



Forest Plot in Metaanalysis

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What is Meta analysis?

- A way to calculate an average
- Estimates an 'average' or 'common' effect
- Improves the precision of an estimate by using all available data




Why Metaanalysis..

Analysis of analyses More reliable information

Precision in estimating effects Garbage in garbage out
File drawer effect

How to plan metaanalysis

- Determine the research question
- Identification of relevant studies
- Select the studies
- Data extraction
- Data analysis**
- Examine heterogeneity/publication bias
- Interpretation & Reporting



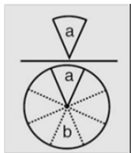
Data Analysis

Effect Measures

- Relative Risk/Risk Ratio (RR)
- Odds Ratio (OR)
- Hazard Ratio (HR)

Risk & Odds

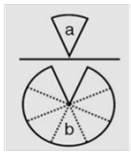
Risk



$\text{Risk} = \frac{a}{a+b}$


Relative Risk: risk patients/risk controls

Odds



$\text{Odds} = \frac{a}{b}$


Odds Ratio: odds patients/odds control

 **Risk**

- ♦ 24 people skiing down a slope, and 6 fall
- ♦ Risk of a fall
 - = 6 falls/24 who could have fallen
 - = $6/24 = \frac{1}{4} = 0.25 = 25\%$


Risk = $\frac{\text{number of events of interest}}{\text{total number of observations}}$

Basics of Metaanalysis; Cochrane Statistical Methods Group

 **Odds**

- ♦ 24 people skiing down a slope, and 6 fall
- ♦ odds of a fall
 - = 6 falls/18 did not fall
 - = $6/18 = 1/3 = 0.33$ (not usually as %)

Odds = $\frac{\text{number of events of interest}}{\text{number without the event}}$

 **Expressing in words**

Risk

- the chances of falling were one in four, or 25%

Odds

- the chances of falling were one third of the chances of not falling
- one person fell for every three that didn't fall
the chances of falling were 3 to 1 against

Relative Risk

$$\frac{\text{Probability of getting disease if exposed}}{\text{Probability of getting disease if not exposed}}$$

Odds Ratio

$$\frac{\text{Odds that the disease were exposed}}{\text{Odds that the controls were exposed}}$$

An example..

<i>Blum et al</i>	Still dyspeptic	Not still dyspeptic	Total
Treatment	119	45	164
Control	130	34	164
Total	249	79	328

Risk ratio (Relative Risk)

<i>Blum et al</i>	Still dyspeptic	Not still dyspeptic	Total
Treat	119	45	164
Control	130	34	164
Total	249	79	328

- risk of event on treatment = **119/164**
- risk of event on control = **130/164**

risk ratio = $\frac{119/164}{130/164} = \frac{0.726}{0.793} = 0.92$

= $\frac{\text{risk on treatment}}{\text{risk on control}}$

Where risk ratio = 1, this implies no difference in effect

Odds Ratio

<i>Blum et al</i>	Still dyspeptic	Not still dyspeptic	Total
Treat	119	45	164
Control	130	34	164
Total	249	79	328

- odds of event on treatment = **119/45**
- odds of event on control = **130/34**

• odds ratio = $\frac{119/45}{130/34} = \frac{2.64}{3.82} = 0.69$

= $\frac{\text{odds on treatment}}{\text{odds on control}}$

Where odds ratio = 1, this implies no difference in effect

Expressing risk ratios and odds ratios

Risk ratio 0.92

- the risk of still being dyspeptic on treatment was about **92%** of the risk on control
- treatment reduced the risk by about **8%**
- treatment reduced the risk to **92%** of what it was

Odds ratio 0.69

- treatment reduced the odds by about **30%**
- the odds of still being dyspeptic in treated patients were about **two-thirds** of what they were in controls

