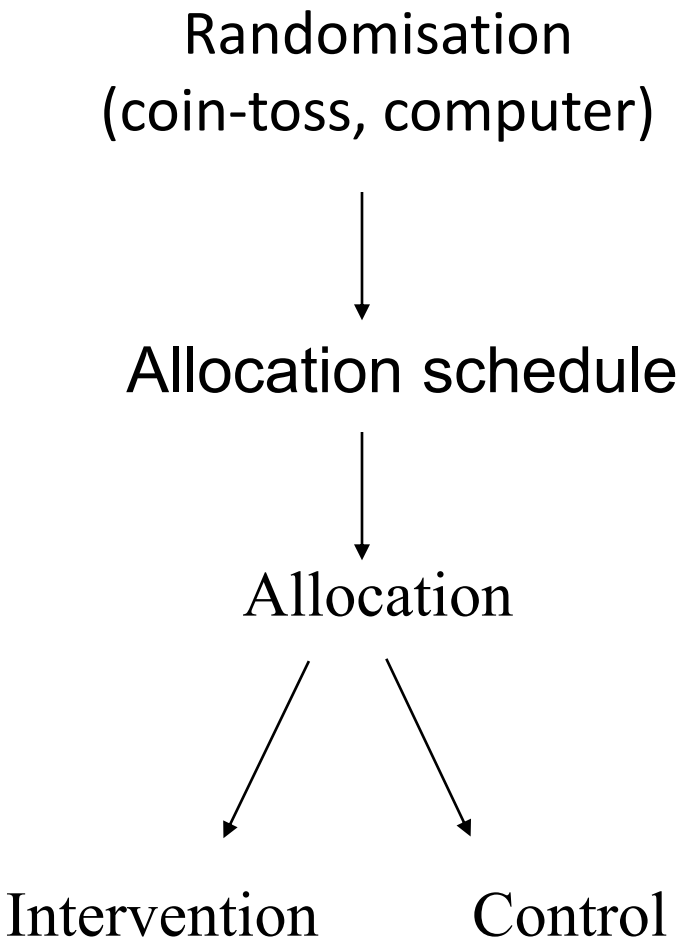
Why randomise?

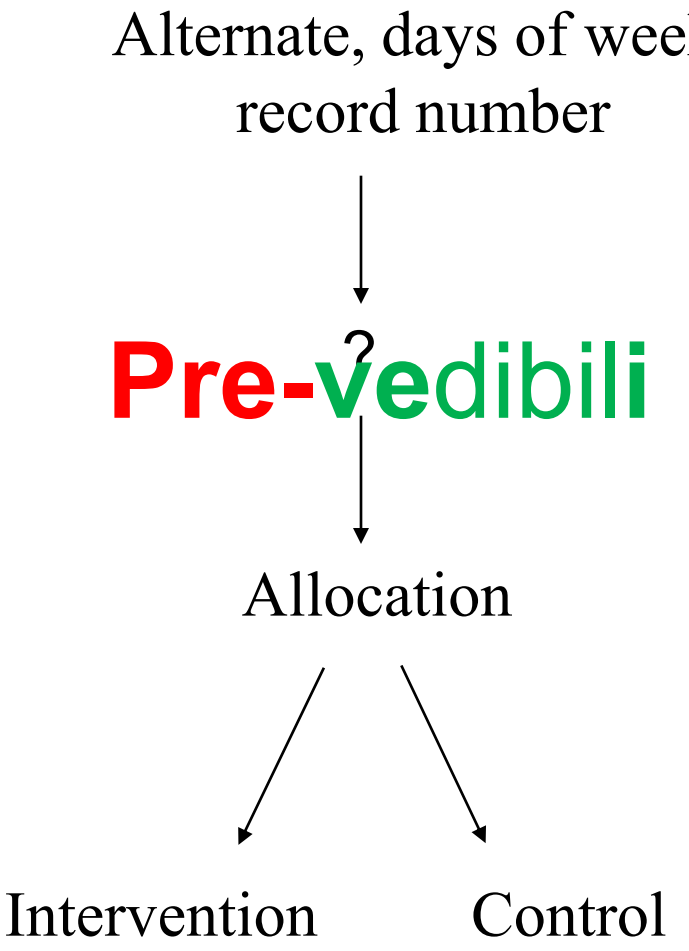
End of a clinical trial

- **We find** a **difference in outcomes** between **intervention** and **control groups**
- **Possible explanations:**
  - the intervention exhibits a **real effect**
  - the outcome difference is due to **chance**
  - there is a **systematic difference** (or **bias**) between the groups due to **factors other than** the **intervention**
- Randomisation prevents the third possibility

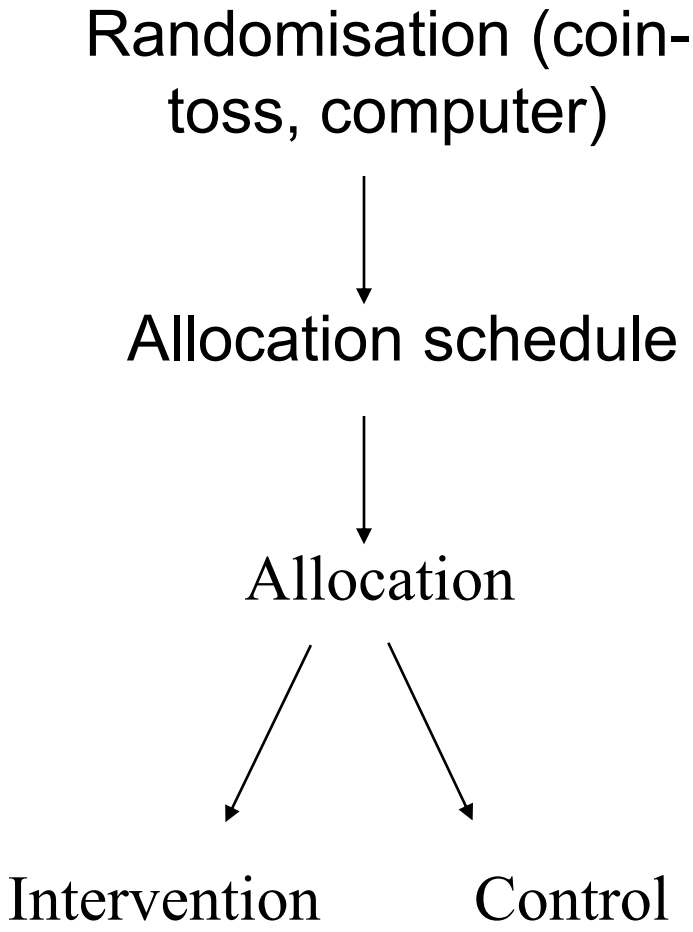
Randomisation ensures **similar** levels of all **risk factors** (**known and unknown**)

RANDOMIZATION BIAS





RANDOMIZATION BIAS



- **Recruiting selected individuals due to knowledge of the next allocation**

- **Manipulating allocations of people based on personal believing**

- **Exclusion of certain patients based on their prognosis**

Selection bias

1. **generazione della sequenza di randomizzazione**

- **Adequate methods :**random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice. **(Low risk of bias)**
- **Inadequate methods**: odd or even date of birth; date (or day) of admission; hospital or clinic record number; alternation; judgement of the clinician; results of a laboratory test or a series of tests; availability of the intervention **(High risk of bias). «quasi randomised studies «**

Selection bias

Mascheramento della assegnazione

- Chi recluta i pazienti e verifica se rispondono ai criteri di inclusione non sa a che gruppo verranno assegnati
- Chi assegna i pazienti ai gruppi non sa chi sono i pazienti

Selection bias

2. Mascheramento della assegnazione

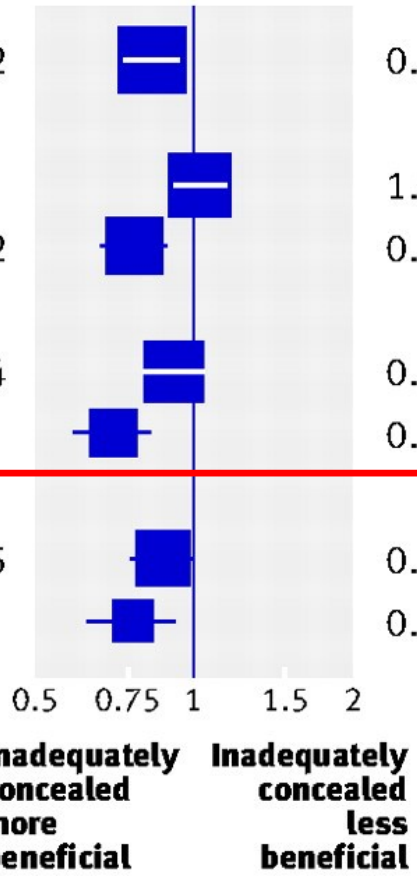
Adequate methods: central allocation (including telephone, web-based, and pharmacy-controlled, randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes. **Low risk of bias**

Inadequate methods: open random allocation schedule (e.g. a list of random numbers); assignment envelopes without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure . **High risk of bias**


SORE THROAT?

