Systematic review and Meta-analysis

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Narrative reviews, Systematic reviews, Meta-analyses

NARRATIVE REVIEWS tend to be:

- mainly descriptive
- do not involve a systematic search of the literature
- often focus on a subset of studies in an area chosen based on availability or author selection.

PROBLEMS: Thus narrative reviews while informative, can often include an element of selection bias.
They can also be confusing at times, particularly if similar studies have diverging results and conclusions.

Narrative reviews, Systematic reviews, Meta-analyses

SYSTEMATIC REVIEWS, as the name implies, typically involve a detailed and comprehensive plan and search strategy derived a priori, with the goal of reducing bias by identifying, appraising, and synthesizing all relevant studies on a particular topic. Often, systematic reviews include a meta-analysis component.

META-ANALYSES involve using statistical techniques to synthesize the data from several studies into a single quantitative estimate or summary effect size.

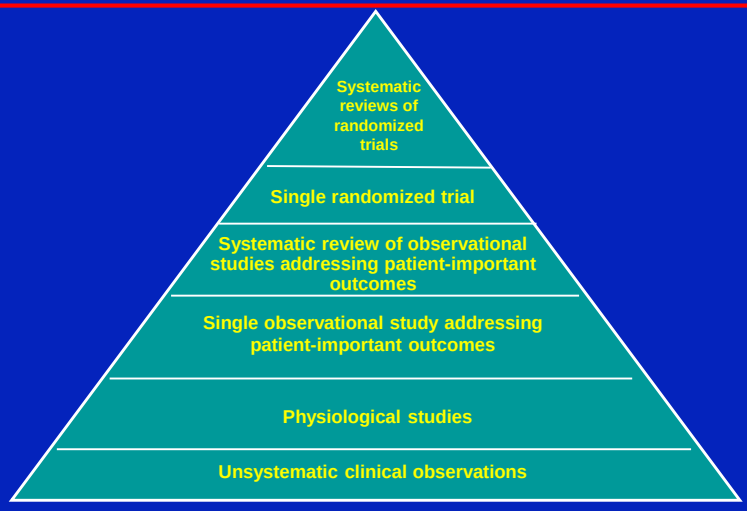
Uman SU. Systematic Reviews and Meta-Analyses. J Can Acad Child Adoesc Psychiatry 2011; 20(1):57-59

Meta-analysis

- Meta-analysis is a kind of observational/ecological study, where single studies are statistical units.
- It is a two-step process. In the first step, an appropriate effect measure is computed for each study. In the second step, the above-mentioned statistics are combined to compute a pooled estimate.

NB: an ECOLOGICAL STUDY investigates the time and/or spatial relation between outcome and exposure at population level (e.g. town, region, country), rather than at individual level.

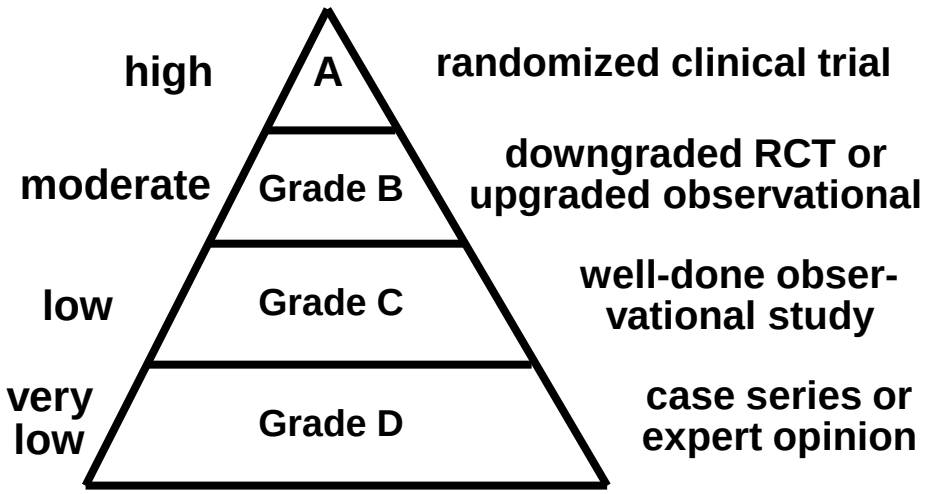
A Hierarchy of Strength of Evidence in Interventional Clinical Trials



Adapted from: Guyatt et al (2000) for the Evidence-Based Medicine Working Group. *JAMA* 284:1290-6

Also the quality of single studies should be assessed

Pyramid of evidence according to the GRADE system



The quality of observational studies is evaluated by the Newcastle-Ottawa Scale (NOS) score [Wells et al],

While the quality of experimental studies is assessed by the Jadad score [Jadad et al, 1996].

