

# Altre dimensioni della qualità

Applicabilità, eterogeneità,  
imprecisione e bias di pubblicazione

# What are we grading?

- two components
- quality of body of evidence
  - extent to which confidence in estimate of effect adequate to support decision
    - high, moderate, low, very low
- strength of recommendation
  - strong and weak

# 1. risk of bias

## Deferasirox for managing transfusional iron overload in people with sickle cell disease (Review)

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding (performance bias and detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Vichinsky 2007	?	+	-	-	-	?
Vichinsky 2011	?	?	-	-	+	?

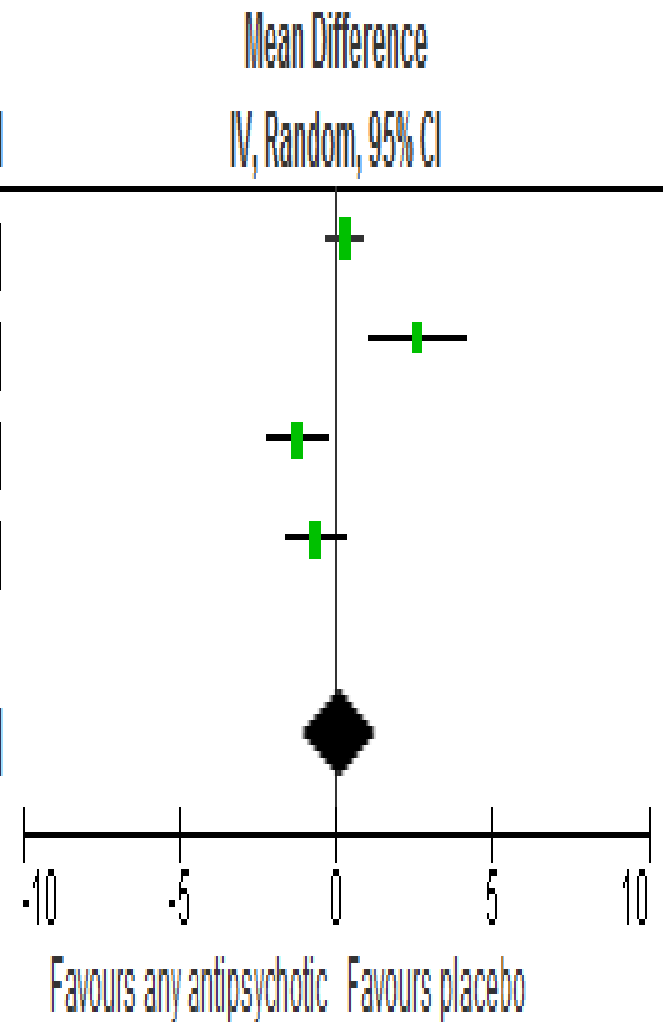
## 2. Inconsistency (heterogeneity) between studies results

- Variation in size of effect ( **Point estimates vary widely** across studies)
- **Confidence intervals** (CIs) show minimal or **no overlap**
- The statistical test for heterogeneity which tests the null hypothesis that all studies in a meta-analysis have the same underlying magnitude of effect shows a low **P-value (< 0.05)**
- The  $I^2$  which quantifies the proportion of the variation in point estimates due to among-study differences (< 40% : low, 30 e 60% : moderate, **50%** e 90% :substantial, 75 e 100% : considerable)
- **All statistical approaches have limitations**, and their **results should be seen in the context of a subjective** examination of the variability in point estimates and the overlap in CIs.

Study or Subgroup	Any antipsychotic			Placebo			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
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]
<b>Total (95% CI)</b>			<b>120</b>			<b>120</b>	<b>100.0%</b>	<b>0.13 [-1.08, 1.35]</b>

Heterogeneity:  $\tau^2 = 1.26$ ;  $\chi^2 = 19.78$ ,  $df = 3$  ( $P = 0.0002$ );  $I^2 = 85\%$

Test for overall effect:  $Z = 0.22$  ( $P = 0.83$ )

