Meta-analysis – an introduction

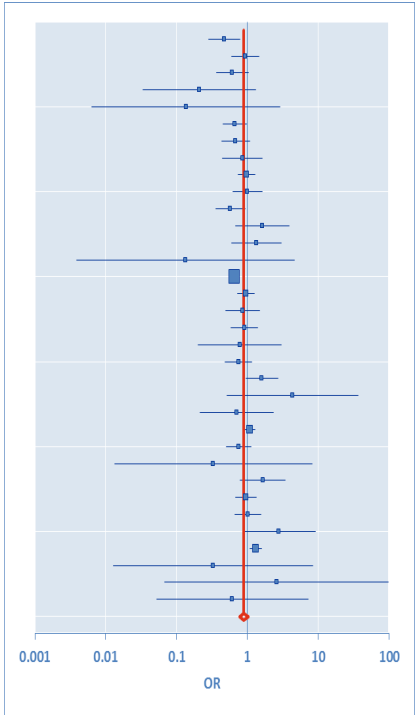
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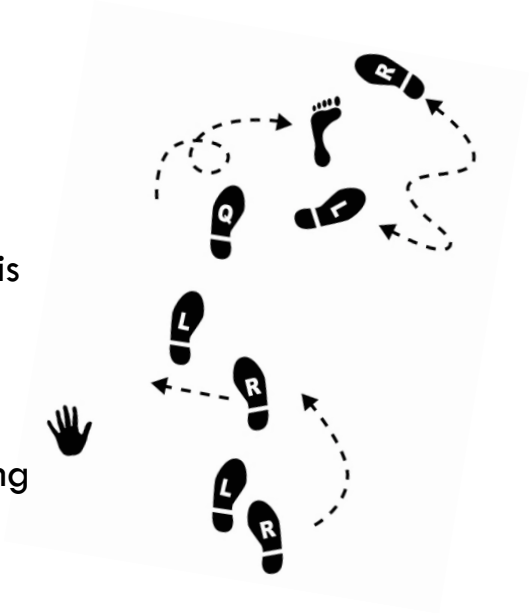
Outline

- The research context
- Meta-analysis workflow
- Meta-analysis concepts
- Software options
- Worked example using metafor in R
- Recap



What is a workflow?

- Every statistical analysis is different, but all follow similar paths. It can be useful to know what these paths are
- We have developed practical, step-by-step instructions that we call '*workflows*', that can you can follow and apply to your research
- We have a general research workflow that you can follow from hypothesis generation to publication
- And statistical workflows that focus on each major step along the way (e.g. experimental design, power calculation, model building, analysis using linear models/survival/multivariate/survey methods)



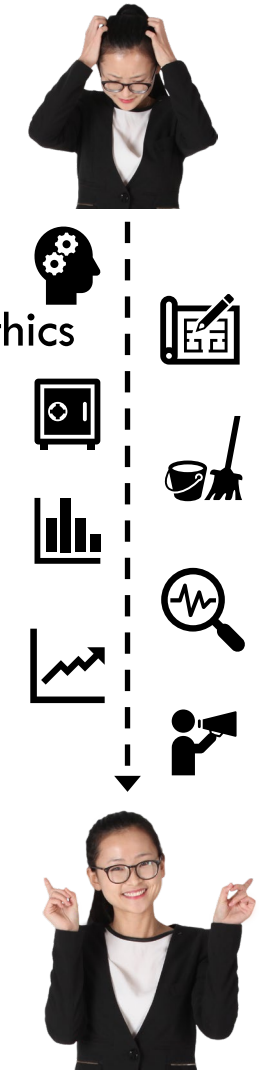
Statistical Workflows

- Our **statistical workflows** can be found within our workshop slides
- **Statistical workflows** are software agnostic, in that they can be applied using any statistical software
- In this workshop there is an accompanying **software workflow** that shows you how to perform the statistical workflow using R



General Research Workflow

1. **Hypothesis Generation** (Research/Desktop Review)
2. **Experimental and Analytical Design** (sampling, power, ethics approval)
3. **Collect/Store Data**
4. **Data cleaning**
5. **Exploratory Data Analysis (EDA)**
6. **Data Analysis aka inferential analysis**
7. **Predictive modelling**
8. **Publication**



Systematic Review – the research context

Before 1993: Narrative reviews were common and accepted

1993: Cochrane (Collaboration) founded to promote systematic review of randomised controlled trials

Since 2010: Systematic review is the dominant synthesis method in many fields

	Narrative Review	Systematic Review
Research articles covered	An overview of a field of research	A well-defined research question
Methodology for finding articles	Not defined	Search methodology defined in a protocol (eg PRISMA prisma-statement.org)
Assessment of quality	Subjective and unstated	Formal and clearly defined (e.g. GRADE)
Meta-analysis	Not applicable	May be included

Systematic Review - the research context

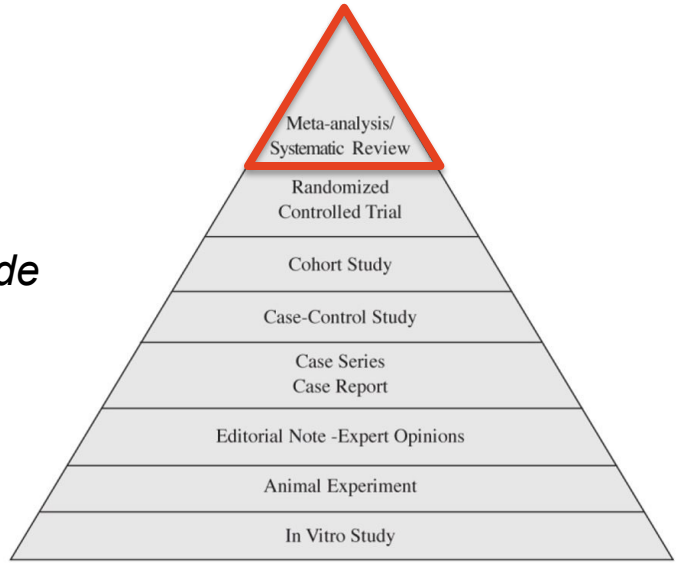
Why choose to do Systematic Review and meta-analysis?

A well conducted meta-analysis sits at the top of the evidence pyramid

"Potential advantages of meta-analyses include an improvement in precision, the ability to answer questions not posed by individual studies, and the opportunity to settle controversies arising from conflicting claims."

Cochrane 2024

Evidence pyramid for medical studies



Systematic Review – step by step overview



1. Before you Start
2. Define a research question
3. Develop a protocol
4. Plan your literature search
5. Perform your search
6. Screen your results
7. Extract and appraise data
8. Analyse and interpret data
   - Meta-analysis
9. Writing and publishing

The University of Sydney library guides

Literature Review – Library support



- The Sydney University library is the best place to get support on the wider questions of Literature Review and Systematic Review
- Resources available at the Systematic Review Support Page and Library Services
- Library has dedicated support staff – eligible staff and students can request a consultation with an Academic Liaison Librarian review the Systematic review service charter for details
- Workshops run include "Literature Reviews: Systematic Methodology" – check the workshops calendar (filter category by "systematic review")
- Canvas OLE modules available online - Writing a Literature Review OLEO5130

Workflow

Meta-analysis workflow



Meta Analysis – concepts and workflow step by step

Meta-Analysis workflow steps

0. (From systematic review workflow) Define a research question and perform data extraction on included studies
1. Import the data (into the software)
2. Calculate Effect Size
3. Meta-Analysis summary (Fixed-Effect and Random-Effects)
4. Explore Heterogeneity (Q statistic, I^2, tau)
5. Publication bias (Funnel plot)
6. Sub-group analysis and/or meta-regression (if warranted)

0. Outline a research question

Because of the limitations of reported summaries methods, meta-analyses primarily address quite simple comparisons:

1. Continuous outcome (e.g. weight loss) measured in two groups
2. Binary outcome (e.g. myocardial infarction [heart attack] yes/no) measured in two groups
3. Correlation between two continuous variables (e.g. blood lead levels in children and IQ scores).

