Health Technology Engineering
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Meta-analysis Lab

We will use same sample datasets to walk through the basic steps of conducting a meta-analysis, specifically:
(1) estimating a mean effect size;
(2) quantifying heterogeneity;
(3) interpreting the results.

Step 1:

Download OpenMetaAnalyst
If you have not already done so, download the free OpenMetaAnalyst software from the following website:
http://www.cebm.brown.edu/open_meta/download.html

http://www.cebm.brown.edu/static/oma/open_meta_analyst_windows.zip
(WIN)
http://www.cebm.brown.edu/static/oma/open_meta_analyst_mac.zip
(MAC)

For help, you could see the following web page:
http://www.cebm.brown.edu/static/oma/doc/OpenMA_help.html

Step 2:

Open the first Example Dataset
Once you have installed OpenMetaAnalyst software on your laptop, you can open the software, and then ‘open an existing project’ data file, using the “BCG.oma” file that was distributed in the sample data.

This dataset contains data from a number of studies on the effect of a vaccine (called BCG) in preventing the development of tuberculosis (TB)

The file contains data of n = 13 studies (rows). The columns represent variables related to the studies and study findings.

For this example dataset, assume that you have conducted a systematic review of the literature and identified these 13 studies as eligible for inclusion in a meta-analysis. Your eligible outcome of interest is the number of subjects who developed the TB.

You have extracted statistical data from each of these studies reported in the table below:

Study	Treated events	Treated subjects	Control events	Control subjects
Aaronson (1948)	4	123	11	139
Ferguson & Simes (1949)	6	306	29	303
Rosenthal (1960)	3	231	11	220
Hart & Sutherland (1977)	62	13598	248	12867
Frimodt-Moller (1973)	33	5069	47	5808
Stein & Aaronson (1953)	180	1541	372	1451
Vandiviere (1973)	8	2545	10	629
TB Prevention Trial (1980)	505	88391	499	88391
Coetzee & Berjak (1968)	29	7499	45	7277
Rosenthal (1961)	17	1716	65	1665
Comstock (1974)	186	50634	141	27338
Comstock & Webster (1969)	5	2498	3	2341
Comstock (1976)	27	16913	29	17854

In this example, the effect of the vaccine will be measured by the relative risk - the risk of contracting TB in the treatment group divided by the risk of contracting TB in the control group. The relative risk (RR) is defined by:

$$RR = \frac{\frac{a}{(a+b)}}{\frac{c}{(c+d)}}$$

Where:

a = Treated events - number of subjects in the treatment group who contracted TB.
b = Treated subjects - total number of subjects in the treatment group
c = Control events - number of subjects in the control group who contracted TB.
d = Control subjects - total number of subjects in the treatment group

For statistical reasons, the effect sizes for relative risk (RR) are calculated in log scale:

$$\log(RR) = log\left(\frac{\frac{a}{(a+b)}}{\frac{c}{(c+d)}}\right)$$

The variance of the effect size is:

$$v_{(\log(RR))} = \frac{1}{a} - \frac{1}{a+b} + \frac{1}{c} - \frac{1}{c+d}$$

Step 3:

Analyze the Data:

Estimate the fixed-effect weighted mean effect size. Report and interpret the mean effect size and its 95% confidence interval.

Estimate the random-effects weighted mean effect size and its 95% confidence interval. Compare your results to those you found in previous point.