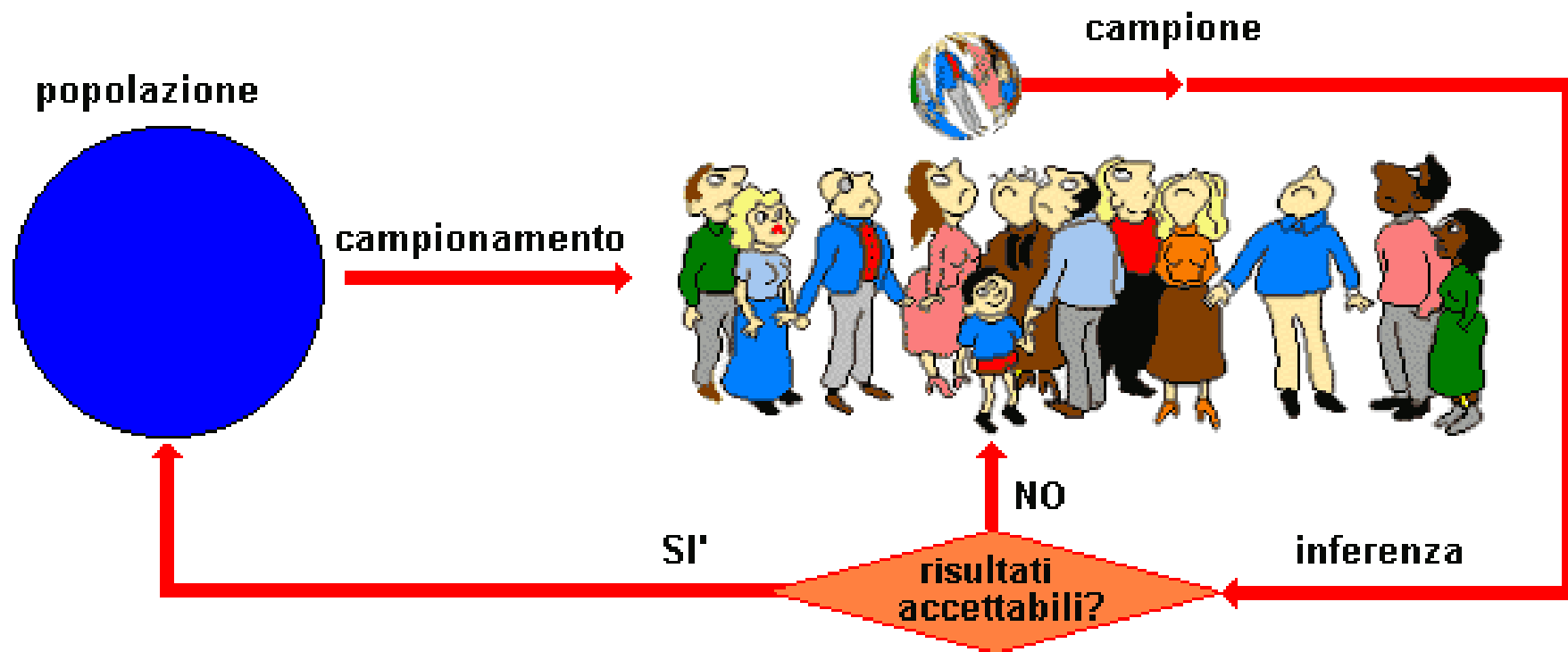


# 3. Directness of Evidence

## generalizability, transferability, applicability

- differences between PICO and available evidence in
  - populations/patients (interested in children found adults population)
  - interventions (interested in high dosage, found low dosage, interested in long treatment, found short, etc)
  - outcomes (interested in important but we found surrogate; e.g hip fracture vs bone density; interested in long term but found short term results)
- indirect comparisons
  - interested in A versus B
  - found A versus C and B versus C

# **5. Imprecision of the overall estimate**



*Da una popolazione viene estratto un campione e, con adatti test, ne viene controllata la validità: se è positiva, si può inferire che il campione rappresenta con un certo errore la popolazione da cui è stato estratto; se il test è negativo, occorre procedere ad un nuovo campionamento.*