The types of variables and the study design determine the type of effect size that is synthesised in the meta-analysis.

0. Outline a research question

Similarity of Studies

The studies included for meta-analysis will generally be of one type only, for example:

1. Studies where the treatment is assigned (eg RCT)
2. Observational studies – no assignment to groups

They should be similar in such a way as to relate to the specific research question (refer back to steps 1 and 2 of the systematic review workflow).

For example (from Borenstein Ch 40)
What is the effect of an intervention? → Randomised controlled trials
What is the cause of a rare disease? → Case-control studies
What is the prevalence of a condition? → Cross-sectional studies

1. Import the data Function of Variables

For any analysis we need to be clear what the functional classification of the variables in the data set is, e.g. we want to investigate the effect of smoking on lung disease:





Smoking (yes/no)

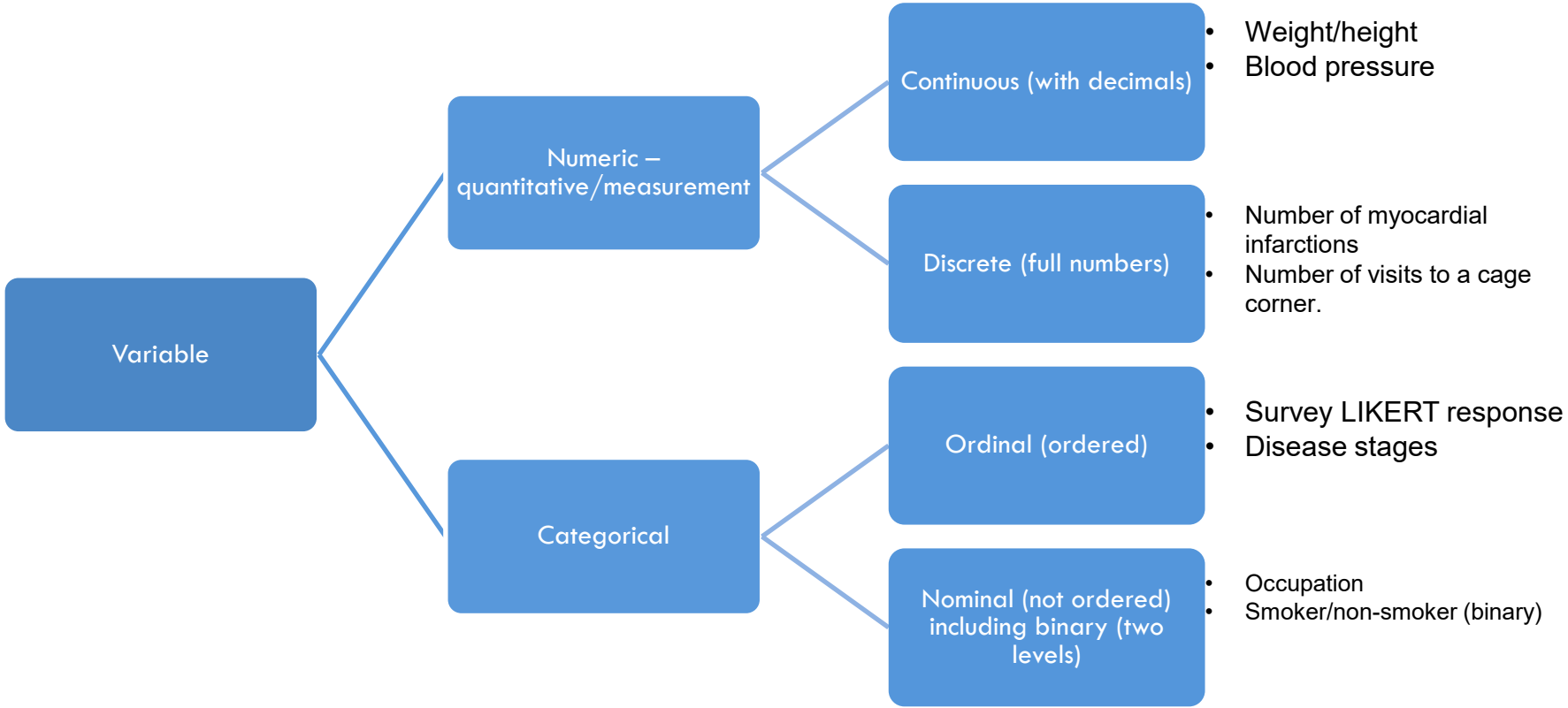
Predictor
Explanatory variable
Risk factor
Independent variable

Lung disease (yes/no)

Response
Outcome
Dependent variable

Depending on who taught you statistics, your discipline, stats software or textbook you may have come across any of these terms or more!

1. Import the data variable types



The type of variable will influence what type of effect size is appropriate

1. Import the data continuous outcome example

Basic clean layout

study_id	author	year	mean_t	sd_t	n_t	mean_c	sd_c	n_c
S01	Smith	2015	74.2	12.1	85	68.7	11.8	83
S02	Jones	2016	65.4	15.7	42	59.6	14.2	39
S03	Chen	2017	81.3	10.5	120	77.1	10.8	118
S04	Brown	2017	69.7	13.4	56	63.8	13	54
S05	Patel	2018	72.8	11.6	91	69.2	12.4	88
S06	Wilson	2018	78.1	9.7	67	72.3	10.1	65
S07	Garcia	2019	62.9	16.8	48	58.1	15.9	47
S08	Lee	2019	75.6	12.2	103	70.8	12.5	101
S09	Martin	2020	71.1	14	77	67.5	13.6	75
S10	Taylor	2021	79.5	10.8	132	74.9	11.2	128

For each study extract mean, SD and n for each group (t=treatment, c=control)

1. Import the data binary outcome example

Basic clean layout

Study_ID	author	year	group1_event	group1_no_event	group1_n	group0_event	group0_no_event	group0_n
1	Smith	1992	28	176	204	51	151	202
2	Jones	1962	70	215	285	38	109	147
3	Chen	1963	37	119	156	40	79	119
4	Brown	1981	2	86	88	3	27	30
5	Patel	1969	0	30	30	3	30	33
6	Wilson	1988	61	218	279	82	194	276
7	Garcia	1970	41	165	206	55	151	206
8	Lee	1965	20	103	123	24	105	129
9	Martin	1989	111	907	1018	113	902	1015
10	Taylor	1968	81	346	427	27	116	143

For each study extract counts of ‘yes’, counts of ‘no’ and total n for each group. Optionally, you can leave out the ‘no_event’ columns as this can be calculated from the other columns.

1. Import the data layout example – Sleep studies

StudyID	Author	Year	Country	Mean Age	Female Pct	RiskOfBias	Outcome	TimePoint	N_Treat	Mean_Treat	SD_Treat	N_Control	Mean_Control	SD_Control
S001	Smith	2021	Australia	58.3	62	Low	Sleep Efficiency (%)	3 Months	45	82.4	8.3	44	77.1	9.1
S001	Smith	2021	Australia	58.3	62	Low	Wake After Sleep Onset (min)	3 Months	45	42.1	18.5	44	55.3	20.4
S002	Garcia	2022	Spain	55.7	51	Moderate	Sleep Efficiency (%)	6 Months	38	79.8	10.2	41	73.5	11.5
S003	Chen	2020	China	49.8	47	Low	Sleep Efficiency (%)	3 Months	52	84.1	7.8	50	78.4	8.7
S003	Chen	2020	China	49.8	47	Low	Insomnia Severity Index	3 Months	52	8.7	4.1	50	12.5	4.8
S004	Patel	2023	United Kingdom	61.2	58	High	Sleep Efficiency (%)	12 Months	61	80.3	11	63	76.8	10.5
S005	Wilson	2024	Canada	57.9	60	Low	Sleep Efficiency (%)	6 Months	75	85	8.9	73	79.2	9.4

Real world layout

Different measured outcomes in a single study – Sleep efficiency and WASO. Possible separate meta-analyses.