Results: **Binary Fixed-Effect Model - Inverse Variance (Relative Risk)**

Model Results

Estimate	Lower bound	Upper Bound	p-Value
0.650	0.601	0.704	< 0.001

Heterogeneity

Q(df=12)	Het. p-Value	I^2
152.233	<0.001	92%

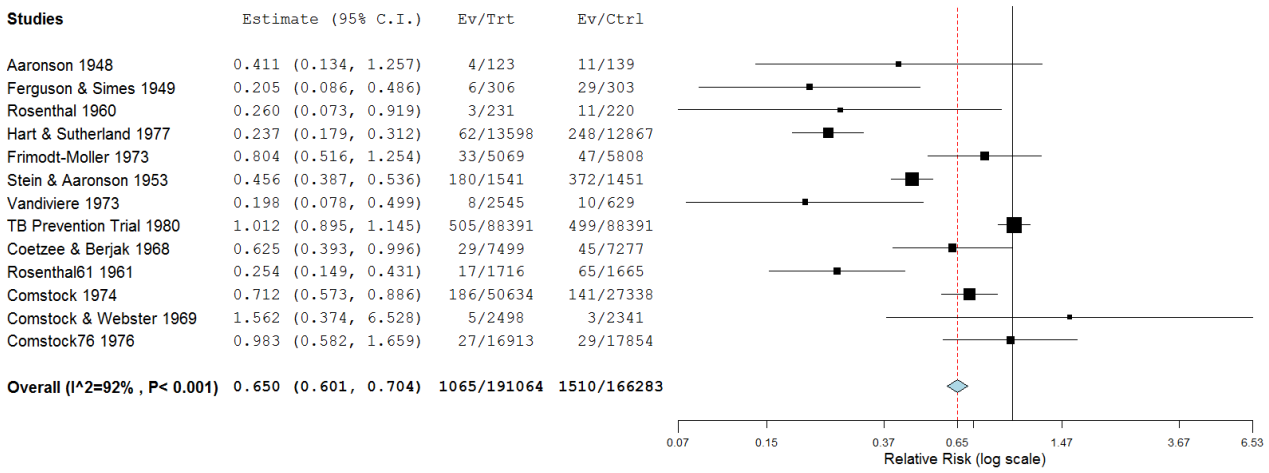
Results (log scale)

Estimate	Lower bound	Upper Bound	Std. error
-0.430	-0.510	-0.351	0.040

Study names	Weights
Aaronson	0.504 %
Ferguson & Simes	0.843%
Rosenthal	0.395 %
Hart & Sutherland	8.197 %

Frimodt- Moller	3.203 %
Stein & Aaronson	23.751 %
Vandiviere	0.735 %
TB Prevention Trial	41.401 %
Coetzee & Beriak	2.906 %
Rosenthal61	2.246 %
Comstock	13.214 %
Comstock & Webster	0.308 %
Comstock76	2.297 %

Forest Plot



Binary Random-Effects Model (Relative Risk)

Model Results

Estimate	Lower bound	Upper Bound	p-Value
0.490	0.345	0.695	<0.001

Heterogeneity

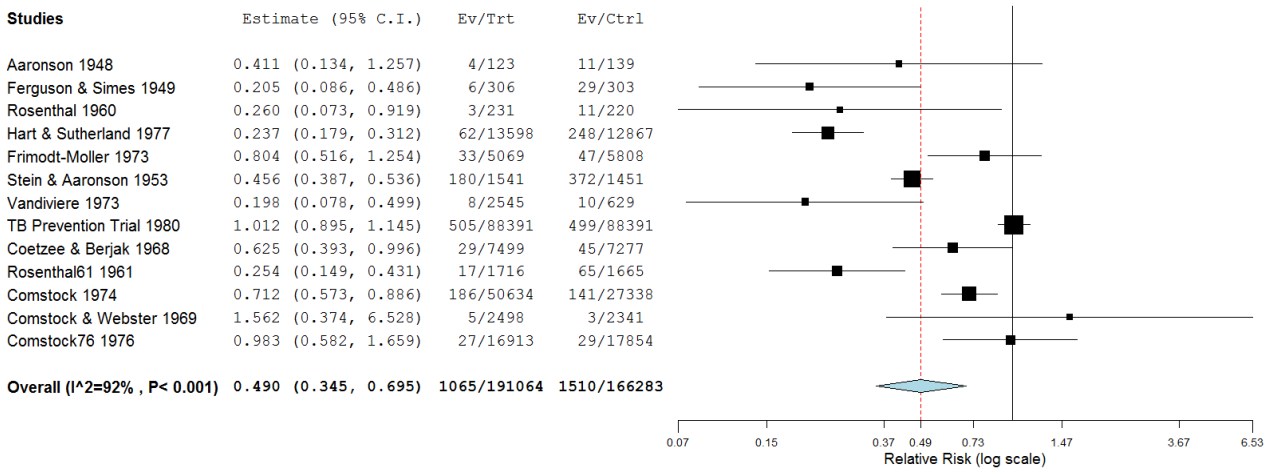
Tau^2	Q(df=12)	Het. p-Value	I^2
0.309	152.233	<0.001	92%