Ratios of odds ratios comparing estimates of intervention effects 532 trials with inadequate or unclear allocation concealment versus 272 trials with adequate concealment

Comparison (No of meta-analyses)	No of trials*	Ratio of odds ratios	Ratio of odds ratios (95% CI)	P value of test of interaction	Variability in bias† (P value)
Overall (102)	532 *v* 272		0.83 (0.74 to 0.93)	–	0.11 (<0.001)
All cause mortality (23)	119 *v* 90		1.01 (0.90 to 1.15)	0.002	0.02 (0.24)
Other outcomes (79)	415 *v* 182		0.76 (0.66 to 0.87)		0.14 (<0.001)
Objective outcomes (62)	310 *v* 174		0.91 (0.80 to 1.03)	0.009	0.11 (<0.001)
Subjective outcomes (40)	222 *v* 98		0.69 (0.59 to 0.82)		0.07 (0.011)
Drug intervention (65)	411 *v* 205		0.87 (0.76 to 1.00)	0.27	0.09 (<0.001)
Other intervention (37)	121 *v* 67		0.77 (0.64 to 0.93)		0.16 (<0.001)



* Inadequately or unclearly concealed *v* adequately concealed

† Between-meta-analysis heterogeneity variance

Wood, L. et al. BMJ 2008;336:601-605

CECITA’

6 ragioni per introdurre la cecità

- Se dite al paziente che è stato randomizzato al placebo, non è contento
- Se dite alle persone che l'efficacia del trattamento è dovuto all'effetto placebo, si arrabbiano
- Se dite al clinico che il paziente prende il trattamento, il clinico vedrà un miglioramento (anche in assenza di cambiamento)
- Se dite al paziente che non si dovrebbe grattare, si gratta uguale, ma vi dice che si gratta di meno (Effetto Rosenthal)
- Illusione di specifici effetti come le tradizioni millenarie sono molto radicate (agopuntura nei meridiani vs a caso)
- Avete inventato la panacea che, ogni volta che la somministrate, fallisce miseramente… cercate cercate fino a analizzare il beneficio su 100 variabili…(così funziona la statistica)

Benefici Della CECITA

- Usually reduces differential assessment
- May improve compliance and retention
- May reduce biased supplemental care or treatment (co-intervention) [and testing]

Confused Terminology of Single, Double, and Triple Blinding Permeates the Literature

- Physicians, textbooks, and journal articles vary greatly in interpretations and definitions

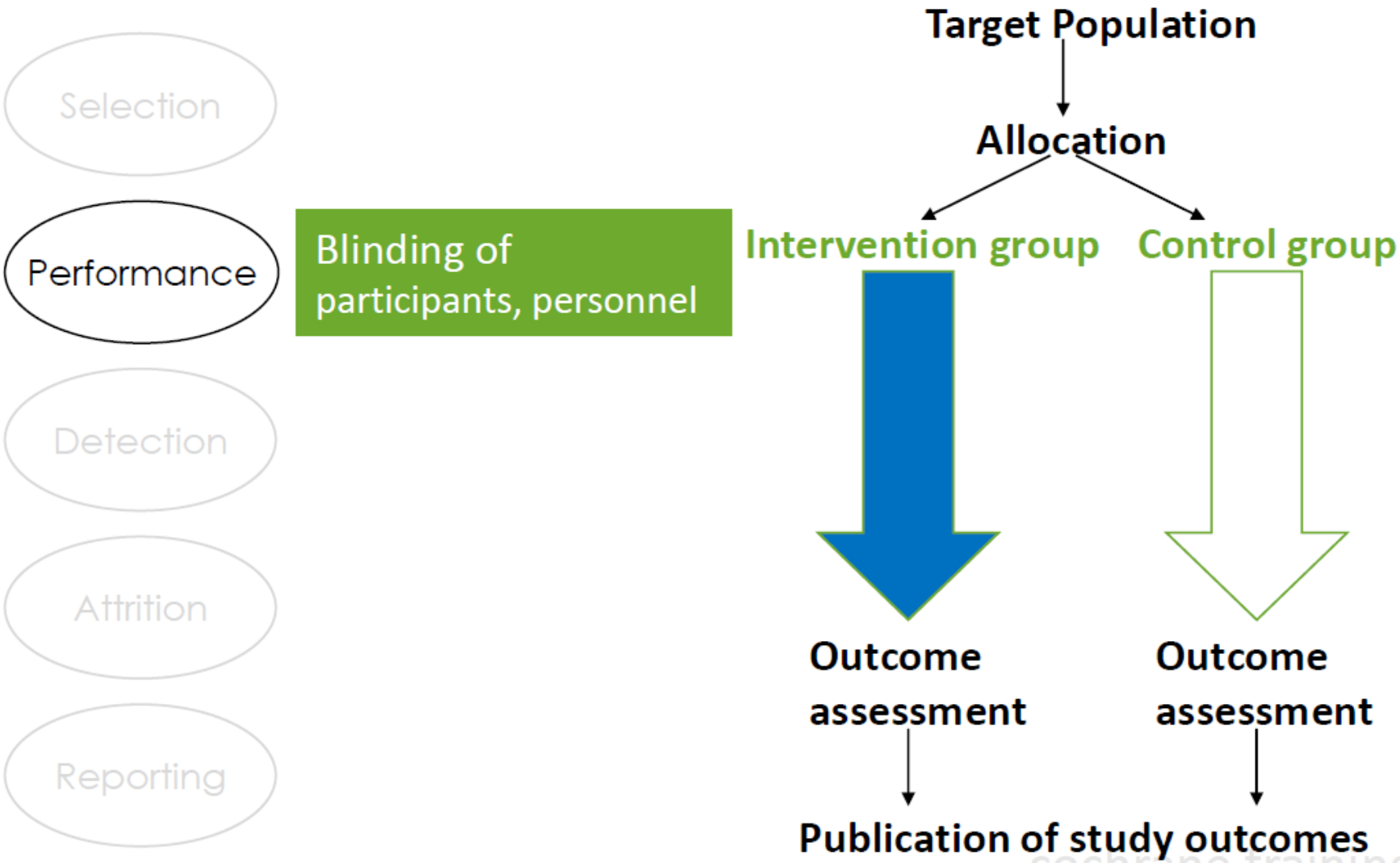
  [Devereaux et al. JAMA 2001; 285: 2000-3]

- Define "double-blind" inconsistently
  - Authors frequently fail to report their definitions clearly

- When I use "double-blind", participants, investigators, and assessors are blinded

- In reporting RCTs, authors should explicitly state what steps were taken to keep whom blinded

Sources of bias



Performance bias

Rischio di bias dipende dal tipo di outcome !!

Low risk of bias :

- **Blinding** of **participants** and ***providers*** and unlikely that the blinding could have been broken
- **No blinding** or incomplete blinding, but the outcome is not likely to be influenced by lack of blinding (e.g. mortality, cancer incidence)

High risk of bias:

- **No blinding** or incomplete blinding, and the outcome is likely to be influenced by lack of blinding;
- **Blinding** of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding

Sources of bias

Selection

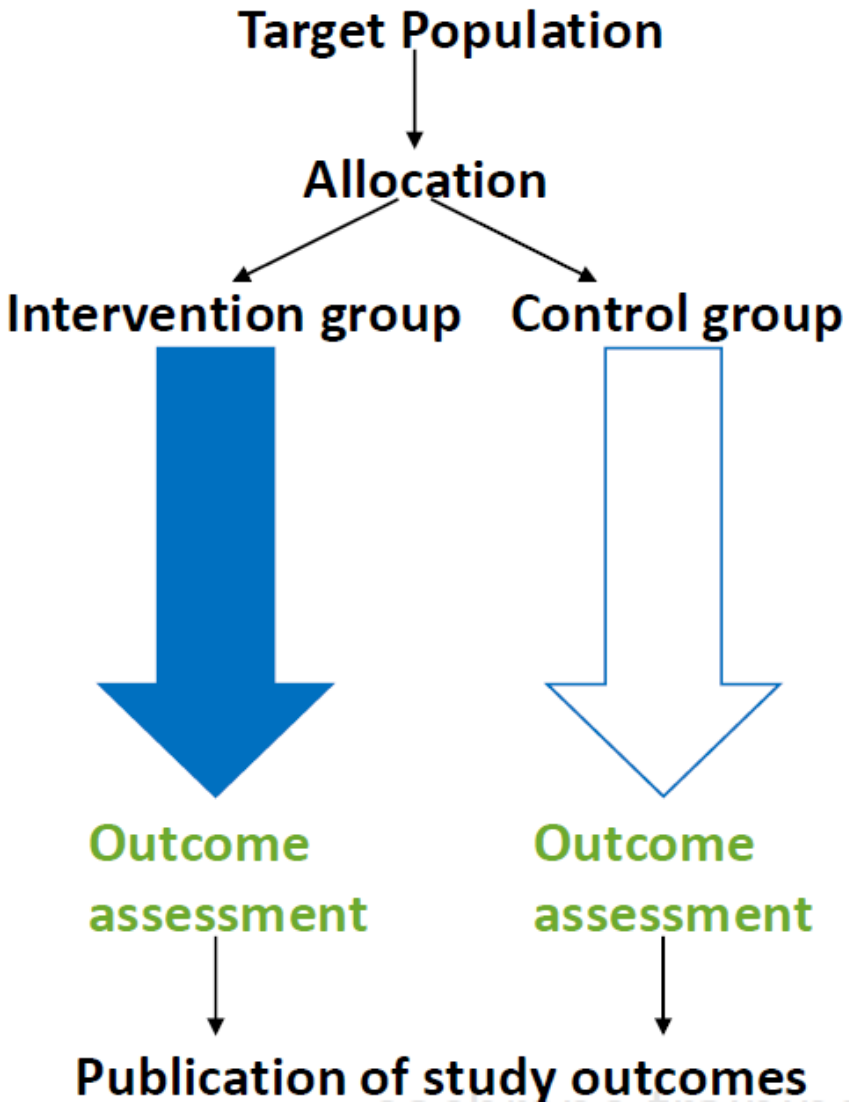
Performance

Detection

Blinding of outcome assessment

Attrition

Reporting



Detection bias

- When **knowledge** of the treatment **assignment** (by participants already recruited into a trial, investigators, or persons who analyze and report trial results) **leads to systematic differences** on the way the outcomes are assessed

Detection bias

Blinding of outcome assessor

Rischio di bias dipende dal tipo di outcome !!