Information for possible sub-group analyses or meta-regression

Different follow up durations

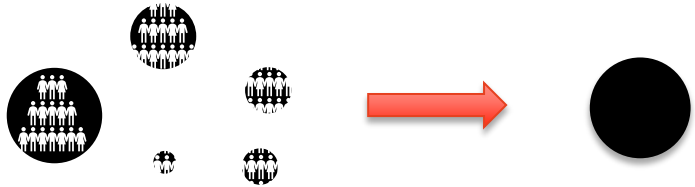
Possibly many other columns for: SE's, CI's, p-values, GRADE assessment, comments, etc.

2. Calculate Effect Size

What is an effect size?

An effect size is a measure of some difference or association of interest, e.g. mean difference between groups, odds ratio, correlation coefficient

- In primary research studies estimate population effect sizes using individual study samples
- In meta-analysis our goal is to combine these individual effect sizes across study samples to estimate an **overall effect** (sometimes called the pooled estimate, summary effect, true effect), hence 'an analysis of analyses'/meta-analysis



Individual study effects

Overall effect

2. Calculate Effect Size

Types - Difference in means

This is common when the explanatory variable is categorical (groups) and the response variable is numeric.

Example:

The study question is a comparison of the effectiveness of *low fat diets* vs *low carbohydrate diets* for *weight loss*

Explanatory variable is diet type – categorical (low fat or low carbohydrate). Outcome variable is weight loss – numeric (kg).

The effect size is the difference in mean weight loss between the two groups.

$$MD_{between} = \bar{x}_{LF} - \bar{x}_{LC}$$

2. Calculate Effect Size

Types – Proportions

These are typically used where you have groups with a binary outcome.

Example: The study question is a comparison of: survival rates in males and females at risk of myocardial infarctions (MI)

Explanatory variable is binary, two groups: male and female
Response variable is binary, survival: alive or dead
p_{female}= proportion of females died from MI
p_{male}= proportion of males died from MI

Risk difference:

$$p_{female} - pmale$$

We can express this as a risk ratio (RR)

$$RR = \frac{p_{female}}{p_{male}}$$

2. Calculate Effect Size Types – Odds Ratio

The same outcome can also be expressed as an Odds Ratio (OR)

	Death (event)	Survival (no event)	Proportion (Risk)	Odds
Female	a	b	$p_{female}=a/(a+b)$	a/b
Male	c	d	$p_{male}=c/(c+d)$	c/d

$$OR = \frac{a/b}{c/d} = \frac{ad}{bc}$$

When the risk of the event (eg death) is low, then the OR will be similar in value to the RR

Analysis of an OR effect size is often preferred to RR because of superior statistical properties and/or sample selection (in case control studies the risk cannot be estimated because the sample includes cases from a general population)

Computations are performed on the natural log of the RR or OR

2. Calculate Effect Size Odds Ratio - combining



Suppose we want to combine Study A and B

Study	OR
A	2.0
B	4.0
Average(A:B)	

What is the average odds ratio of A and B?

2. Calculate Effect Size Odds Ratio - combining



Suppose we want to combine Study A and B

Study	OR	ln(OR)
A	2.0	0.693
B	4.0	1.386
Average(A:B)		

What is the average odds ratio of A and B?

2. Calculate Effect Size Odds Ratio - combining



Suppose we want to combine Study A and B

Study	OR	ln(OR)
A	2.0 →	0.693
B	4.0 →	1.386
Average(A:B)	2.83 ←	1.040

To get the average odds ratio, you have to go via the log odds ratio

Whenever your effect size is a *ratio* you will need to combine them on the log scale.
What are some examples?

2. Calculate Effect Size

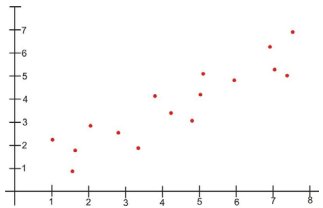
Types - Correlation

This is common when both variables are numeric.

Example:

Blood lead levels in children and IQ scores.

Both variables are numeric (IQ score and plasma lead concentration). We use the correlation coefficient.



$$r_{xy} = \frac{\sigma_{xy}^2}{\sigma_x \sigma_y}$$

2. Calculate Effect Size

Types - Correlation

Like with Odds Ratios, combining correlation coefficients needs to be done using the right scale. In this case we use the Fisher's Z transformation

$$z = \frac{1}{2} ln\left(\frac{1+r}{1-r}\right) \text{ and back transform } \quad r = \frac{exp(2z)-1}{exp(2z)+1}$$

Study	(Pearson's) r	(Fisher's) z
A	0.20 →	0.2027
B	0.40 →	0.4236
Average (A:B)	0.3033 ←	0.3132

2. Calculate Effect Size

Combining Effect Sizes - considerations

How do we get our overall effect size from our individual study effect sizes?

We need to consider a few issues:

1. Standardisation
2. Weighting
3. Different types of effect sizes

2. Calculate Effect Size

Standardisation

It may or may not be necessary to use standardised effect sizes.

Example 1: Selected studies examining effects of a supplement on fasting glucose levels may always measure the plasma glucose concentration.

Combine without standardisation

Example 2: Selected studies might examine ratings of anxiety among carers of people living with dementia vs matched control individuals. Some studies used the Generalised Anxiety Disorder Questionnaire (GAD-7), while other studies used the Hamilton Anxiety Rating Scale (HAM-A).

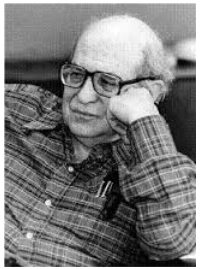
Standardise before combining

Standardised effect sizes are a way to transform effect sizes into a form where they can be compared and summarised.

2. Calculate Effect Size

Standardisation – difference in means

Many standardised effect sizes were defined by Jacob Cohen (1923-98).
For example, Cohen's *d*:



$$d = \frac{\overline{x_1} - \overline{x_2}}{s}$$

Where s is the pooled within-group standard deviation

Cohen's d is analogous to the number of standard deviation's difference or the z-score difference

Cochrane reviews refer to the "Standardised Mean Difference" (SMD) and use a variation of d, called Hedges' (adjusted) *g*.

$$g = \left(1 - \frac{3}{4df - 1}\right) d \qquad df = n_1 + n_2 - 2$$

2. Calculate Effect Size

Standardised effect sizes

Tip from the consulting room:

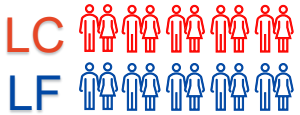
- The question of whether to standardise comes up frequently in consulting.
- It may be that almost all the studies examined used the same scale, but a couple of studies used a different scale. Should you standardise?
- The downside is that standardised measurements are on a 'unitless' scale, and so the interpretation of your overall effect may be less clear
- The upside is that more studies can be included, whatever the scale they measured on
- We can't 'compare apples with oranges', but a unitless scale allows us to do just that. The interpretation is no longer on a domain-specific scale

2. Calculate Effect Size Weighting

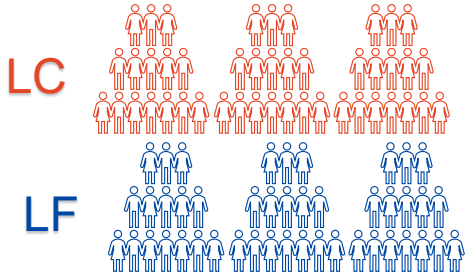
Example:

The study question examines weight loss in a low carbohydrate diet (LC) vs a low fat (LF) diet.

Study 1 The difference in weight loss was 9.0 kg. The number of participants was 10 in each dietary group.



Study 2 The difference in weight loss was 7.0 kg. The number of participants was 50 in each dietary group.