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. Available at http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm

Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–12

The Jadad score to evaluate clinical trials

It ranges between 0 (poor) and 5 (very good)

+1) *Was the study described as randomized?* **YES**

+1) *The method of randomisation was described in the paper, and that method was appropriate* (e.g. random numbers taken from tables or computer software)

-1) *The method of randomisation was described, but was inappropriate* (e.g. patients are alternatively allocated to either group according to increasing date of birth)

+1) *Was the study described as double blind?* **YES**

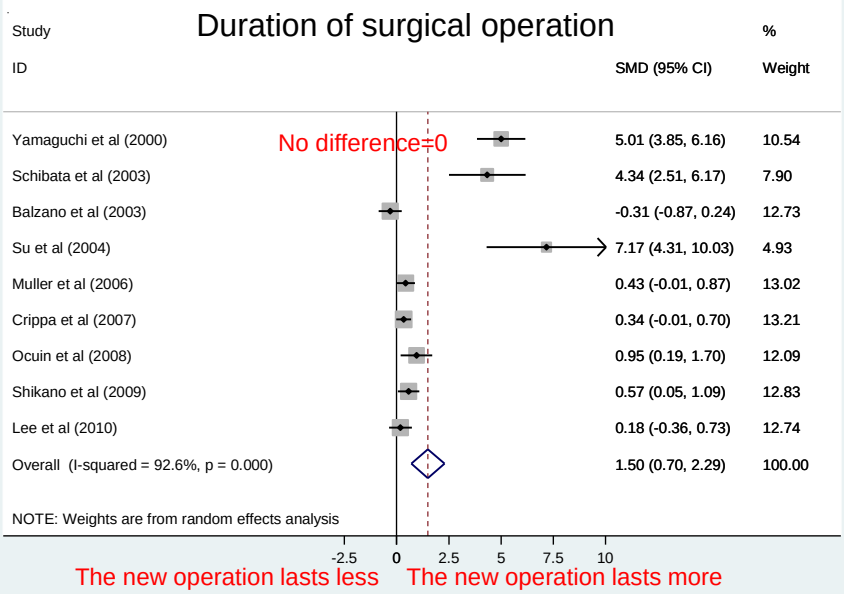
+1) *The method of blinding was described, and it was appropriate* (e.g. double dummy)

-1) *The method of blinding was described, but was inappropriate* (e.g. placebo per os while drug intravenously)

+1) *Was there a description of withdrawals and dropouts?* **YES**

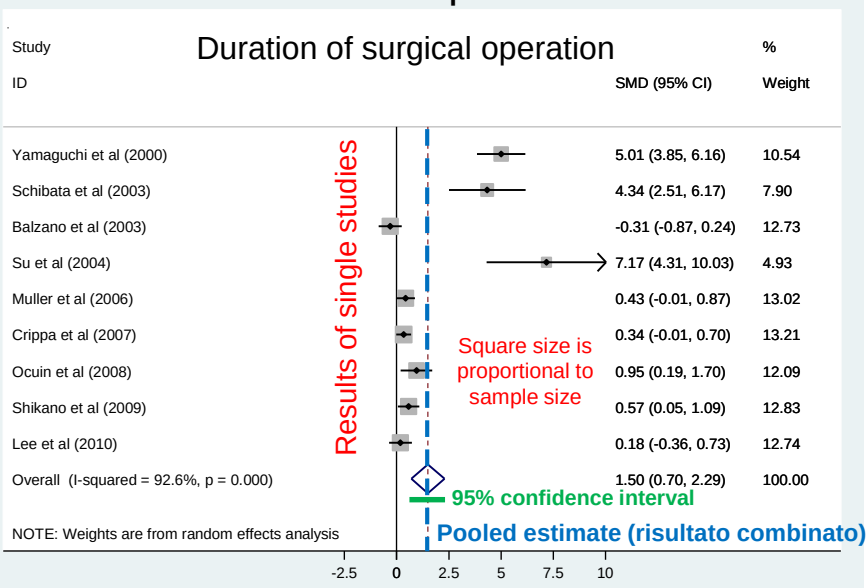
The results of a meta-analysis are synthetized through the Forest plot