Low risk of bias:

- Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken
- No blinding of outcome assessment, but the outcome measurement is not likely to be influenced by lack of blinding

High risk of bias:

- No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding;
- Blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding

Detection bias

- Blinding? Double blinding? Triple blinding?
- Who needs to be blinded?
- Is the outcome sensitive to blinding?
  - Blinding: clearly very difficult in many intervention trials (i.e. surgical)
  - **Solution: Blinded assessors should be used routinely for measuring outcome**

Outcome assessor

- Participants (subiective outcomes)
- Investigator who collects outcome data
- Data manager
- Statistician
- Quando l'intervento non può essere fatto in cieco ma l'outcome è soggettivo è fondamentale cercare di garantire la cecità di chi rileva i dati
- **Non tutela dal detection bias del paziente**
- **Non tutela dal performance bias del medico**

Single-blinded studies

- the **patient should be unaware** of which treatment they are taking
- the **investigators are aware**
- **Risk of bias**: Providers may give advice or prescribe additional therapy to the control group if they feel that these patients are disadvantaged in comparison to the active group(**performance bias**)

Double-blinded studies

- neither the patient nor the provider knows the identity of the assigned intervention
- the validity of the study depends on the providers and participants remaining really blinded throughout the study .
- A study of a drug is easily unblinded if the medications are not identical in appearance

Double blind - double dummy

- retaining the blind
- when two treatments cannot be made identical.
- Subjects then take two sets of treatment; either A (active) and B (placebo), or A (placebo) and B (active).

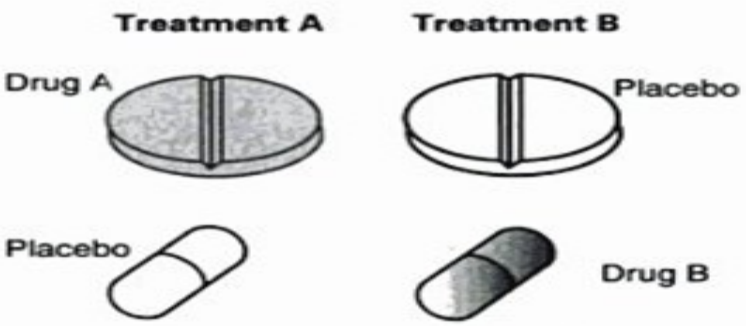


Fig. 2.7 The double-dummy technique. The patient always takes a tablet and a capsule. In treatment A, the tablet contains the active drug and the capsule contains the placebo. In treatment B, the capsule contains the active drug and the tablet contains the placebo.

Triple-blinded studies

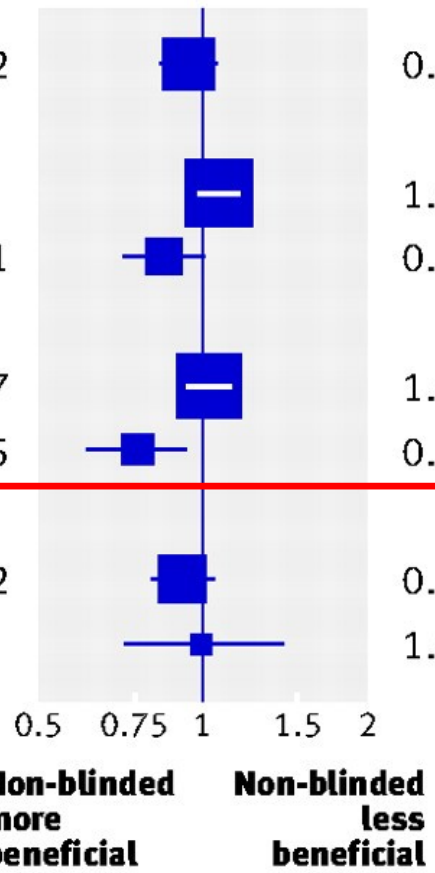
- Providers blinded
- Participants blinded
- **All** the sponsor's project team (eg, the project clinician, outcome assessor , statistician, and data manager) **blinded**
- **Appropriate** if risk of adverse events (new or standard treatment) is low
- **Not Appropriate** where safety is a critical issue

Assessing trial blindness

- asking the patients to guess which group they were assigned to.
- If the mean is close to 50% correct, the study was well blinded.
- A similar enquiry could be done with providers also.

Ratios of odds ratios comparing intervention effect estimates in 314 non-blinded trials versus 432 blinded trials.

Comparison (No of meta-analyses)	No of trials*	Ratio of odds ratios	Ratio of odds ratios (95% CI)	P value of test of interaction	Variability in bias† (P value)
Overall (76)	314 *v* 432		0.93 (0.83 to 1.04)	–	0.11 (<0.001)
All cause mortality (18)	79 *v* 121		1.04 (0.95 to 1.14)	0.011	0.01 (0.27)
Other outcomes (58)	235 *v* 311		0.83 (0.70 to 0.98)		0.18 (<0.001)
Objective outcomes (44)	210 *v* 227		1.01 (0.92 to 1.10)	0.01	0.08 (<0.001)
Subjective outcomes (32)	104 *v* 205		0.75 (0.61 to 0.82)		0.14 (0.001)
Drug intervention (57)	250 *v* 372		0.92 (0.81 to 1.05)	0.66	0.10 (<0.001)
Other intervention (19)	64 *v* 60		1.00 (0.71 to 1.39)		0.22 (0.003)



* Non-blinded *v* blinded

† Between-meta-analysis heterogeneity variance

Wood, L. et al. BMJ 2008;336:601-605

Allocation concealment

≠

Blinding

- It prevents **selection bias** in intervention assignment by protecting the allocation sequence **before and until** assignment
- It can always be successfully implemented regardless of the study topic

- It seeks to prevent **performance and detection bias** by protecting the sequence **after** assignment
- Not always feasible – for example, in trials comparing surgical with medical interventions

Attrition bias

- Non tutti i soggetti randomizzati completano lo studio
- i soggetti non escono a caso dallo studio: è possibile che quelli che escono siano sistematicamente diversi da quelli che non escono: i gruppi non sono più randomizzati
- **Validità esterna** : es: escono tutti i più giovani, o i meno gravi, o i maschi: posso trarre conclusioni solo su quelli che rimangono
- **Validità interna (Bias):** se la probabilità di uscire dallo studio è legata all'intervento o all'outcome, cioè se quelli che escono hanno sistematicamente probabilità più alte o più basse di avere l'outcome di quelli che restano

Attrition bias

- **Persi al follow up**: il soggetto sparisce non si hanno più info
- **Uscito dallo studio** il soggetto interrompe il trattamento ma è reperibile (eventi avversi? Non efficace?)
- **Bassa compliance**: il soggetto riceve il trattamento ma in dosi e modalità diverse da quelle prescritte (eventi avversi? Trattamento poco accettabile?)
- **Missing data**: misurazioni ripetute: il soggetto riceve il trattamento ma non è presente a tutte le misurazioni dell'outcome (TD non consegnano le urine quando sono positive)

Attrition bias

Intention to treat analysis: all subjects analysed in the treatment group they were originally randomized, regardless if they actually received the assigned treatment or not

Imputation of missing data : es: considerare gli usciti come fallimenti terapeutici (TD); last observation carried forward

Per protocol analysis: only patients who received the treatment as described in the prtocol were analysed

Intention to treat:

- **effectiveness** (efficacia in pratica, efficacia del trattamento prescritto)
- Tiene conto anche della scarsa compliance, della difficoltà a somministrare il trattamento
- Tutela da attrition bias (mantiene la similitudine dei gruppi ottenuta con la randomizzazione

Per protocol:

- **efficacy** (efficacia in condizioni ottimali, efficacia della trattamento ricevuto nelle modalità previste)
- Può dare stime distorte se la non compliance e l'uscita dallo studio è legata al trattamento o all'outcome

Attrition bias

Low risk of bias

- No missing outcome data;
- the **proportion of missing outcomes** compared with observed event risk not enough to have a relevant impact on the intervention effect;
- Missing outcome data balanced in numbers across intervention groups, with similar reasons across groups;
- Missing data imputed using appropriate methods
- All patients analysed in the group they were allocated to by randomisation irrespective of non-compliance and co-interventions (intention to treat)

High risk of bias:

- the proportion of missing outcomes compared with observed event risk enough to induce relevant bias in intervention effect estimate
- Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups;

Attrition bias

Low risk of bias

- Numero di persi (piccolo) ma quanto? (<5-10%)
- Bilanciati fra i gruppi
- Riportate le ragioni (non differenti fra gruppi e non attribuibili agli interventi)
- Intention to treat
- Imputation of missing data

publication bias?

Publication bias is the selective or *multiple* publication *or suppression* of trial results so that the scientific record is distorted

Extension: applied to trial parts - outcomes, subgroups, adverse events reporting bias

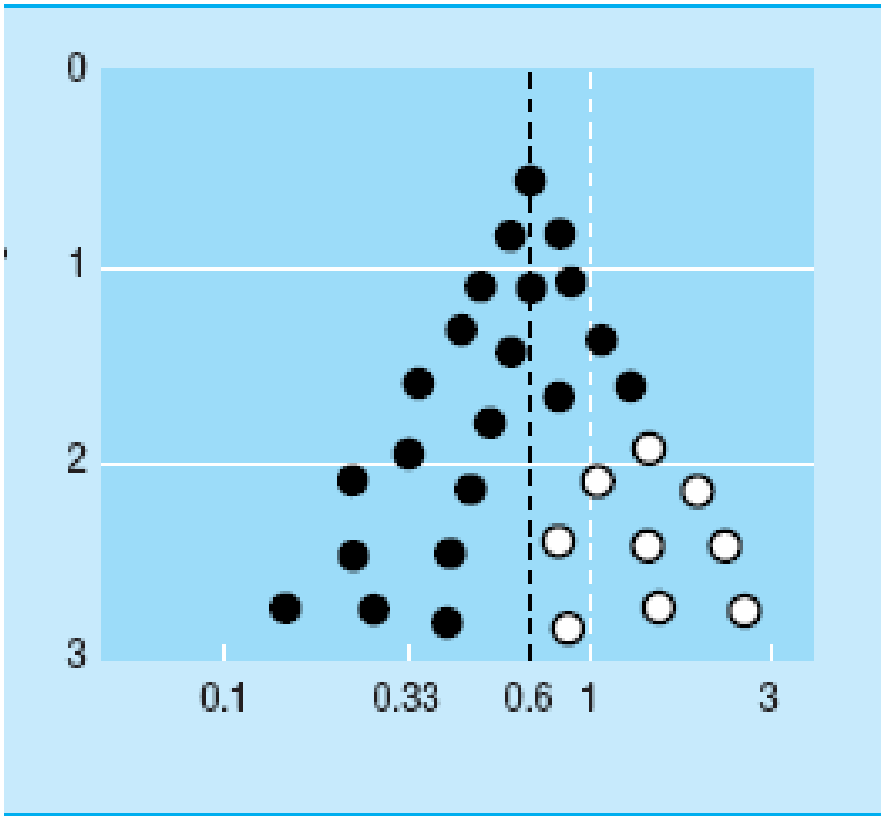
The likelihood of finding studies is related to the results of those studies (positive vs negative/detrimental)

Why does it matter?