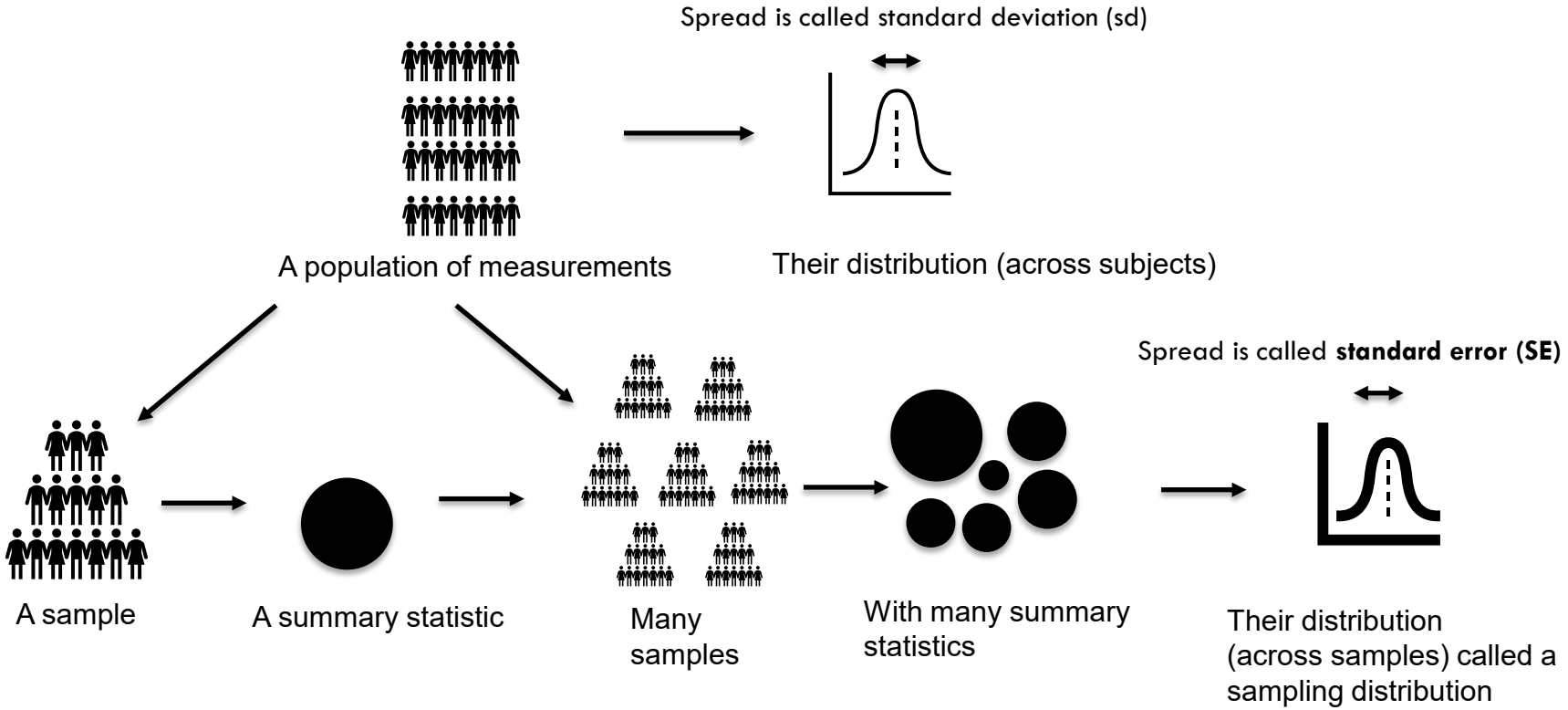


Should each study contribute equally to the calculation of the overall effect size? Is the overall effect size an 8.0 kg weight loss?

2. Calculate Effect Size Weighting

- We need to consider the precision of the estimates for each study
- Sample size is a key component of study precision
- Studies that are more precise should have more weighting in the overall estimate
- Information about study precision is found in the Standard Error

2. Calculate Effect Size What is a standard error?



2. Calculate Effect Size What is a standard error?

It is a measure of the precision of an estimate for a parameter

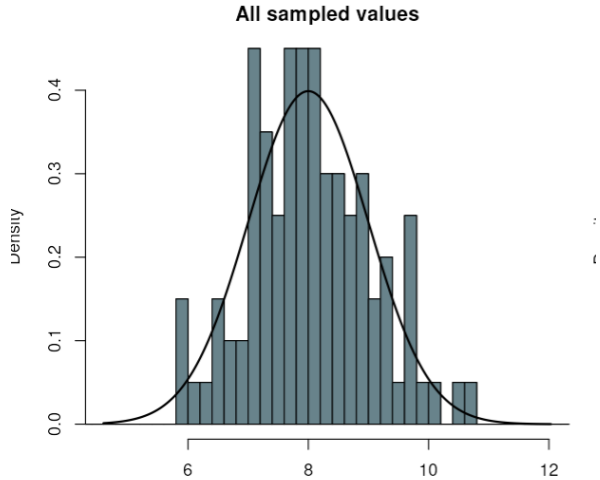
Most commonly we think of the standard error of the mean (SEM)

Simulation: A sample of n=100 drawn from a normally distributed population with:

Population true mean $\mu = 8$
Population true SD $\sigma = 1$

Sample: n = 100
Sample Mean $\bar{X}$=8.04
Sample SD s = 1.038

Conduct your own simulations here:
https://shiny.rit.albany.edu/stat/sampdist/

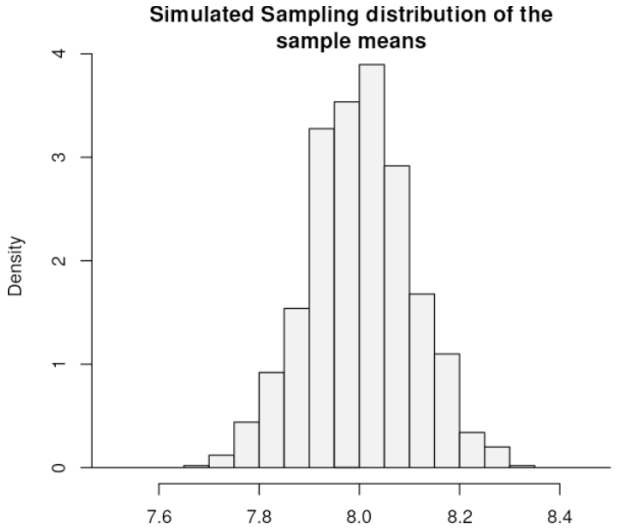


2. Calculate Effect Size What is a standard error?

Standard Error of the Mean (SEM) is the standard deviation of the sample means:

$$SEM = \frac{s}{\sqrt{n}}$$

For the example: $SEM = \frac{1.038}{\sqrt{100}} = 0.104$



Sample Mean $\bar{X}$=8.111 estimates the true mean **μ = 8.000** with a standard error of 0.104

The standard error tells us about the precision of the estimate

2. Calculate Effect Size What is a standard error?

$$SEM = \frac{s}{\sqrt{n}}$$

Increasing the sample size reduces the standard error of the mean (because the denominator, $\sqrt{n}$, is larger).

Increasing the sample size will also reduce the standard error of the effect size (mean difference, OR, or any other)

2. Calculate Effect Size

Standard error for difference in means effect size

$$Difference\ in\ means = \bar{x}_1 - \bar{x}_2$$

$$pooled\ SD, \qquad s = \sqrt{\frac{[(n_1 - 1)s_1^2 + (n_2 - 1)s_2^2]}{(n_1 + n_2 - 2)}}$$

$$Standard\ Error\ for\ Effect\ Size = s\sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$$

2. Calculate Effect Size

Example of a different effect size – log Odds Ratio

	Outcome 1	Outcome 2	Odds
Exposure 1	a	b	a/b
Exposure 2	c	d	c/d

$$ES_{LOR} = ln\left(\frac{ad}{bc}\right)$$

$$SE_{LOR} = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$$

Weighting factor for Log OR

$$w_{LOR} = \frac{1}{SE^2} = \frac{abcd}{ab(c+d) + cd(a+b)}$$

2. Calculate Effect Size

Standard error for difference in means effect size

We want to weight the studies with a smaller standard error more relative to studies with a larger standard error…

…so we use the **inverse variance weight** or weighting factor (w) which is inverse to the effect size variance (i.e. the square of the standard error)

$$w = \frac{1}{SE^2}$$

2. Calculate Effect Size

Using weighting factors to combine effect sizes

$$\overline{ES} = \frac{\sum(w_i ES_i)}{\sum w_i}$$

The weighted mean effect size can then be calculated by summing the individual weighted effect sizes and dividing by the sum of the weighting factors.