Forest plot



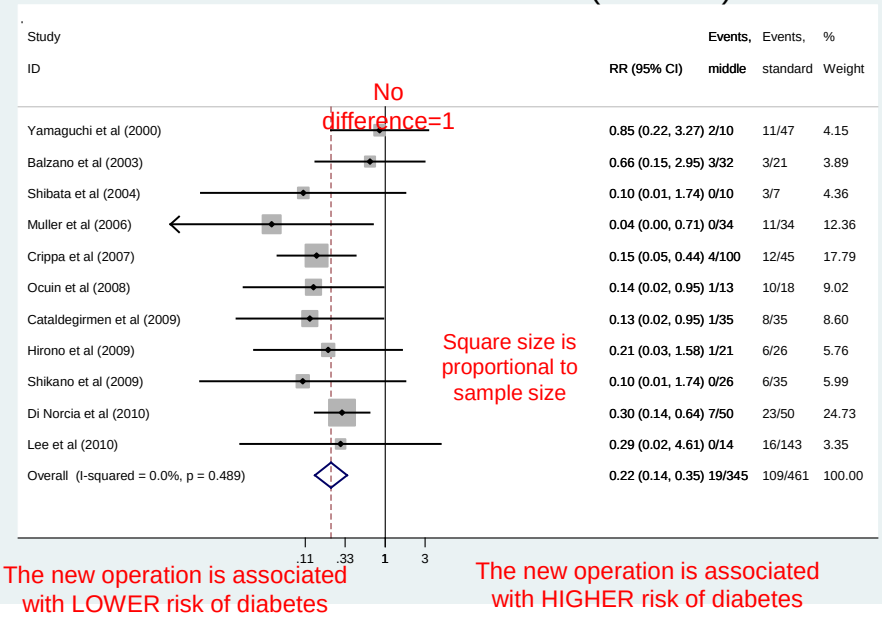
Iacono C, Verlato G, et al. Systematic review of central pancreatectomy - The Dagradi-Serio-Iacono procedure - and meta-analysis versus distal pancreatectomy. Brit J Surg 2013; 100:873-885

Forest plot



Iacono C, Verlato G, et al. Systematic review of central pancreatectomy - The Dagradi-Serio-Iacono procedure - and meta-analysis versus distal pancreatectomy. Brit J Surg 2013; 100:873-885

Risk of endocrine failure (diabetes)



Effect measures in Meta-analysis

Hypothesis testing gives us information about statistical significance, i.e. whether the observed difference can be attributed to random variability or to real difference in the source populations.

Effect sizes measure the strength of the relationship between two variables, thereby providing information about the magnitude of the intervention effect (i.e., small, medium, or large).

The type of effect size calculated generally depends on the type of outcome and intervention being examined as well as the data available from the published trials; however, some common examples include odds ratios (OR), weighted/standardized mean differences (WMD, SMD), and relative risk or risk ratios (RR).

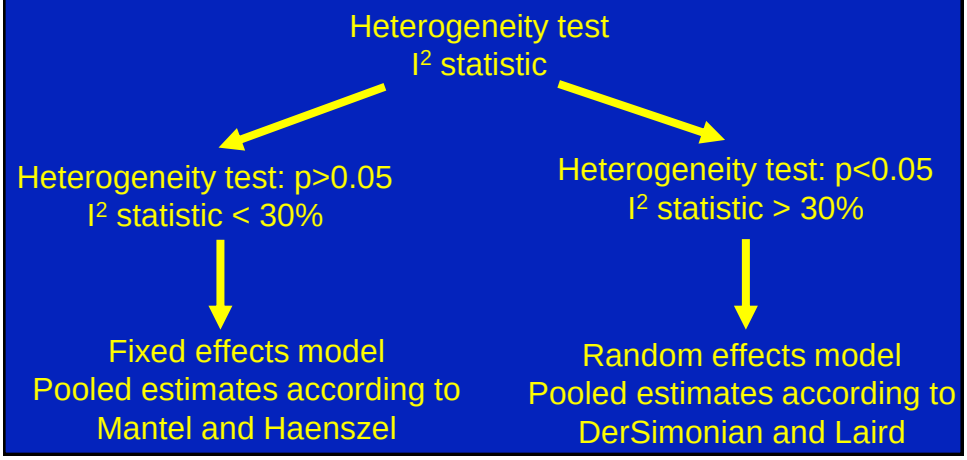
Standardized Mean Difference (SMD) was computed for quantitative variables (operation time, blood loss, length of hospital stay)