Interpretation of RR and OR

RR or OR > 1
Increased likelihood of outcome in treatment group

RR or OR < 1
Decreased likelihood of outcome in treatment group

RR or OR = 1
No difference of outcome between tt & control group

OR or RR should be accompanied by CI

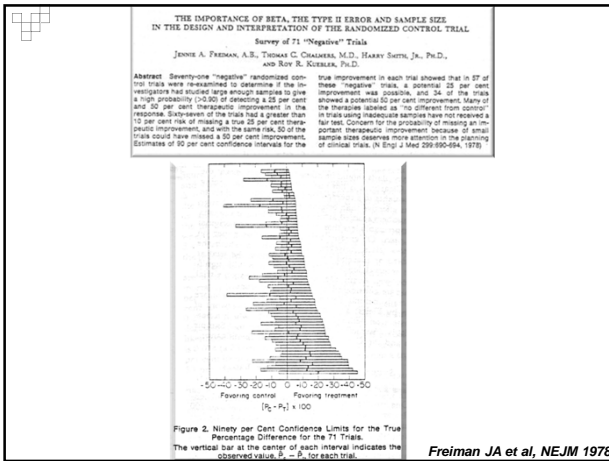
Confidence Intervals

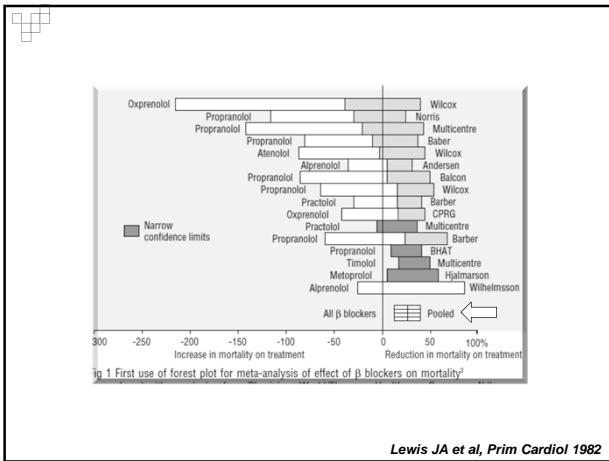
Value	95 % CI are commonly used 90 or 99% CI are sometimes used
Width of CI	Indicates precision of the estimate Wider the interval, less the precision
CI includes 1	No statistically significant difference
CI doesn't include 1	Statistically significant difference

Statistical Significance and CI

a) Statistically significant, low precision
 b) Statistically significant, high precision
 c) Not statistically significant, low precision
 d) Not statistically significant, high precision

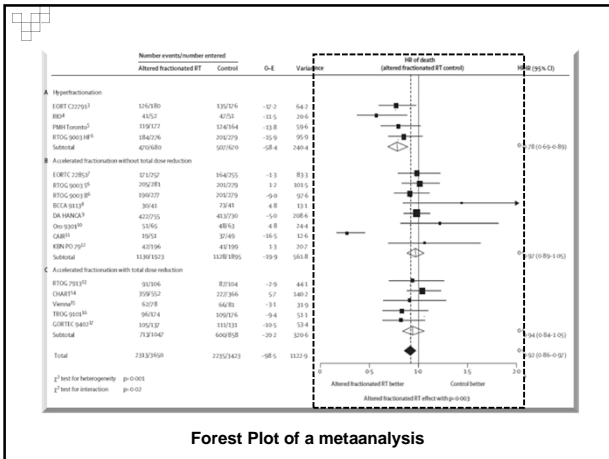
The graph displaying results of metaanalysis
“Forest Plot”