- Distorts the scientific record
- Hides the “truth”
- Influences doctors’ decision making
- Misleads policy makers
- Causes harm to patients
- Costly for the health service
- A form of scientific and research misconduct

- TO U: It will matter if the studies you don’t find differ systematically from the ones you have found
- You might arrive at different answers, or even THE WRONG ANSWER

Publication of All Trials



Publication Bias

- **In this situation the effect calculated in a meta-analysis will overestimate the treatment effect**

- **The more pronounced the asymmetry, the more likely it is that the amount of bias will be substantial.**

Outcome reporting bias

Reporting bias is selection bias

- R.B. is perhaps the greatest source of selection bias
- Originally defined as the publication or non-publication of studies depending on the direction and statistical significance of the results
- Is a complex phenomenon

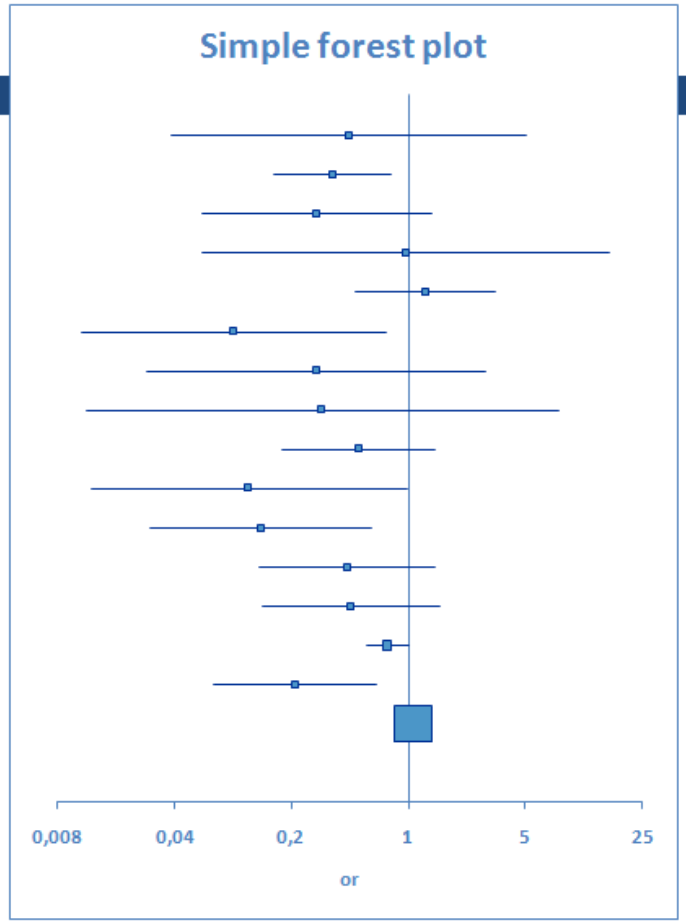
Eterogeneità

E' efficace?

Author(s)		Reference					
Teo et al.		Effects of intravenous magnesium in suspected acute myocardial infarction. BMJ 1991;303:1499–501					
Outcome object	Unit	Intervention (e)		Control (c)			
Mortality	Event	Intravenous magnesium		Control			
Study ID	Ref #	n[e]	n[e](E=1)	n[c]	n[c](E=1)	Study date	-
Morton	1	40	1	36	2	1984	
Rasmussen	2	135	9	135	23	1986	
Smith	3	200	2	200	7	1986	
Abraham	4	48	1	46	1	1987	
Feldstedt	5	150	10	148	8	1988	
Schechter	6	59	1	56	9	1989	
Ceremuzynski	7	25	1	23	3	1989	
Bertschat	8	22	0	21	1	1989	
Singh	9	76	6	75	11	1990	
Pereira	10	27	1	27	7	1990	
Schechter 1	11	89	2	80	12	1991	
Golf	12	23	5	33	13	1991	
Thogersen	13	130	4	122	8	1991	
LIMIT-2	14	1159	90	1157	118	1992	
Schechter 2	15	107	4	108	17	1995	
ISIS-4	16	29011	2216	29039	2103	1995	

Forest plot (meta-graph) analitico

author	year	n[I]	N[I]	n[C]	N[C]	Weight	or	ci-	ci+	p
Morton	1984	1	40	2	36	0,06%	0,44	0,04	5,02	0,51
Rasmussen	1986	9	135	23	135	0,54%	0,35	0,15	0,78	0,01
Smith	1986	2	200	7	200	0,14%	0,28	0,06	1,36	0,11
Abraham	1987	1	48	1	46	0,05%	0,96	0,06	15,77	0,98
Feldstedt	1988	10	150	8	148	0,39%	1,25	0,48	3,26	0,65
Schechter	1989	1	59	9	56	0,08%	0,09	0,01	0,74	0,02
Ceremuzynsk	1989	1	25	3	23	0,07%	0,28	0,03	2,88	0,28
Bertschat	1989	0	22	1	21	0,03%	0,30	0,01	7,88	0,47
Singh	1990	6	76	11	75	0,32%	0,50	0,17	1,43	0,19
Pereira	1990	1	27	7	27	0,08%	0,11	0,01	0,97	0,05
Schechter 1	1991	2	89	12	80	0,15%	0,13	0,03	0,60	0,01
Golf	1991	5	23	13	33	0,24%	0,43	0,13	1,44	0,17
Thogersen	1991	4	130	8	122	0,24%	0,45	0,13	1,54	0,21
LIMIT-2	1992	90	1159	118	1157	4,33%	0,74	0,56	0,99	0,04
Schechter 2	1995	4	107	17	108	0,28%	0,21	0,07	0,64	0,01
ISIS-4	1995	2216	29011	2103	29039	92,99%	1,06	1,00	1,13	0,07



META-ANALYSIS

General

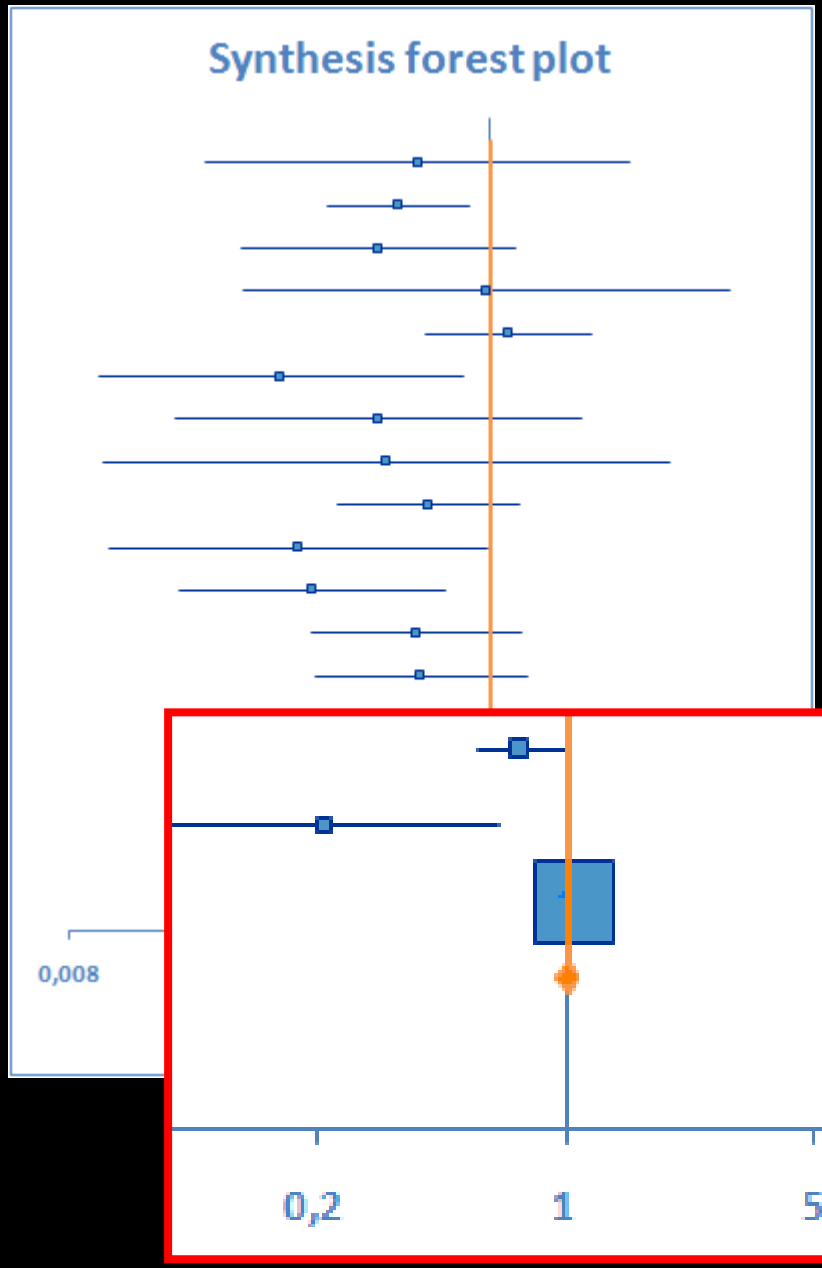
Number of studies	16
Number of participants	62607 (62607)

OR (MH) - Fixed effect model

Meta-analysis outcome	1,0063
95% CI lower limit	0,9482
95% CI upper limit	1,068
z	0,2073
p-value (two-tailed)	0,8358

Heterogeneity

Q	47,1363
p-value (two-tailed)	< 0,0001
I^2	68,18%
95% CI lower limit	46,53%
95% CI upper limit	81,06%



Could we just add the data from all the trials together?