Results (log scale)

Estimate	Lower bound	Upper Bound	Std.error
-0.714	-1.064	-0.364	0.179

Study names	Weights
Aaronson	5.036 %
Ferguson & Simes	6.347 %
Rosenthal	4.412 %
Hart & Sutherland	9.718 %
Frimodt- Moller	8.875 %
Stein & Aaronson	10.121 %
Vandiviere	6.008 %
TB Prevention Trial	10.216 %
Coetzee & Beriak	8.748 %
Rosenthal61	8.368 %
Comstock	9.948 %
Comstock & Webster	3.798 %
Comstock76	8.404 %

Forest Plot:



Conclusion: High Heterogeneity => difference from random vs fixed effect model => The heterogeinity could be explained by Meta-regression

Meta-Regression

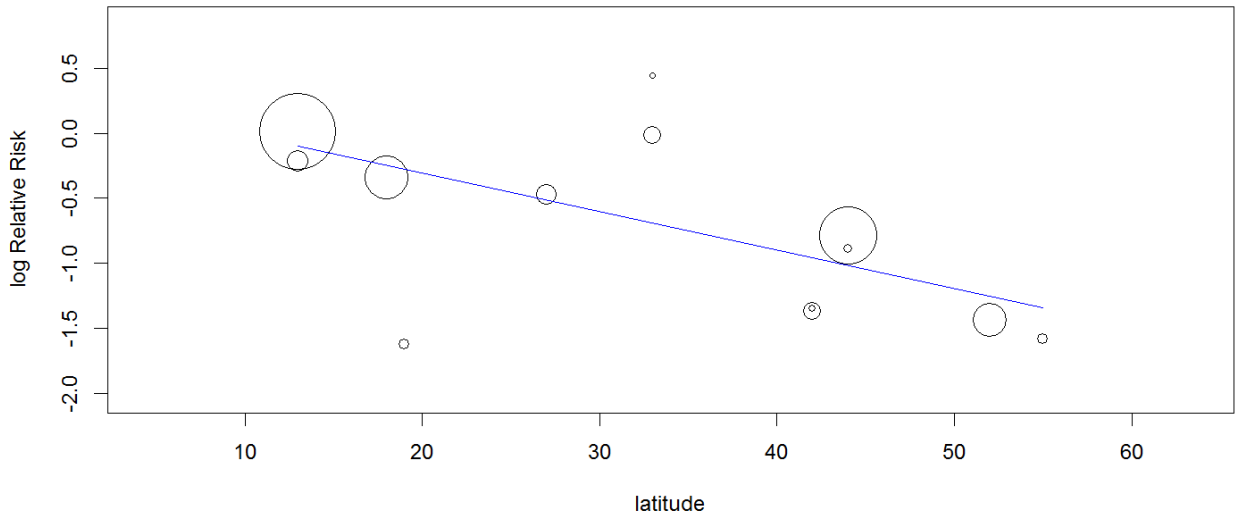
Metric: Relative Risk

Model Results

Covariate	Coefficients	Lower Bound	Upper bound	Std. error	p-Value
Intercept	0.282	-0.085	0.649	0.187	0.132
latitude	-0.030	-0.040	-0.019	0.005	<0.001

Omnibus p-Value
0.000

Regression Plot:



Step 4:

Open the Second Example Dataset “continuous.oma”
You can now open another dataset, using the menu ‘file’, open and select the file ‘continuous.oma’.

This dataset contains data from a number of studies on the operative time of a surgical procedure performed by two different techniques (A and B).

The file contains data of n = 6 studies (rows).

For this example dataset, assume that you have conducted a systematic review of the literature and identified these 6 studies as eligible for inclusion in a meta-analysis. Your eligible outcome of interest is the difference in operative time.