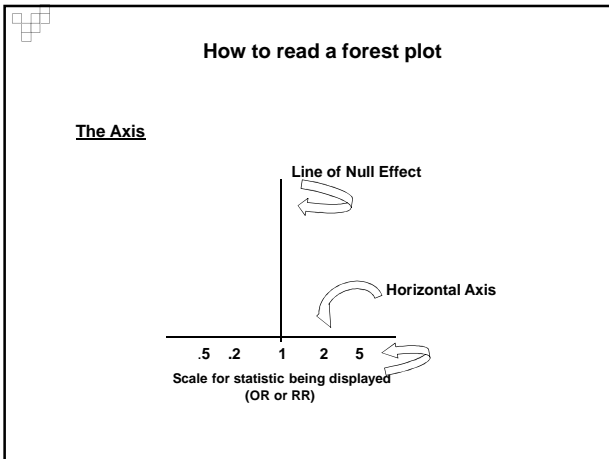


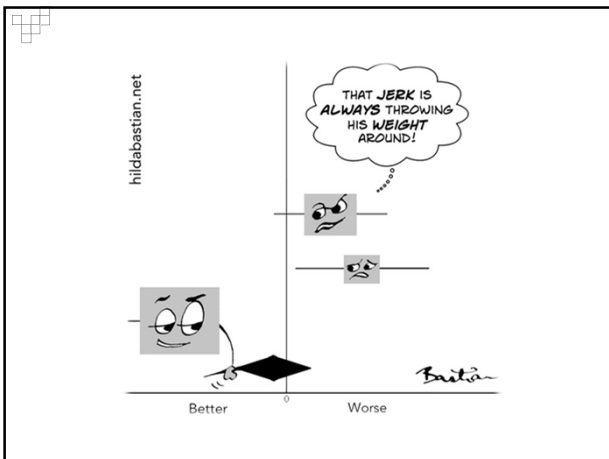


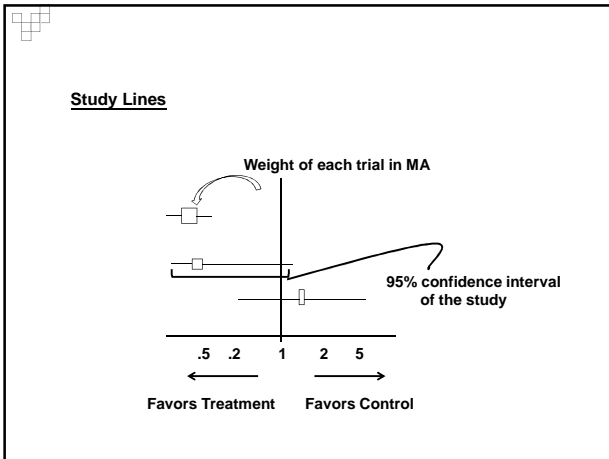
What's in a name?
That which we call a rose
By any other name
would smell as sweet.

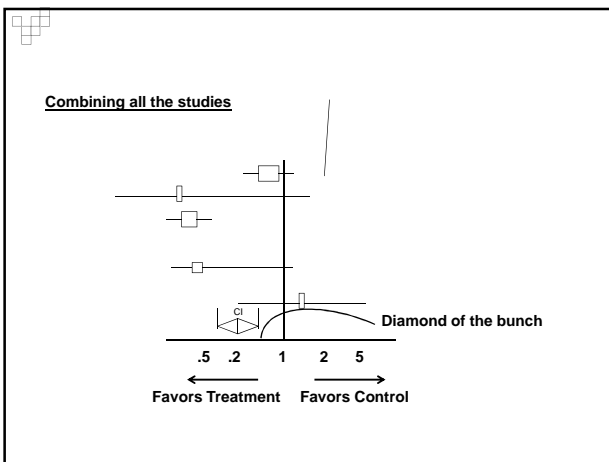
Forest Plot or Forrest Plot!!