- One approach to combining trials would be to add all the treatment groups together, add all the control groups together, and compare the totals
- This is wrong for several reasons, and it can give the wrong answer

MetaView 3.1 - [Death at end of follow up period (Corticosteroids for acute traumatic brain injury)]

File Display Sort Statistic Window Next Outcome Prev Outcome

Comparison: **Any steroid administered in any dose against no steroid**
Outcome: **Death at end of follow up period**

Study	Expt n/N	Ctrl n/N	Relative Risk (95%CI Fixed)	Weight %	RR (95%CI Fixed)
Alexander 1972	16 / 55	22 / 55		6.6	0.73 [0.43,1.23]
Braakman 1983	44 / 81	47 / 80		14.2	0.92 [0.70,1.21]
Chacon 1987	1 / 5	0 / 5		0.2	3.00 [0.15,59.89]
Cooper 1979	26 / 49	13 / 27		5.0	1.10 [0.69,1.77]
Dearden 1986	33 / 68	21 / 62		6.6	1.43 [0.94,2.19]
Faupel 1976	16 / 67	16 / 28		6.8	0.42 [0.24,0.71]
Gaab 1994	19 / 133	21 / 136		6.2	0.93 [0.52,1.64]
Giannotta 1984	34 / 72	7 / 16		3.4	1.08 [0.59,1.98]
Grumme 1995	38 / 175	49 / 195		13.9	0.86 [0.60,1.25]
Hernesniemi 1979	35 / 81	36 / 83		10.7	1.00 [0.70,1.41]
Pitts 1980	114 / 201	38 / 74		16.7	1.10 [0.86,1.42]
Ransohoff 1972	9 / 17	13 / 18		3.8	0.73 [0.43,1.25]
Saul 1981	8 / 50	9 / 50		2.7	0.89 [0.37,2.12]
Stubbs 1989	13 / 98	5 / 54		1.9	1.43 [0.54,3.80]
Zagara 1987	4 / 12	4 / 12		1.2	1.00 [0.32,3.10]
xZarate 1995	0 / 30	0 / 30		0.0	Not Estimable
Total (95%CI)	410 / 1194	301 / 925		100.0	0.96 [0.85,1.08]

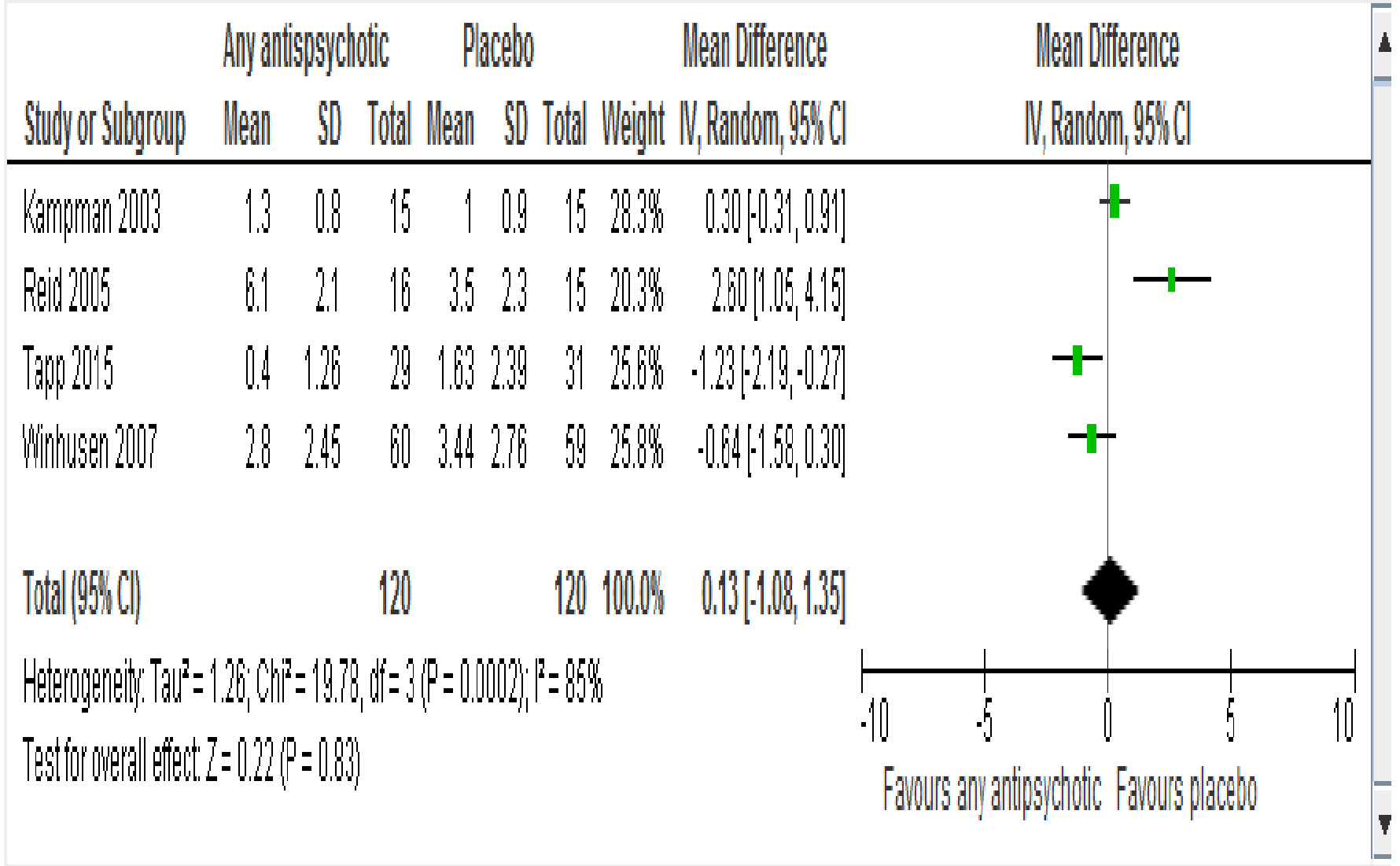
Chi-square 18.11 (df=14) Z=0.68

.1 .2 1 5 10

Steroid better Steroid worse

If we add up the columns we get 34.3% vs 32.5% , a RR of 1.06, a higher chance of death in the steroids group

From a meta-analysis, we get RR=0.96 , a lower chance of death in the steroids group


Any antispsychotic
Placebo
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Kampman 2003 1.3 0.8 15 1 0.9 15 28.3% 0.30 [-0.31, 0.91]
Reid 2005 6.1 2.1 16 3.5 2.3 15 20.3% 2.60 [1.05, 4.15]
Tapp 2015 0.4 1.26 29 1.63 2.39 31 25.6% -1.23 [-2.19, -0.27]
Winhusen 2007 2.8 2.45 60 3.44 2.76 59 25.8% -0.64 [-1.58, 0.30]
Total (95% CI) 120 120 100.0% 0.13 [-1.08, 1.35]
Heterogeneity: Tau² = 1.26; Chi² = 19.78, df = 3 (P = 0.0002); I² = 85%
Test for overall effect: Z = 0.22 (P = 0.83)
-10
-5
0
5
10
Favours any antipsychotic
Favours placebo

Va a scua il mar

Mettere insieme … studi diversi… che testano quesiti diversi… considerando popolazione diverse… usando interventi lievemente diversi…
ma partendo da protocolli profondamente diversi… e dando risultati …

Eterogeneità

What is heterogeneity?

- Heterogeneity is variation between the studies' results

What is heterogeneity?

Differences between studies with respect to:

Clinical heterogeneity (clinical diversity)

- *Participants*
  - e.g. conditions under investigation, eligibility criteria for trials, geographical variation
- *Interventions*
  - e.g. intensity / dose / duration, sub-type of drug, mode of administration, experience of practitioners, nature of the control (placebo/none/standard care)
- *Outcomes*
  - e.g. definition of an event, follow-up duration, ways of measuring outcomes, cut-off points on scales

What is heterogeneity?

Differences between studies with respect to:

Methodological heterogeneity (methodological diversity)

- *Design*
  - e.g. randomised vs non-randomised, crossover vs parallel group vs cluster randomised, pre-test and long follow up
- *Conduct*
  - e.g. allocation concealment, blinding etc, approach to analysis, imputation methods for missing data

What is heterogeneity?

What do we do if there ***is*** statistical heterogeneity?

- Variation in the *true effects* underlying the studies
- ...which may manifest itself in more observed variation than expected by chance alone

- May be due to clinical diversity (different treatment effects) or methodological diversity (different biases)

Come si misura questa eterogeneità?