This formula can be compared to the simple (unweighted) average where each of the n studies gets an equal weighting (of 1)

$$\overline{ES} = \frac{\sum((1) ES_i)}{n}$$

2. Calculate Effect Size

Using weighting factors to combine effects sizes

LF vs LC diets for weight loss

Study 1: (small) n=10

$ES_1 = \bar{x}_{LC} - \bar{x}_{LF} = 9.0kg$, **SD=2.9, therefore** $\text{SE} = \frac{2.9}{\sqrt{10}} = 0.917$

and $w_1 = \frac{1}{SE^2} = \frac{1}{0.917^2} = 1.189$

Study 2: (large) n=50

$ES_2 = \bar{x}_{LC} - \bar{x}_{LF} = 7.0kg$, **SD=2.9, therefore** $\text{SE} = \frac{2.9}{\sqrt{50}} = 0.410$

and $w_2 = \frac{1}{SE^2} = \frac{1}{0.410^2} = 5.945$

$$\overline{ES} = \frac{(w_1.ES_1)+(w_2.ES_2)}{(w_1+w_2)} = \frac{(1.189x9)+(5.945x7)}{(1.189+5.945)}$$

Overall effect size $\overline{ES} = 7.3\ kg$

2. Calculate Effect Size

Studies reporting different types of effect sizes

Research question

Is lead exposure, as measured by plasma lead concentrations, associated with the IQ of children?

1. Study type A

The lead was measured in the plasma of children and their IQ was tested.

Two continuous variables (plasma concentration and IQ)

Effect size – *correlation*

2. Study type B

The lead concentration in the plasma of children was used to classify the children into two groups – lead exposed and unexposed – and the IQ of the children was tested.

One categorical (explanatory) variable (lead exposure) One continuous (outcome) variable (IQ)

Effect size – *difference in means*

2. Calculate Effect Size

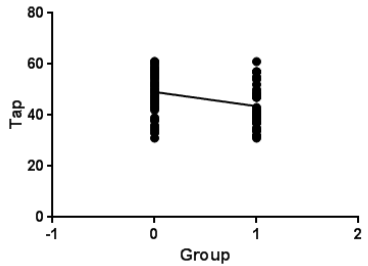
Studies reporting different types of effect sizes

Choices

1. Do analysis on different types of effect sizes separately
2. Use methods to estimate one type of effect size from another

For example:

The Point-Biserial Correlation is a special case of the Pearson's Correlation Coefficient. It is used when one variable is continuous and the other variable is categorical (binomial). For the categorical outcome, one exposure or outcome is assigned 0 and the alternative outcome or exposure is assigned 1.



Example
Group 0 not exposed
Group 1 Lead exposed
Y= IQ score

ES or r = -0.325

2. Calculate Effect Size

Studies reporting different types of effect sizes

2. Use methods to estimate one type of effect size from another

Tip from the consulting room

- These methods are an approximation and introduce more complexity and uncertainty in determining effect sizes
- For example, a Point-Biserial Correlation is often an underestimate of a correlation coefficient using two continuous variables
- There are many other potential conversions, such as RR to OR, or even hazard ratio (HR) to OR
- As in the above example there are formulae to convert a continuous effect size into a categorical effect size (e.g. SMD into OR)
- Note: Studies typically that use different measures may differ in other substantive ways. This needs to be considered. Just because we *can* convert from one effect size to another, it doesn't mean we *should*. How does it change the interpretation of our overall estimate?

2. Calculate Effect Size

Extracting the effect size from other information

In a perfect world…

Standardised effect size for difference in means between two groups, its SE and the weighting factor would be calculated from these values.

Group	n	Mean	SD
A	34	42.4	6.7
B	28	34.6	2.8

However, it is possible to estimate the standardised effect size from a t statistic or a p-value for a known hypothesis test. Eg.

$$Cohen's\ d = t_{(n_A+n_B-2)}\sqrt{\frac{1}{n_A}+\frac{1}{n_B}}$$

Occasionally, results get reported in insufficient detail for effect size calculation/estimation (e.g. "$p < 0.05$")

2. Calculate Effect Size Extracting Effect Sizes

Another situation when effect sizes can be difficult to determine is from a multivariable analysis (e.g. multiple regression)

The regression model might contain the explanatory variable of interest, however, its relationship with the response variable is adjusted by the presence of other explanatory variables in the model.

It is difficult to extract an effect size when only partial regression weights are presented without any kind of univariate analysis.

2. Calculate Effect Size

Precision of the overall effect

2. Calculating a confidence interval for the overall effect size.

The 95% Confidence Interval for a mean effect is calculated so that 95% of the time* the interval contains the population effect size.

It is calculated from the standard error of the overall effect size.

$$SE_{\overline{ES}} = \sqrt{\frac{1}{\sum w_i}}$$

The SE is multiplied by the critical z value representing the desired confidence level (z=1.96 for 95%).

$$95\%\ CI\ for\ \overline{ES} = \overline{ES} \pm 1.96 * SE_{\overline{ES}}$$

If the 95% CI does not contain 0 then there is a statistically-significant effect at $\alpha = 0.05$.

Some meta-analyses report this as a Z-test with a p-value

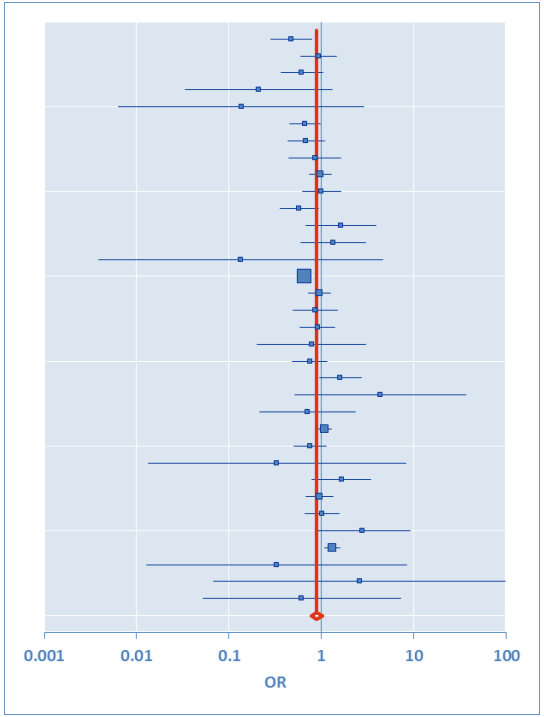
* If you repeated the meta-analysis 100 times (and had different primary studies for each – *unlikely in reality*) – *on average 95 times the CI would contain the true population effect size*