# Uncertainty Estimation

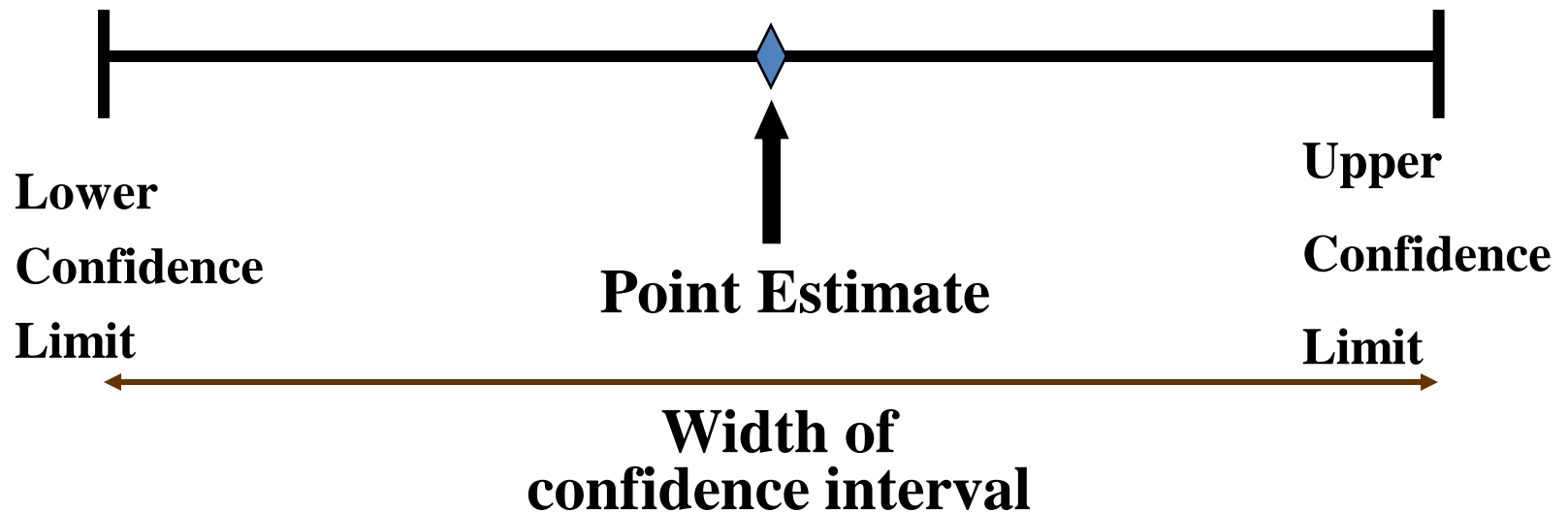
- When we measure some physical quantity with an instrument and obtain a numerical value, we want to know how close this value is to the true value. The difference between the true value and the measured value is the error. Unfortunately, the true value is unknown and unknowable. If we knew it, we wouldn't need the experiment. Since this is the case, the exact error is never known. We can only estimate it.

# Imprecision

- Gli errori casuali condizionano la ***precisione della stima campionaria***

# imprecision

- INTERVALLO DI CONFIDENZA



# Imprecision of the overall estimate

- **Wide confidence intervals** (CIs inform the impact of random error on evidence quality; CI expresses the range in which the truth plausibly lies)
- **Small number of events** (total number of events is less than 300 )
- **Small sample size**
- recommendation or **clinical course of action would differ** if the **upper versus the lower boundary** of the CI represented the truth

# Optimal information size

- We suggest the following: if the total number of patients included in a systematic review is less than the number of patients generated by a **conventional sample size calculation** for a single adequately powered trial, consider rating down for imprecision. Authors have referred to this threshold as the “**optimal information size**” (OIS)

# What is publication bias (1)?

- Definition

“Publication bias refers to the greater likelihood that studies with positive results will be published”

# What is publication bias (2)?

- An alternative definition:

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**

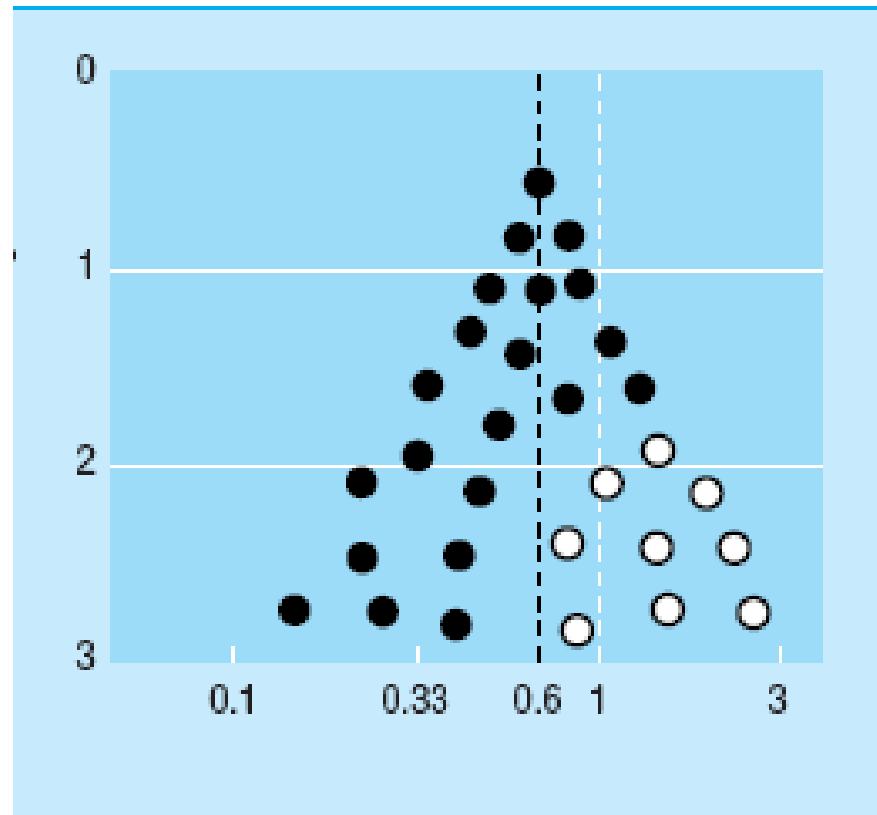
The likelihood of finding studies is related to the results of those studies (positive vs negative/detrimental)

# 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

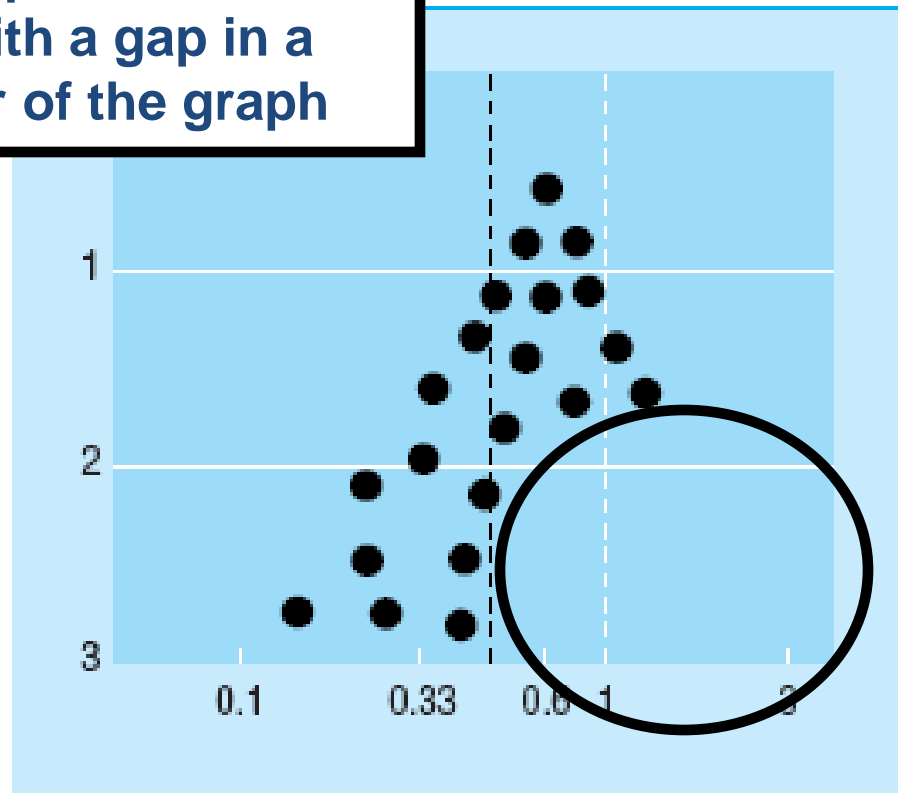


# Publication of All Trials



# Publication Bias

**Asymmetrical appearance of the funnel plot with a gap in a bottom corner of the graph**



# Funnel plots

- A funnel plot is a scatter plot of treatment effect against a measure of study size / precision.
  - Precision in the estimation of the true treatment effect increases as the sample size increases.
  - Small studies scatter more widely at the bottom of the graph
  - In the absence of bias the plot should resemble a symmetrical inverted funnel



# 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.**