You have extracted statistical data from each of these studies (mean and standard deviation).

In this example, the effect of the chosen surgical procedure will be measured by the mean difference in the operative time.

Step 5:

Analyze the Data:

Estimate the fixed-effect weighted mean effect size. Report and interpret the mean effect size and its 95% confidence interval.

Estimate the random-effects weighted mean effect size and its 95% confidence interval. Compare your results to those you found in previous point.

Results: Continuous **Fixed**-Effect Model (Mean Difference)

Model Results

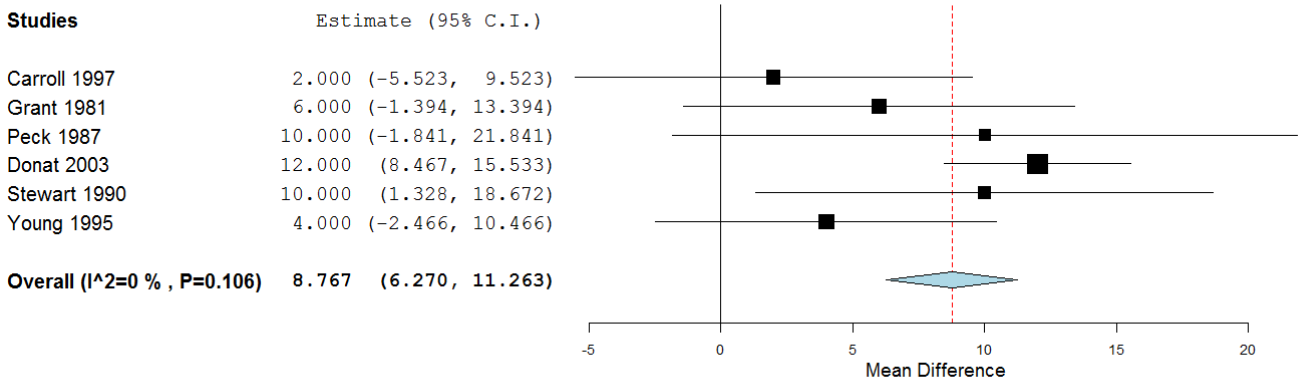
Estimate	Lower bound	Upper Bound	Std. error	p-Value
8.767	6.270	11.263	1.274	<0.001

Heterogeneity

Q(df=5)	Het. p-Value
9.070	0.106

Study names	weights
Study 1	11.015 %
Study 2	11.404 %
Study 3	4.446 %
Study 4	49.933 %
Study 5	8.290 %
Study 6	14.912 %

Forest Plot:


Studies
Estimate (95% C.I.)
Carroll 1997 2.000 (-5.523, 9.523)
Grant 1981 6.000 (-1.394, 13.394)
Peck 1987 10.000 (-1.841, 21.841)
Donat 2003 12.000 (8.467, 15.533)
Stewart 1990 10.000 (1.328, 18.672)
Young 1995 4.000 (-2.466, 10.466)
Overall (I^2=0 % , P=0.106) 8.767 (6.270, 11.263)
-5
0
5
10
15
20
Mean Difference

Continuous **Random**-Effects Model (Mean Difference)

Model Results

Estimate	Lower bound	Upper Bound	Std. error	p-Value
7.617	3.823	11.411	1.936	<0.001

Heterogeneity

Tau^2	Q(df=5)	Het. p-Value	I^2
9.510	9.070	0.106	44.871 %

Study names	weights
Study 1	15.455 %
Study 2	15.782 %
Study 3	8.144 %
Study 4	29.363 %
Study 5	12.882 %
Study 6	18.374 %

Forest Plot

Studies	Estimate (95% C.I.)
Carroll 1997	2.000 (-5.523, 9.523)
Grant 1981	6.000 (-1.394, 13.394)
Peck 1987	10.000 (-1.841, 21.841)
Donat 2003	12.000 (8.467, 15.533)
Stewart 1990	10.000 (1.328, 18.672)
Young 1995	4.000 (-2.466, 10.466)
Overall (I^2=44.87 % , P=0.106)	**7.617 (3.823, 11.411)**