- Confidence interval overlapping Eyeball test

- Cochran's Q: to assess whether observed differences in results are compatible with change alone

χ^2 distribution; low power (small number of studies, small sample size)

p=<0.10 (heterogeneity)

- I^2 quantifing heterogeneity (describes the percentage of variation across studies that is due to heterogeneity rather than chance)

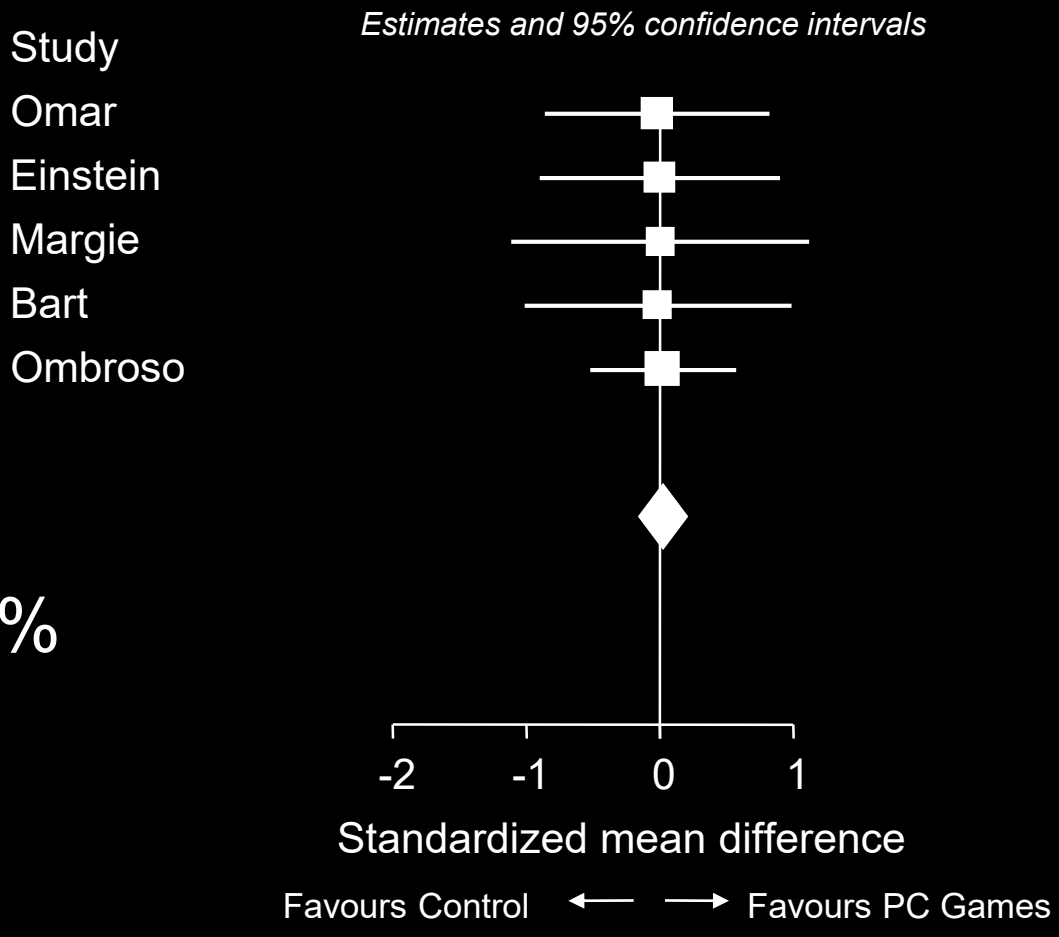
0-40% might not be important
30-60% may represent moderate heterogeneity
50-90% may represent substantial heterogeneity
75-100% considerable heterogeneity

- Tau….

How to deal with heterogeneity

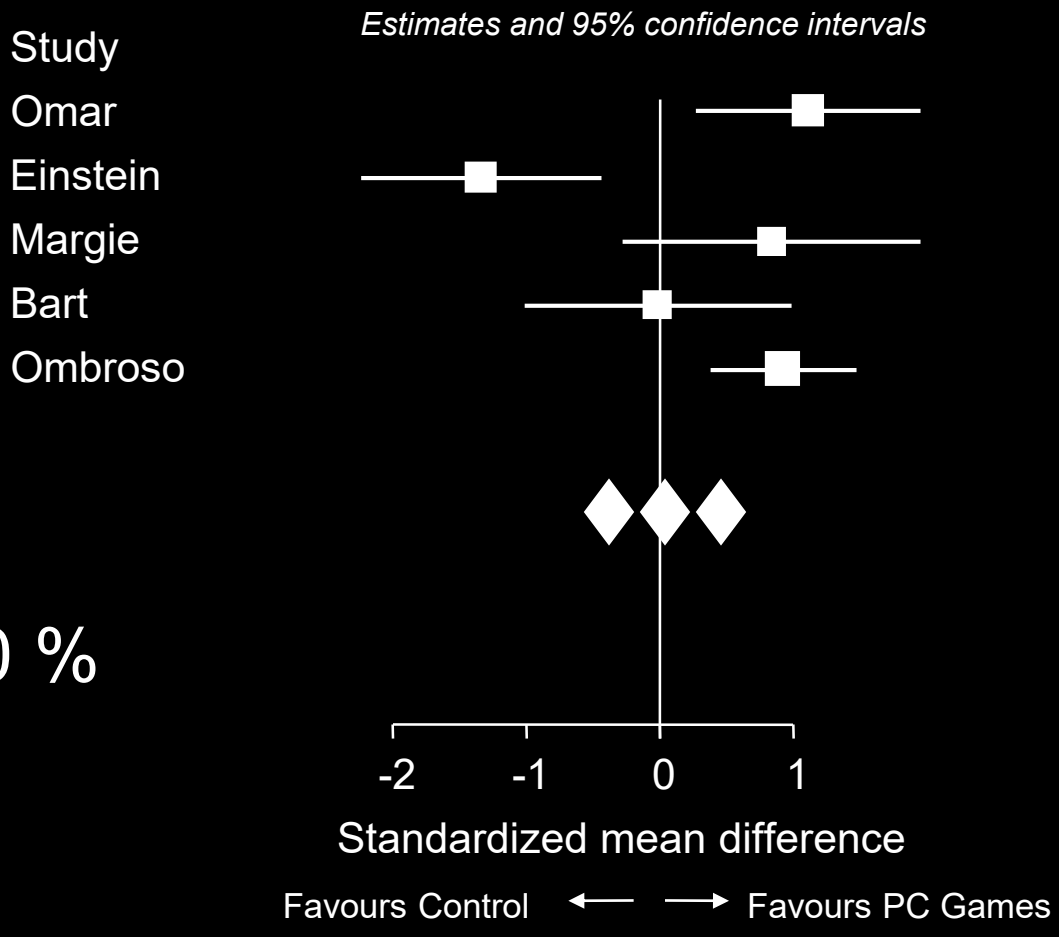
1. Do not pool at all
2. Ignore heterogeneity: use ***fixed effect model***
3. Allow for heterogeneity: use ***random effects model***
4. Explore heterogeneity: subgroups analysis or meta-regression (tricky)