Relative risk (RR) was computed for qualitative variables (overall morbidity, exocrine failure, endocrine failure, pancreatic fistula, re-operation).

Choice of the statistical model in Meta-analysis

Fixed effects model = single studies can be considered as samples drawn from the same population.

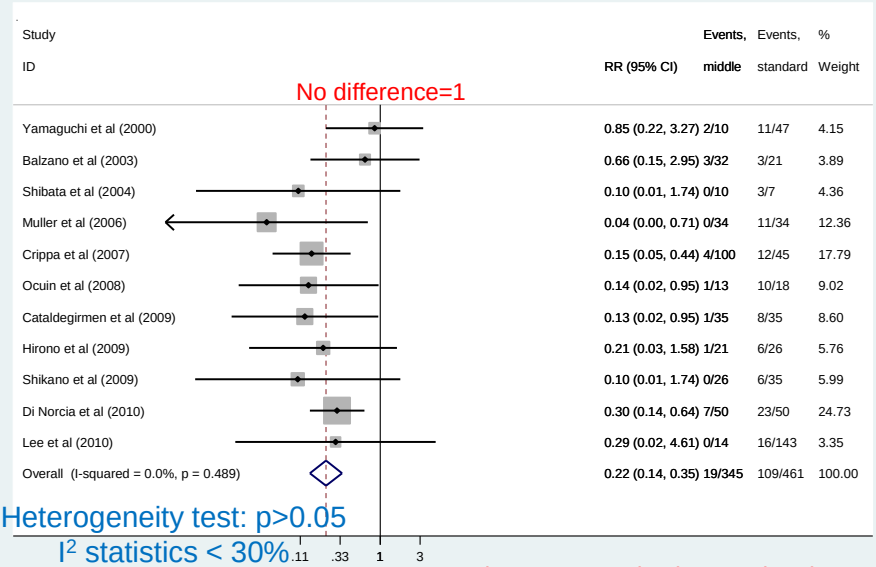
Random effects model = single studies should be viewed as samples drawn from different populations.



ENGLISH: The I-squared statistic indicates the proportion of total variation among the effect estimates attributed to heterogeneity rather than sampling error.

ITALIAN: La statistica I-quadrato indica la proporzione di variabilità tra le stime dei singoli studi che va attribuita all'eterogeneità anziché alla variabilità campionaria.

All studies found a lower risk of diabetes with the new procedure, which spares the pancreas tail, rich in islets producing insulin