3. Meta-Analysis summary

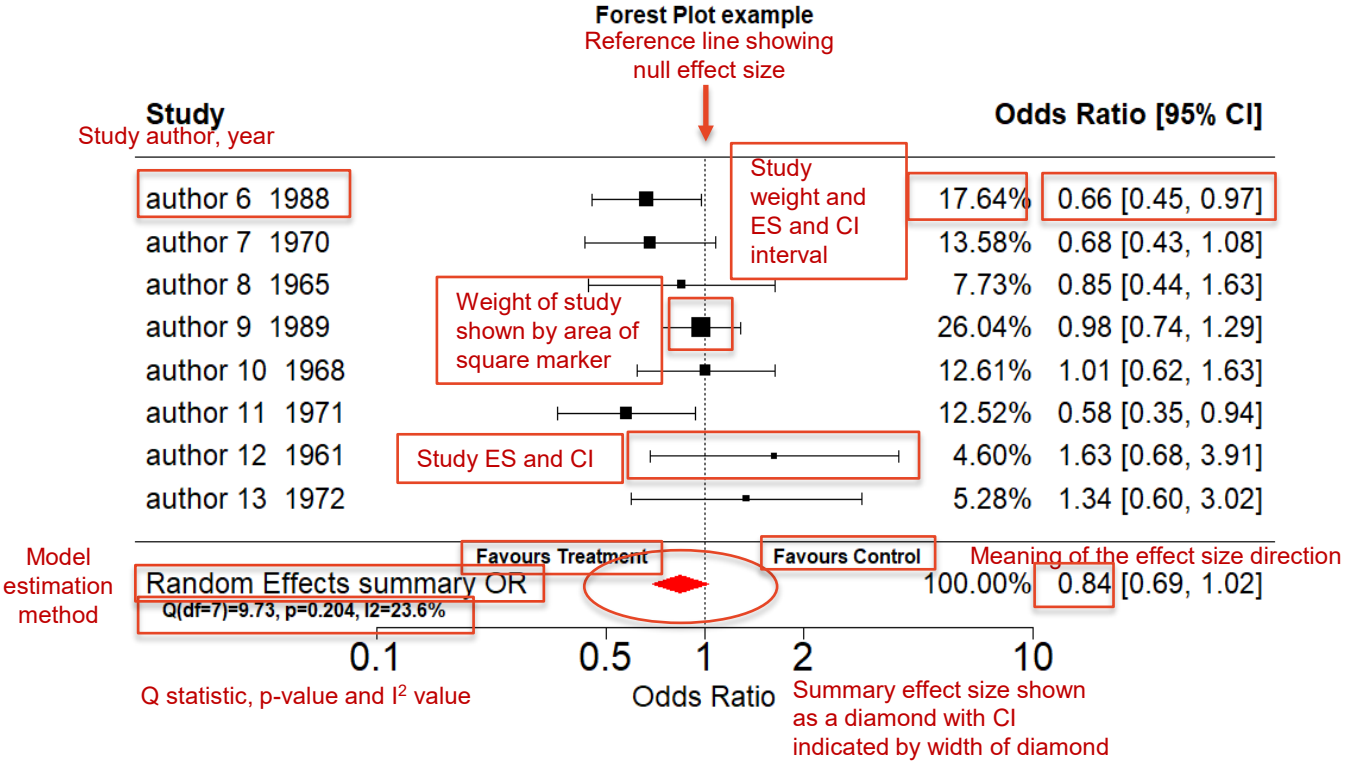
The meta-analysis summary combines all the information we have put together on the study effect sizes, the summary effect size, their associated uncertainties, and information about their spread (or heterogeneity)

The Forest plot is a common tool for displaying this information.

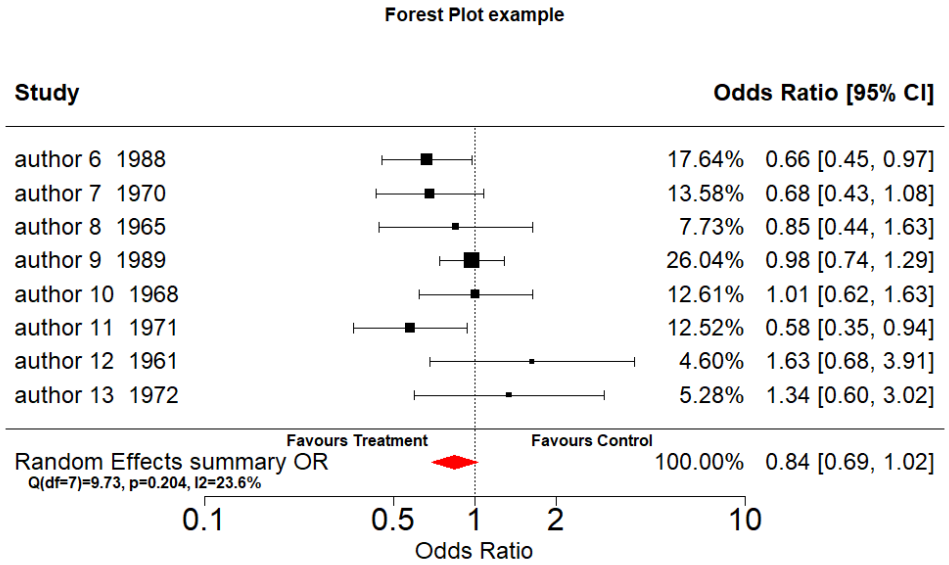
The name refers to the “forest” of lines produced.



3. Meta-Analysis summary Forest Plot



4. Explore Heterogeneity



Do these individual study effect sizes estimate the same underlying true effect size?

4. Explore Heterogeneity Fixed-Effect Models

This model assumes there is one underlying population effect size. The variation in individual effect sizes is due to random sampling.

For example, the population effect of a low fat diet (compared to LC diet) is a weight loss of 8 kg.

Due to random sampling error, the individual studies show an effect size ranging from 6 to 10 kg.

The true effect size is 8 kg. If we had infinitely large sample sizes for each study, then we would have ES=8.0 every time, and the standard errors would be zero.

Assumption of homogeneity

4. Explore Heterogeneity

Assumption of Homogeneity – Q statistic

The homogeneity test is based on the (Cochran's) Q statistic

$$Q = \sum_{i=1}^{k} w_i (ES_i - \overline{ES})^2$$

The Q statistic has a chi-square distribution with *k-1* degrees of freedom where *k* is the number of effect sizes (studies).

If the observed Q statistic is over the critical value (producing a p value less than α) then the null hypothesis (homogeneity of effect sizes) is rejected.

4. Explore Heterogeneity

Quantifying heterogeneity with the I^2 statistic

Effect sizes are always going to be heterogeneous. Why not quantify the inconsistency rather than test with some arbitrary cut-off?

A common approach is to apportion the amount of variation due to heterogeneity in study effect sizes and the amount of variation due to sampling error.

$$I^2 = 100\% \times \left(\frac{Q - df}{Q} \right)$$

I^2 conveys the amount of variation in the effects sizes that would remain if we could remove sampling error.

4. Explore Heterogeneity

Quantifying heterogeneity with the I^2 statistic

What is a large I^2 value?

Rules of thumb:

from Borenstein:

- 25% is low
- 50% is moderate
- 75% is high

From Cochrane Handbook:

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

4. Explore Heterogeneity Random Effects models

This model assumes that there are differences in the underlying effect sizes whose sources cannot be identified.

Therefore the variation in effects sizes is due to sampling error (as with fixed effect models) but with an additional component that estimates other sources of variability.

$$v_{RE} = v_\theta + v_i$$

Where

v_i is the estimate of the variance associated with sampling error.

v_θ is the estimate of the between-studies variance, also known as tau-squared (τ^2).

4. Explore Heterogeneity Random Effects models



v_θ is the estimate of the between-studies variance, also known as tau-squared (τ^2).

The calculation of τ^2 can get technical. The simplest model for tau-squared is the "DerSimonian and Laird" method.

Other options for τ^2

- REML is the default option in the metafor package
- The Knapp-Hartung adjustment to the summary effect confidence interval is commonly used with random effects models as well.
- For dichotomous data (like Odds Ratio) the Mantel-Haenszel method is an alternative estimation method.
- For a general discussion of the methods refer to the Cochrane Handbook section 10.10.4.4

4. Explore Heterogeneity

The consequences of using a Random Effects Model

The inverse variance weights calculated previously (and thus the mean effect sizes) assumed the fixed effect model.

$$inverse\ variance\ weight = \frac{1}{SE^2}$$

However, with the random effects model that becomes

$$inverse\ variance\ weight = \frac{1}{v_{RE}}$$

Therefore, when switching to a random effects model, all mean effect sizes and confidence intervals are recalculated.

4. Explore Heterogeneity

A commonly used approach for model selection

Approach the analysis using the fixed effect model as the default model and explore the heterogeneity of the effects sizes using a statistical test (Q statistic).