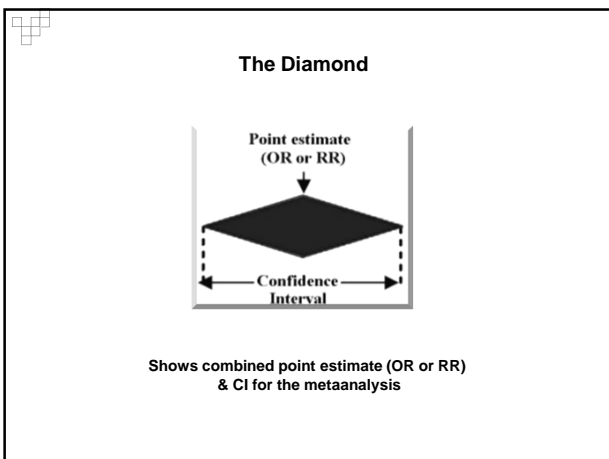


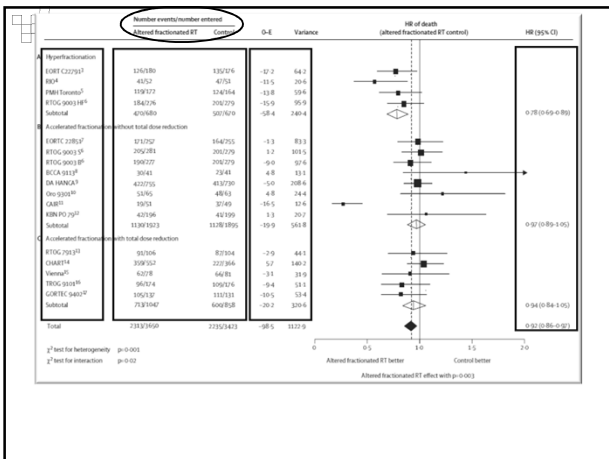


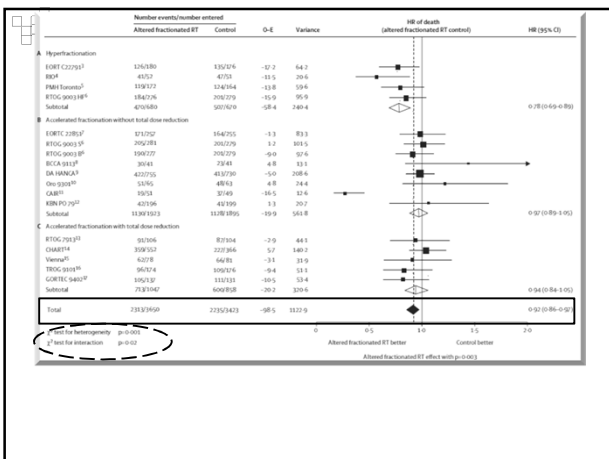












Heterogeneity..
 variation between the studies' results

Differences between studies with respect to:

- ♦ **Patients:** diagnosis, in- and exclusion criteria, etc.
- ♦ **Interventions:** type, dose, duration, etc.
- ♦ **Outcomes:** type, scale, cut-off points, duration of follow-up, etc.
- ♦ **Quality and methodology:** randomised or not, allocation concealment, blinding, etc.

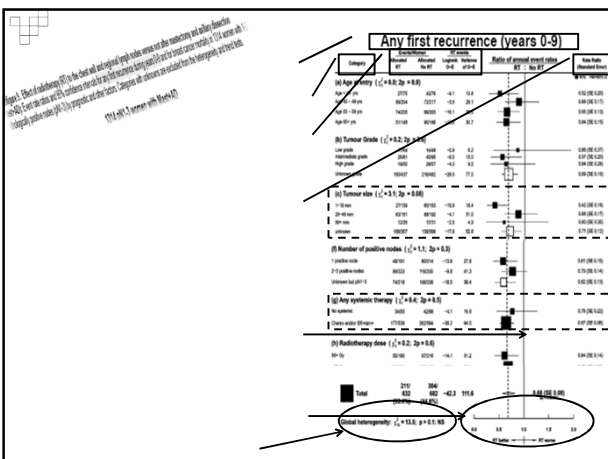
- Measured by I^2
- Located at bottom of the plot
- Should be <50%

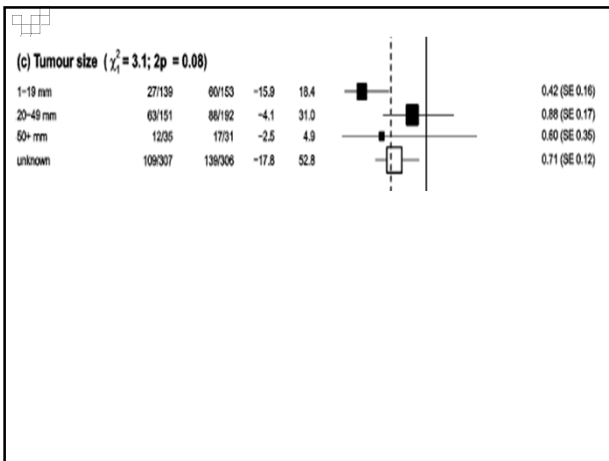
Exercise

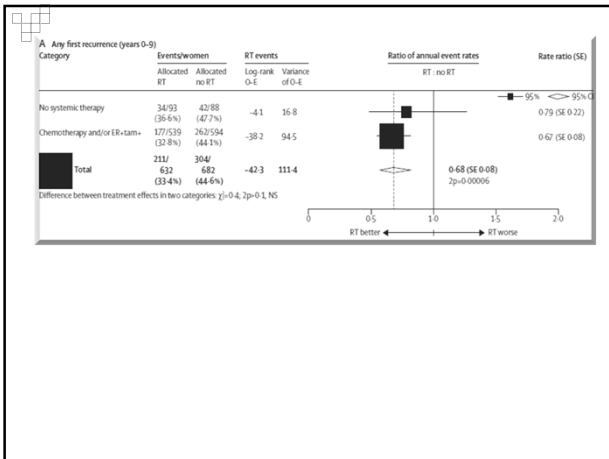
Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials

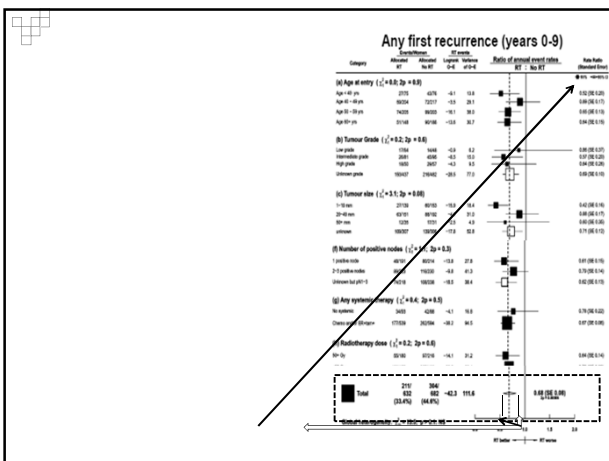
EBCTG (Early Breast Cancer Trialists' Collaborative Group)
 Published Online March 29, 2014

Summary
 Background Postmastectomy radiotherapy was shown in previous meta-analyses to reduce the risks of both recurrence and breast cancer mortality in all women with node-positive disease considered together. However, the benefit in










Exercise



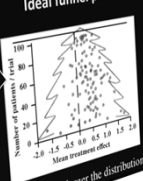
Cochrane Collaboration Logo

Some other plots..

Funnel plots
Bias detected by simple graphical test

- **Plot for each trial** RR or OR on x axis
Sample size on y axis
- **Absence of bias**
Plot should resemble inverted funnel or Christmas tree
- **Presence of bias**
Plot shows asymmetrical & skewed shape

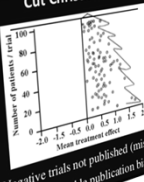
Ideal funnel plot



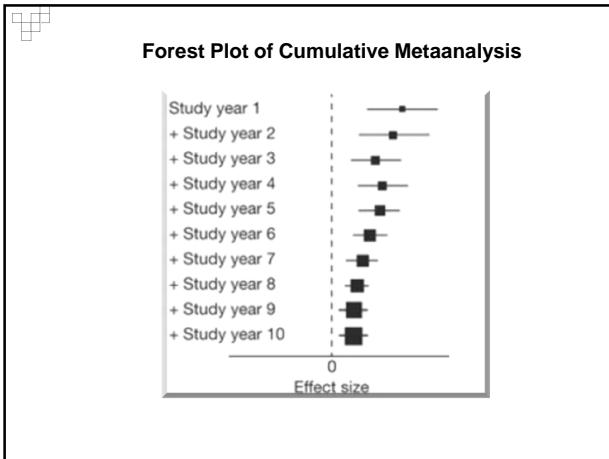
Christmas tree

The smaller the trial, the larger the distribution of results

Cut Christmas tree



Negative trials not published (missing)
Suspicion of considerable publication bias in this MA



Summarize..

Interpretation of Forest Plot

Names on left	First authors of primary studies
Black squares	RR or OR of individual studies
Black square size	Weight of each trial in MA
Horizontal lines	95% confidence intervals
Vertical line	Line of no effect (OR or RR = 1)
Diamond	Overall treatment effect
Diamond Center	Combined treatment effect
Tips of diamond	95% CI

Diamond in Metaanalysis

Diamond on Left of the line of no effect	Less episodes of outcome of interest in treatment group
Diamond on Right of the line of no effect	More episodes of outcome in treatment group
Diamond touches the line of no effect	No statistically significant difference between groups
Diamond does not touch the line of no effect	Difference between two groups statistically significant