Example: PC Games for intelligence



$I^2 = 0\ \%$

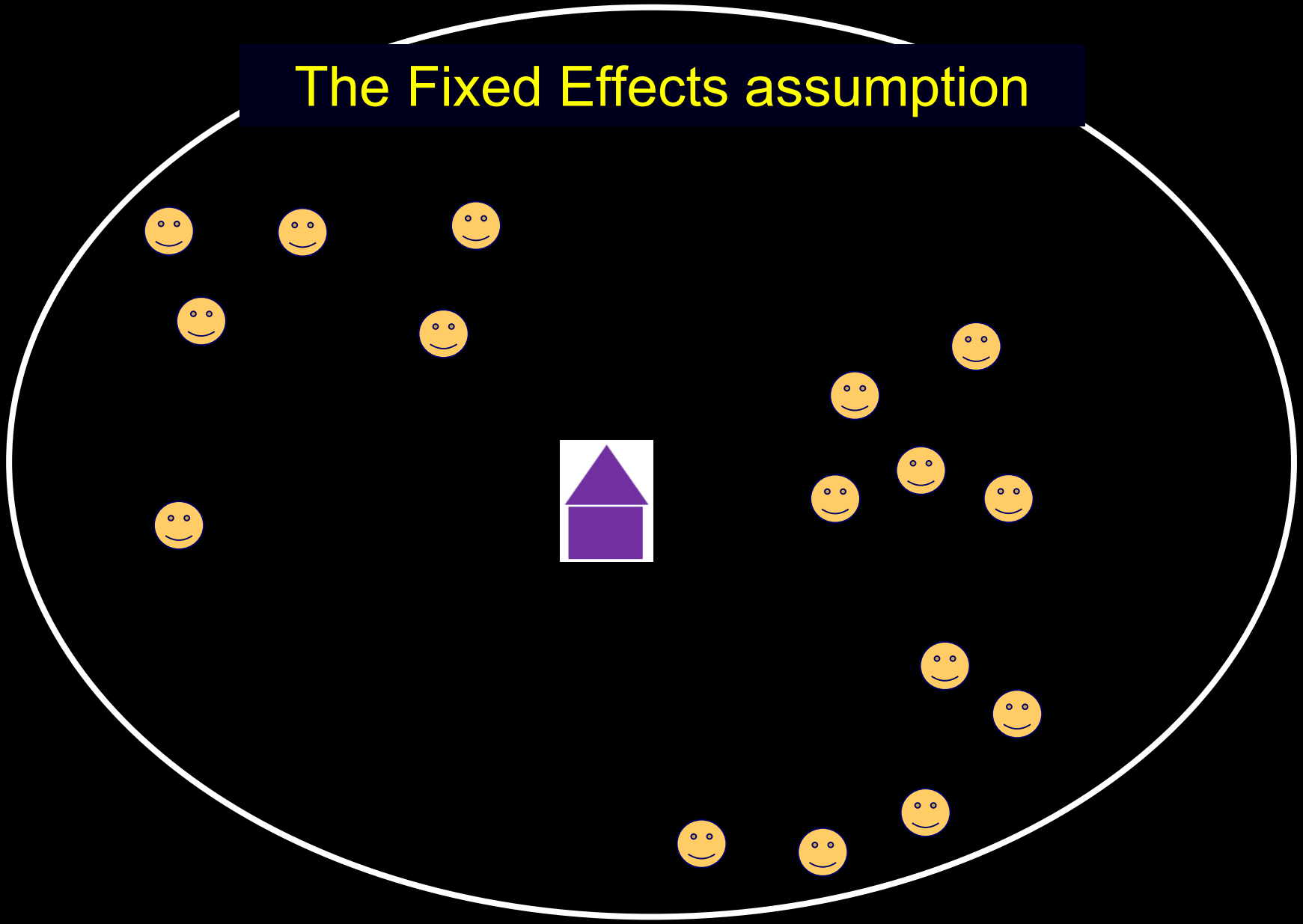
Example: PC Games for intelligence



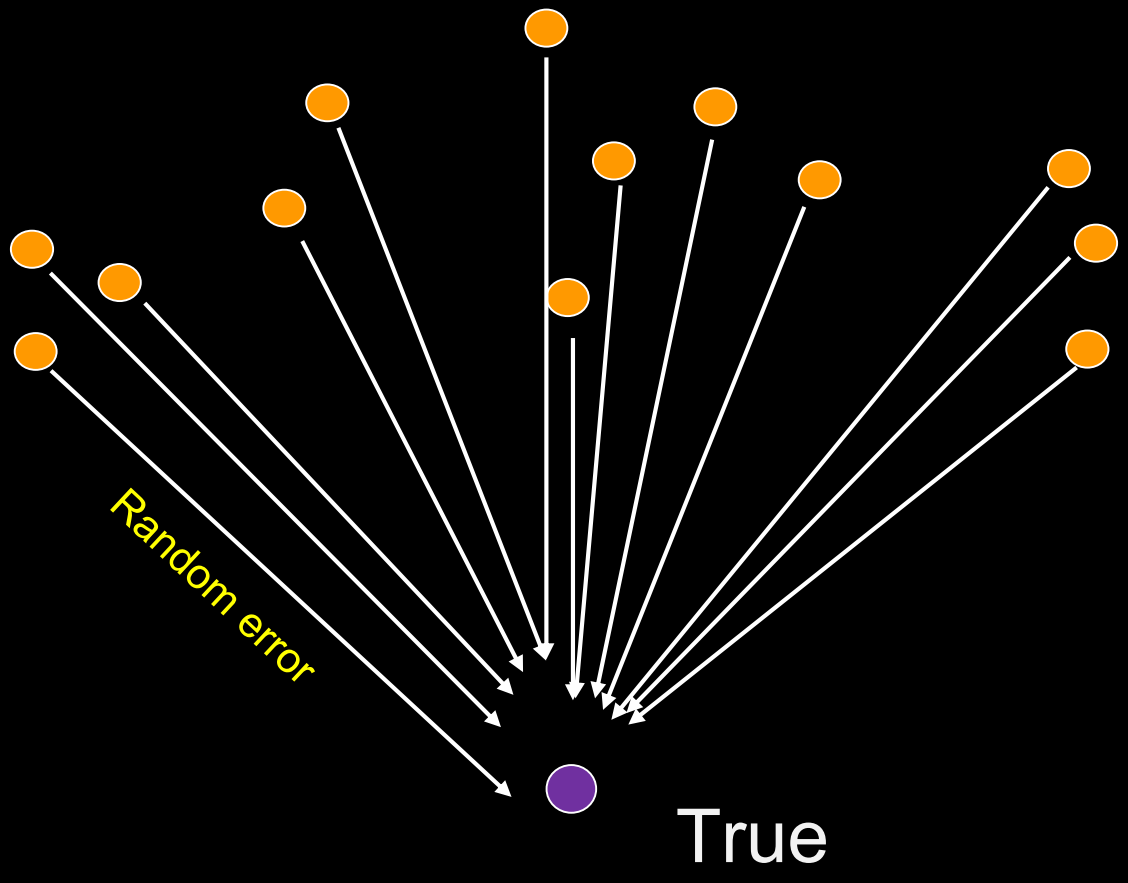
I^2= 80 %

Fixed and random effects

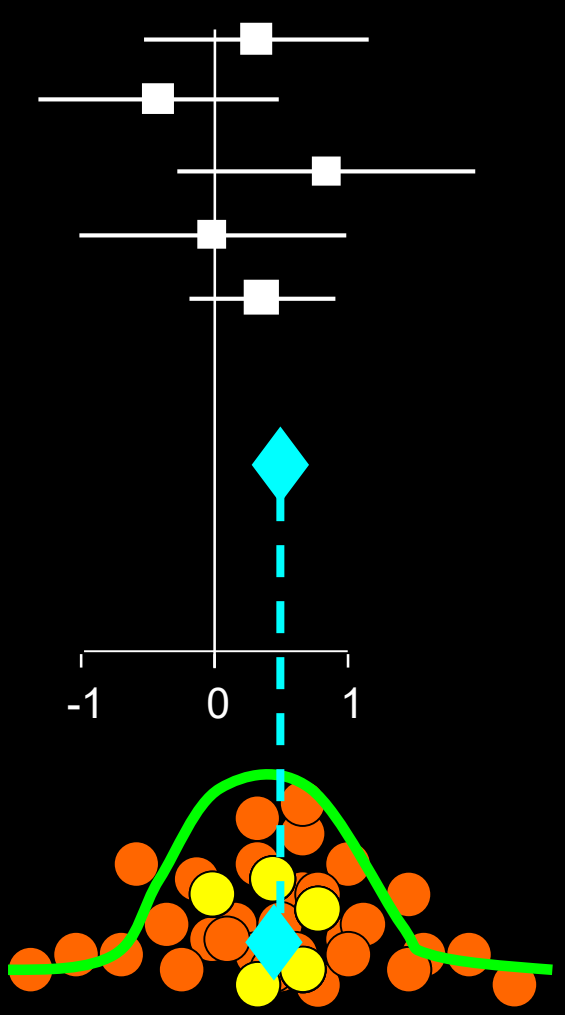
The Fixed Effects assumption



The Fixed Effects assumption



Fixed effects model



In un modello a effetti fissi si assume che tutti gli studi provengano dalla stessa popolazione di studi

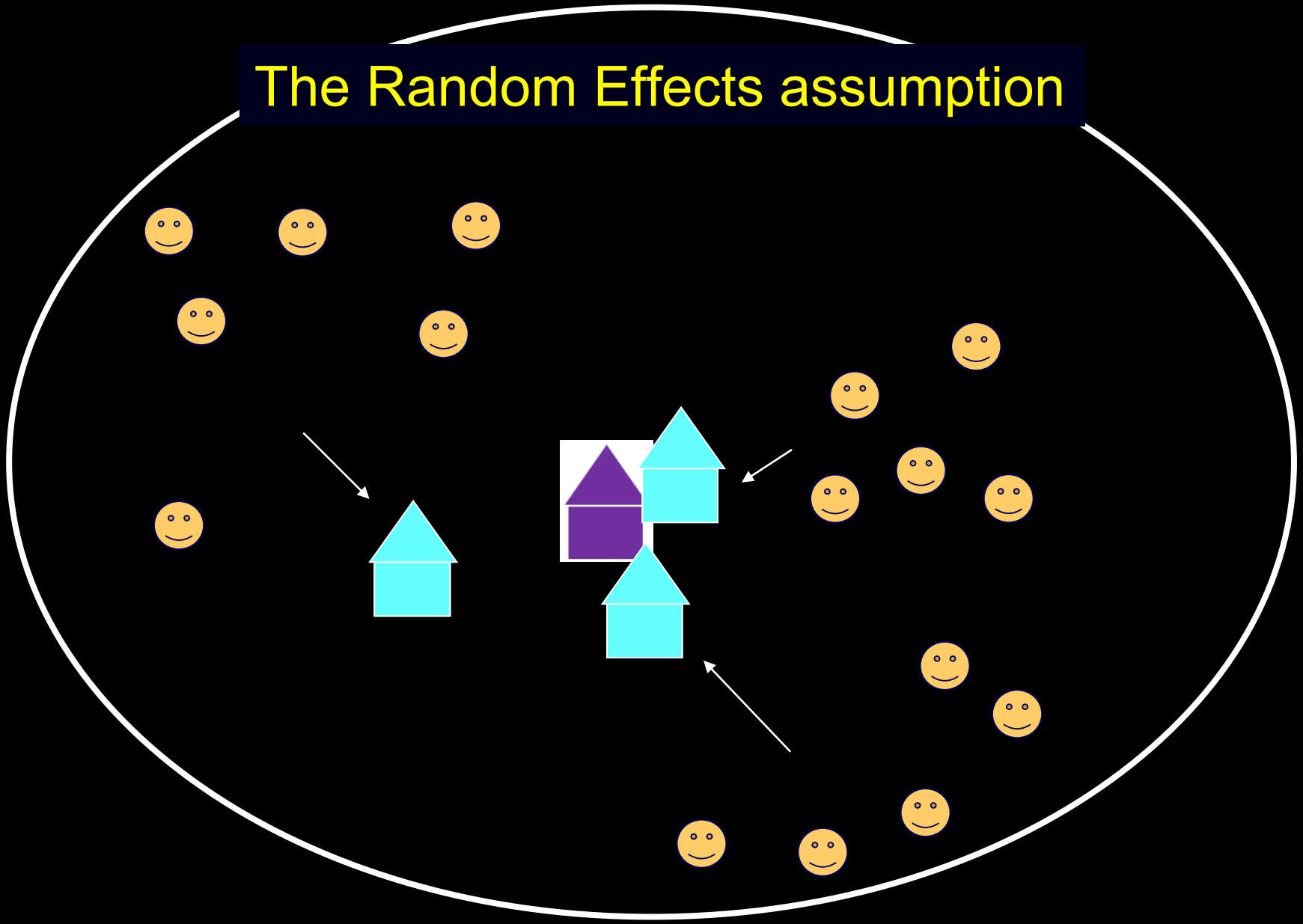
Si assume che ci sia un parametro (es.media) unico, fisso