1. The test for heterogeneity is not significant therefore a fixed effect model is consistent with the data and this model is used; OR

2. The test for heterogeneity is significant so the analysis is repeated with the random effects model.

The problem with this approach…

The non-significant p value does not prove the null hypothesis (that there is one true effect size).

It is recommended that the decision is based on rigorous assumptions regarding the sample of studies.

4. Explore Heterogeneity Prospective Meta-analysis

Cochrane Methods



"A prospective meta-analysis (PMA) is a meta-analysis in which studies (usually randomised controlled trials) are identified, evaluated and determined to be eligible before the results of any of the studies become known. PMA can help to overcome some of the recognised problems of retrospective meta-analyses."

- This approach may lead to low heterogeneity and a justifiable assumption of a Fixed Effect model

4. Explore Heterogeneity

Fixed-Effect and Random-Effects summary



- A fixed-effect meta-analysis estimates a single effect that is assumed to be common to every study, while a random-effects meta-analysis estimates the mean of a distribution of effects.
- Study weights are more balanced under the random-effects model than under the fixed-effect model. Large studies are assigned less relative weight and small studies are assigned more relative weight as compared with the fixed-effect model.
- The standard error of the summary effect and (it follows) the confidence intervals for the summary effect are wider under the random-effects model than under the fixed-effect model.
- The selection of a model must be based solely on the question of which model fits the distribution of effect sizes, and takes account of the relevant source(s) of error. When studies are gathered from the published literature, the random effects model is generally a more plausible match.
- The strategy of starting with a fixed-effect model and then moving to a random-effects model if the test for heterogeneity is significant is a mistake, and should be strongly discouraged.

Borenstein et. al., 2009

How should we select a statistical model?

The choice of a statistical model should depend on the sampling frame that was used to select studies for the analysis. If we are working with one population, then we should use the fixed-effect model. If we are working with a universe of populations, we should use the random-effects model. Consider the following two cases.

Case 1. A pharmaceutical company plans to enroll 1,000 patients. Because the staff can only work with 100 patients at time, it randomly divides the patients into 10 groups of 100 patients, and runs the identical study with each. We know all studies are based on the same population, since that's how we selected them. The fixed-effect model matches the way the studies were sampled.

Case 2. We locate a series of published studies that were performed by different people in different locations at different times. While the studies all looked at similar interventions, it stands to reason that the true impact of this intervention will differ from study to study. If the studies were conducted in different hospitals it's likely that the patient population (age, co-morbid diseases) varied from one hospital to the next, and that the intervention was therefore more effective in some hospitals than in others. It's also possible that the intervention itself (the precise dosage, length of follow-u
from one hospital to the next and that this could have an impact on the effect size. While the difference

Reference: metaanalysis.com

4. Explore Heterogeneity Selecting a model

A random effects model would fit most types of meta-analyses, based on the sources of studies.

At first glance, the random effects model would appear to be the more conservative approach.

However…

Random effects incorporate the between study variance into the denominator of each weight. This has the effect of weighting the studies more evenly and can lead to the effect size being shifted towards the effect size of smaller studies.

Perhaps not a problem unless there is a different effect size observed among the smaller studies compared to the larger studies.

We address this issue in the next step of the workflow.

5. Publication Bias and other sources of bias

There are many forms of bias, but publication bias is of particular relevance to meta-analyses

Selection bias

Only choose studies which they are familiar with or support their view-point

Occurs when the two groups being compared differ systematically, eg. differences in the characteristics between those who are selected for a study.

Performance bias

differences between groups in the care that is provided, or in exposure to factors other than the interventions of interest.

Detection bias

differences between groups in how outcomes are determined.

Attrition bias

differences between groups in withdrawals from a study.

Reporting bias

differences between reported and unreported findings.

→ **Publication bias**

Only select studies which have been published. In general, studies with statistically significant or positive results are more likely to be published than those with non-significant or negative results.

Language bias

Only select studies written in English

Indexing bias

Only search a limited number of databases or use a limited choice of search terms.

5. Publication Bias

"The small proportion of results chosen for publication are unrepresentative of scientists' repeated samplings of the real world."

Young, Ioannidis & Al-Ubaydli, PL0S Medicine, doi:10.1371

"The winner's curse refers to the phenomenon that studies that find evidence of an effect often provide inflated estimates of the size of that effect. Such inflation is expected when an effect has to pass a certain threshold — such as reaching statistical significance — in order for it to have been 'discovered'. Effect inflation is worst for small, low-powered studies, which can only detect effects that happen to be large."

Button et al, Nature Reviews Neuroscience, 2013,14:365

5. Publication Bias



A review by Easterbrook et al quantified the extent of the problem in clinical research

Easterbrook, P.J et al. "Publication Bias in Clinical Research." The Lancet (British edition) 337.8746 (1991): 867–872. Web.

https://sydney.primo.exlibrisgroup.com/permalink/61USYD_INST/2rsddf/cdi_scopus_primary_21140048

5. Publication Bias what can you do?

- As individuals, it's hard to change the forces that cause publication bias.
- Look at studies that are available from other sources and may be more representative.
- Research Grey Literature sources (including pre-prints)
- Avoid indexing bias! (a more thorough literature search will generate a more valid meta-analysis)

5. Publication Bias Funnel Plot

A funnel plot is a scatter plot of each study's Effect Size vs a measure of the study's size or precision e.g. SE of the effect size.

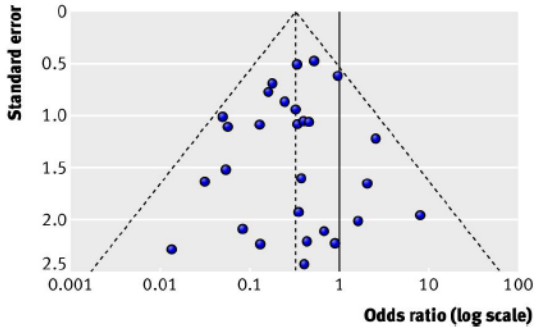


Fig 1 Example of symmetrical funnel plot. The outer dashed lines indicate the triangular region within which 95% of studies are expected to lie in the absence of both biases and heterogeneity (fixed effect summary log odds ratio±1.96×standard error of summary log odds ratio). The solid vertical line corresponds to no intervention effect

Sterne, Jonathan A C et al. "Recommendations for Examining and Interpreting Funnel Plot Asymmetry in Meta-Analyses of Randomised Controlled Trials." BMJ 343.7818 (2011): c4737–307. Web.

5. Publication Bias Funnel Plot Asymmetry

It has been observed that small studies report larger effect sizes compared with large studies. This may be due to publication bias but could also be due to other factors e.g. different subgroups in the smaller studies.

A different effect size in the small studies can be observed as asymmetry in the funnel plot.

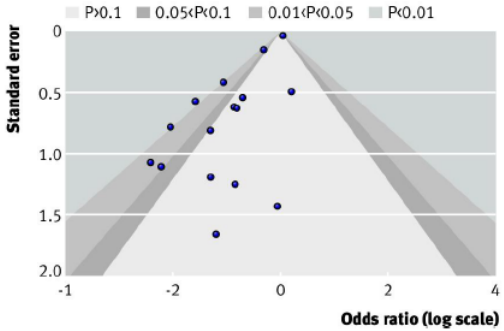


Fig 4 Contour enhanced funnel plot for trials of the effect of intravenous magnesium on mortality after myocardial infarction

5. Publication Bias Test for funnel plot asymmetry

It is possible to test for asymmetry but check the recommendations as it may not be advisable.

For example,

- The minimum number of studies should be substantially greater than 10.
- The asymmetry test should not be used if the studies are of similar size/precision.
- The plots need to be considered in the context of the other characteristics of the studies.

If there is significant asymmetry, the effect estimate should be compared under the fixed and random-effects model as the random effects model might be skewing the mean effect size towards the smaller studies.

Refer to the Cochrane Handbook section 13.3.5.2 for further advice.