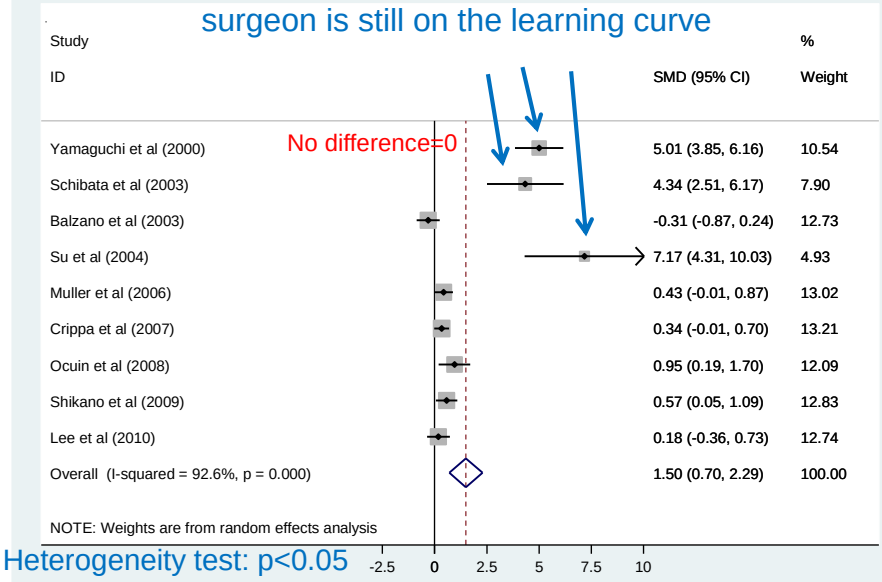
Heterogeneity test: p>0.05

I^2 statistics < 30%

The new operation is associated with LOWER risk of diabetes

The new operation is associated with HIGHER risk of diabetes

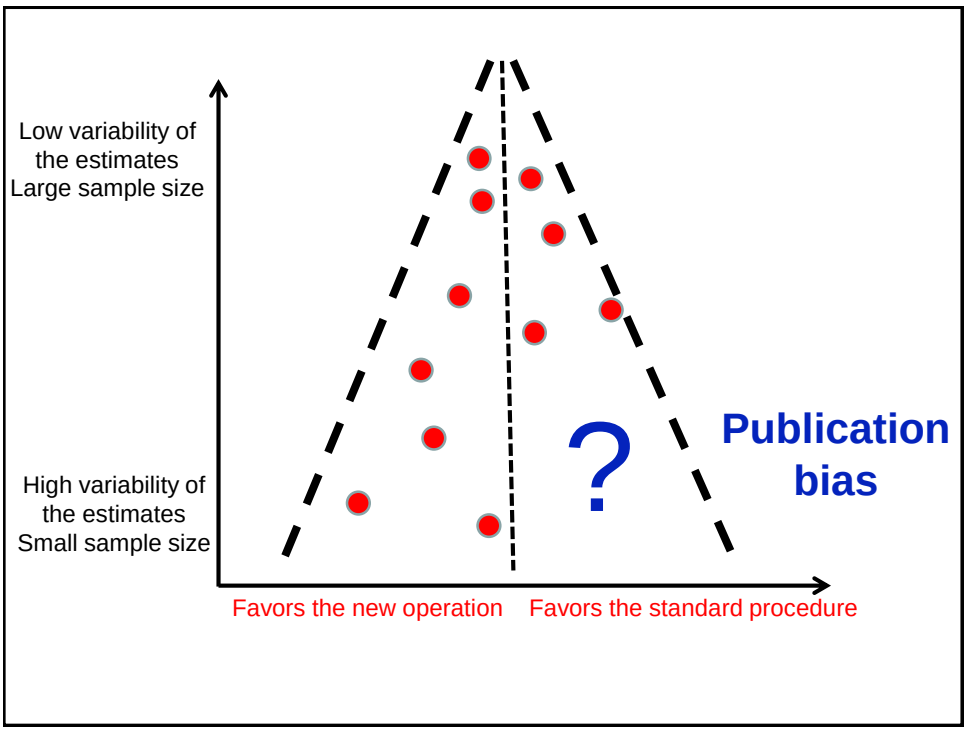
The new operation lasts longer in small series, where the surgeon is still on the learning curve



Heterogeneity test: $p<0.05$

I^2 statistics > 30%

The new operation lasts less The new operation lasts more

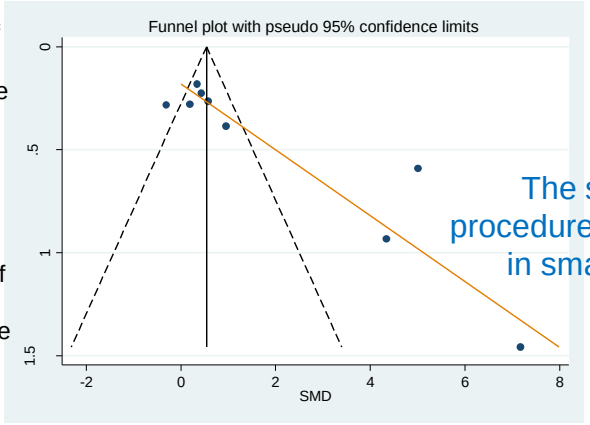


Funnel plot (diagramma a imbuto)

It also allows to highlight small series bias (distorsione da studi di bassa numerosità)

Low variability of the estimates
Large sample size

High variability of the estimates
Small sample size



The surgical procedure lasts longer in small series