Il peso degli studi è funzione della variabilità intra-studio

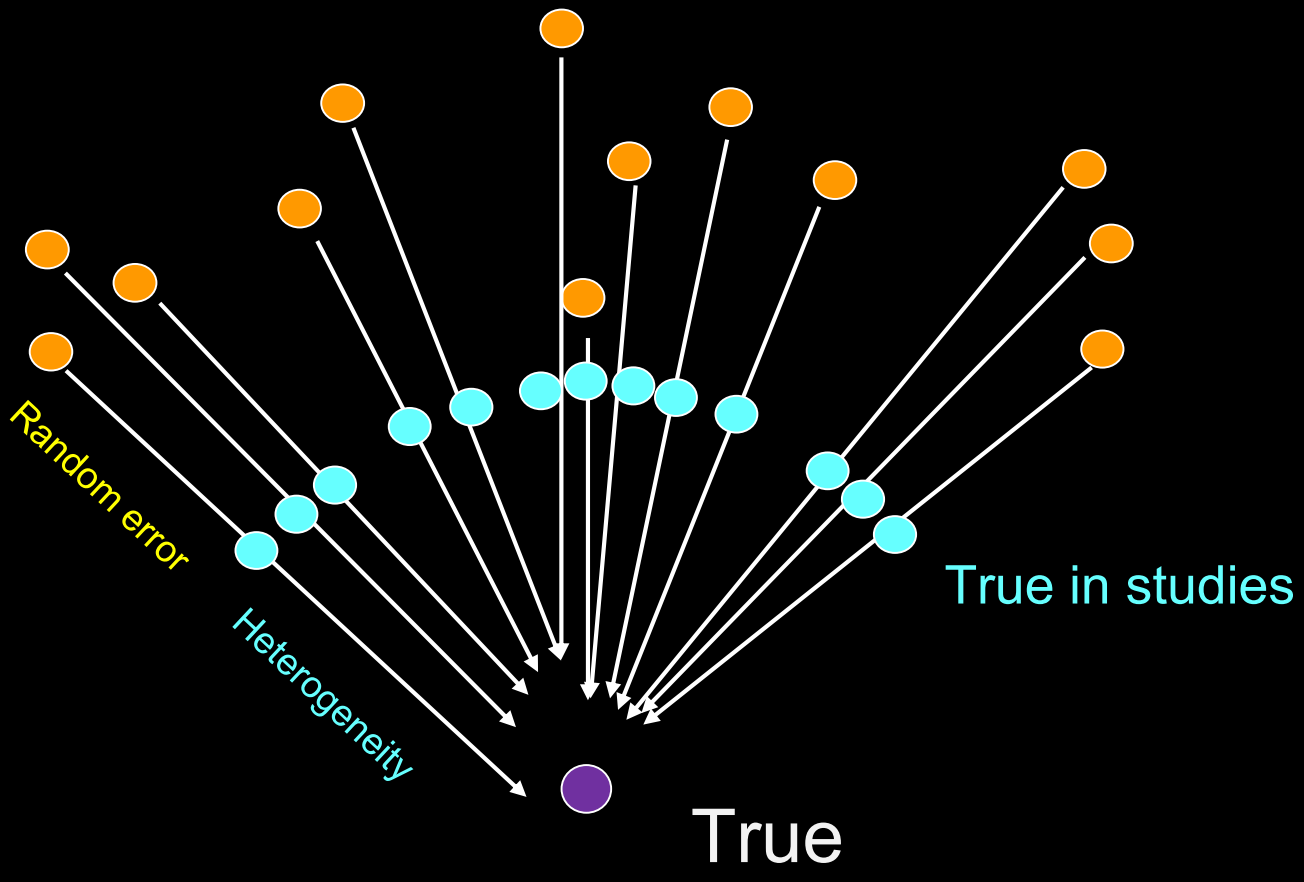
Gli intervalli di confidenza del parametro sono ridotti

Popolazione di riferimento unica, omogenea

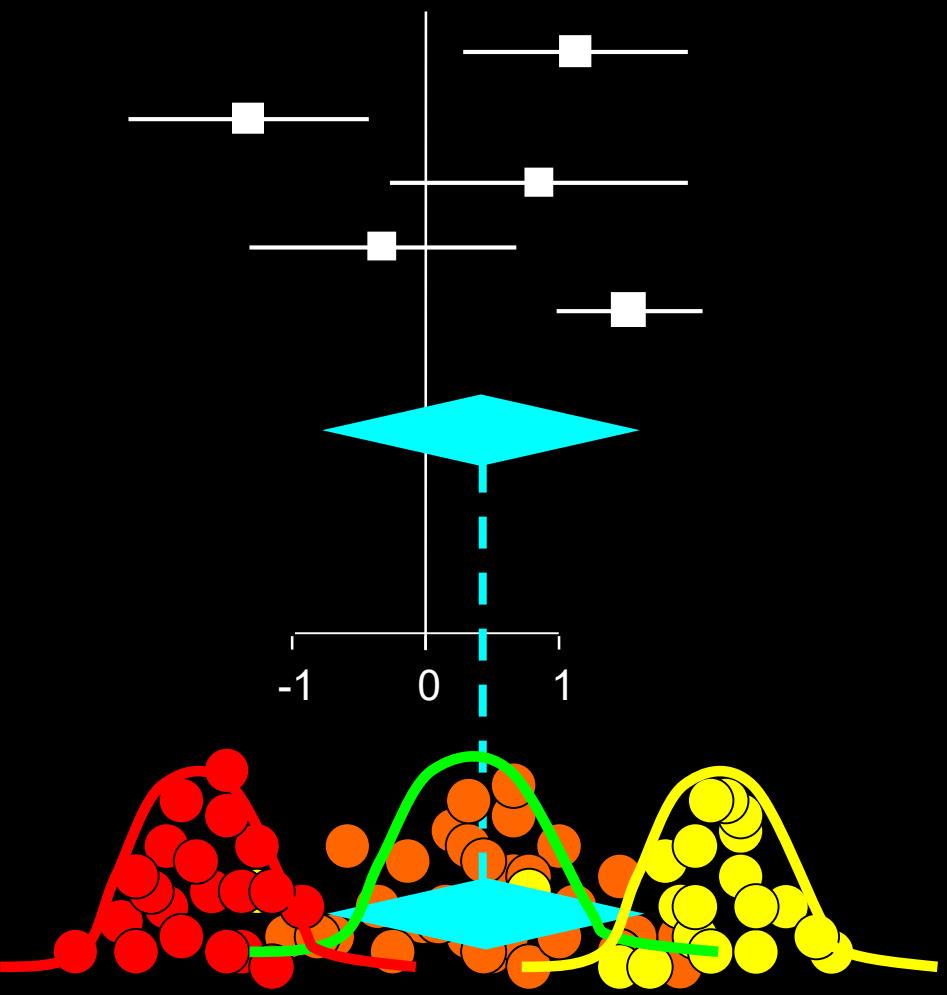
The Random Effects assumption



The Random Effects assumption



Random effects model



In un modello a effetti random gli studi potrebbero provenire da popolazioni di studi diverse

I pesi sono ridistribuiti in modo più omogeneo tra studi grandi e piccoli (il peso non è dovuto solo alla variabilità intra-studio)

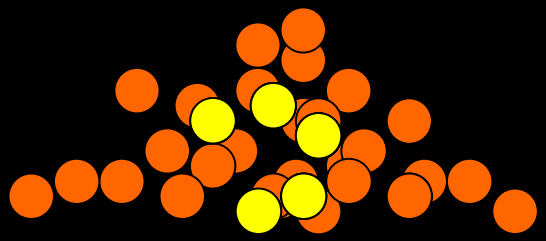
Gli intervalli di confidenza del parametro sono aumentati

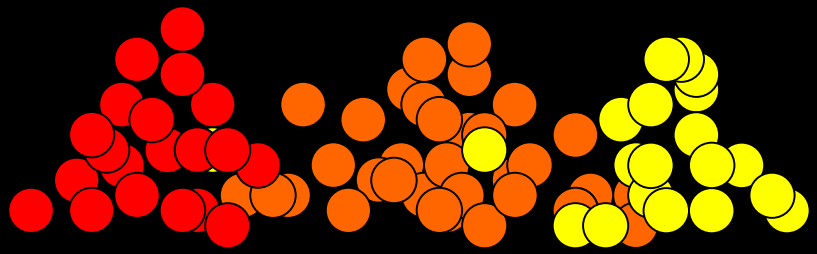
Popolazioni di riferimento molteplici, eterogenee

Quale modello?

Fixed effect

Random effect





Quale modello?

Fixed effect

Random effect

Potente (IC ristretti)

Assume un solo parametro, non facile in ambito biomedico

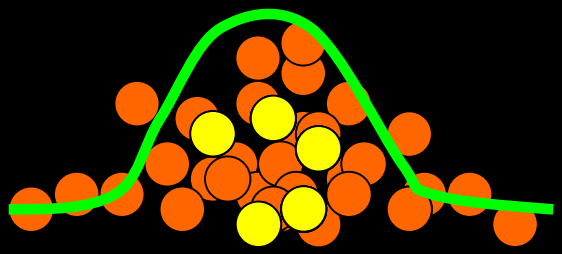
Più facile per sottogruppi

Semplicistico

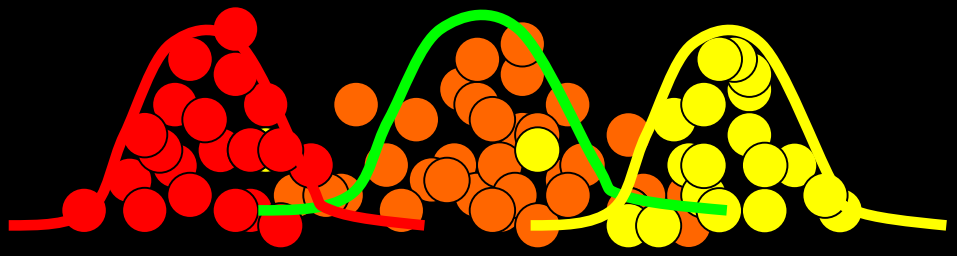
Dà luogo a un aggiustamento dei pesi grezzo (ridistribuzione senza tener conto di nessuna co-variata)

IC realistici

I^2= 20% - 50%



I^2= 50% - 70%



I^2= > 70%