5. Publication Bias Funnel Plot Asymmetry

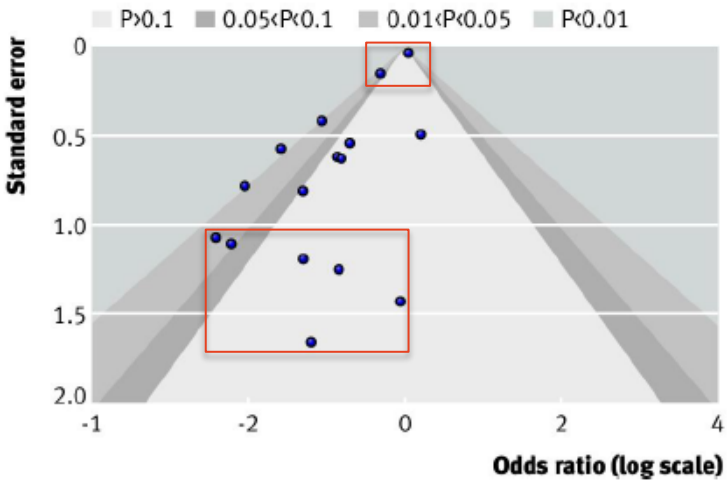


Fig 4 Contour enhanced funnel plot for trials of the effect of intravenous magnesium on mortality after myocardial infarction

If we have large studies showing no beneficial effect of intervention and other small studies showing mostly beneficial effect.

Fixed Effect model – No net effect

Random Effects model – An overall beneficial effect

This is because the missing study data (RHS of plot) results in a smaller between study variance than should be the case.

6. Sub-group analysis moderating factor

1. There is one underlying population effect size. The variation in individual effect sizes is due to random sampling.

For example, the population effect of a low fat diet (compared to LC diet) is a weight loss of 8 kg.

Due to random sampling error, the individual studies show an effect size ranging from 7 to 9 kg.

OR

2. There is variation in the population effect sizes but this is systematic and due to a moderating factor.

For example, the population effect of the LF diet on weight loss is 7.5 kg in older adults whilst the effect is 8.5 kg in younger adults.

6. Sub-group analysis moderating factor

If we suspect a moderating factor is present (and we have the data for it)…

…then the homogeneity analysis can be partitioned according to the grouping factor.

For example,

The categorical or grouping variable is Age Group (older adults or younger adults).

The Q statistic is partitioned into the portion that is explained by Age Group (Q_B) and the residual portion that explains the within group variation (Q_W).

$$Q = Q_B + Q_W$$

6. Sub-group analysis Meta-regression

Meta-regression is a more flexible approach to understanding the factors that might contribute to an effect size because:

- The moderator can be a numeric variable instead of being restricted to a categorical variable.
- Multiple variables (including categorical variables when coded appropriately) can be considered in the same analysis.

Example: Weight loss for LF diet (vs LC diet)

Rather than compare sub-groups for younger vs older adults, if we had information on subject age on a continuous scale then we could incorporate this covariate in a meta-regression model. [However, take care to consider issues such as aggregation/ecological bias! - see Cochrane 10.11.5.5]

Like all multiple regression models, a large ratio of subjects (i.e. studies) to covariates is required (suggestion of 10:1).

The regression model can be formulated using the assumptions of the fixed or random effects model.

Meta Analysis software

Software	Origin/Developer	Interface
SPSS	IBM	Limited built-in meta-analysis; often requires macros.
Stata	StataCorp	Strong for advanced models, meta-regression, and graphics.
RevMan	Cochrane Collaboration	Excellent for Cochrane workflows but more restrictive for non-Cochrane reviews.
Comprehensive Meta-Analysis (CMA)	Biostat Inc.	Highly flexible data entry (100+ formats) and customizable forest plots; supports automated reports.
SAS	SAS Institute	Common in epidemiology and regulatory work.
Meta-Analyst	Brown University	Free, Windows-based, supporting standard and diagnostic meta-analysis.
Meta-DiSc	Clinical Biostatistics Unit, Ramón y Cajal Hospital	Popular for diagnostic test accuracy meta-analysis

Meta Analysis in R

Software or package	Origin	Comments
meta	Schwarzer, 2007	General package, easy to use
metafor	Viechtbauer, 2010	General package with extensive functionality
netmeta	Schwarzer & Rücker, 2015	Add-on package for meta to allow network meta-analysis
metap	Dewey, 2020	Enables meta-analysis using significance values
mada	Doebler, 2020	Meta-Analysis of Diagnostic Accuracy (for summary ROC)
jamovi https://www.jamovi.org/	uses metafor R package	User friendly interface, can save R script

Meta Analysis in R – some more packages

Software or package	Origin / Source	Comments
gemtc	van Valkenhoef et al.	Bayesian Network Meta-Analysis using MCMC (via JAGS).
robumeta	Hedges, Tipton & Johnson	Implements Robust Variance Estimation (RVE) for dependent effect sizes.
compute.es	Del Re	Convenience functions to convert diverse statistics to effect sizes (d, g, r, OR, etc.).
MAd	Del Re & Hoyt	Converts raw summary statistics to effect sizes; complementary to compute.es
metasens	Rücker et al.	Provides tools for sensitivity analyses and bias adjustment (e.g., selection models).
metaSEM	Cheung	Conducts meta-analytic structural equation modeling and multilevel meta-analysis.
metaviz	Kossmeier et al.	Tools for modern visualization of meta-analytic data, including interactive graphics.

Data extraction software

Q. Should you use Excel to extract your data?

A. It depends on the scale of the systematic review.

Project Scale	What tool to use	Tool type
A PhD or Masters thesis (single reviewer)	Excel	Spreadsheet
Small academic review team	Qualtrics or Redcap + Excel	Survey Platform
Multi-reviewer or large collaboration	Covidence	Dedicated review management system

Gen AI tools

Can I get AI to do the whole analysis for me?

Answer: No, not yet...

What it can do: You may be able to use it for screening and extraction of studies

Discuss options with library experts

Refer to the general advice in our other workshops

Worked example

Meta-analysis with metafor in R



THE UNIVERSITY OF SYDNEY

Example: Meta analysis with metafor in R

Sutton-Smith Cholesterol lowering intervention on mortality

This data is taken from the book "Methods of Meta-analysis in Medical Research" by A. J. Sutton

(originally extracted from the article: Smith, George Davey, Fujian Song, and Trevor A Sheldon. "Cholesterol Lowering and Mortality: The Importance of Considering Initial Level of Risk." British Medical Journal 306.6889 (1993): 1367–. Print.)

The data comprises 34 studies assessing the effectiveness of cholesterol treatments on mortality in randomised controlled trials.

Example: Meta analysis with metafor in R

Sutton-Smith Cholesterol lowering intervention on mortality

The following files are provided for you to follow this example on your own device:

The data: Meta_Sutton_Smith.csv

The R script: Metafor example script

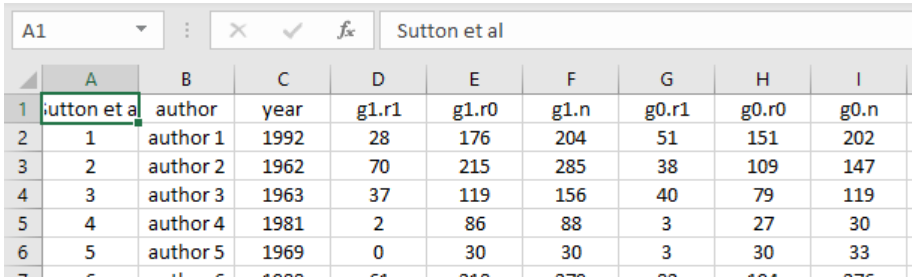
If you are not an R user, just follow the output. A similar workflow can be followed using other software tools.

Example: Sutton-Smith (binary outcome)

Step 1: Import the data

We have the data in a csv file ready to read in using:

```
metadata <- read.csv("Meta_Sutton_Smith.csv", header = T)
```



A1 | Sutton et al

	A	B	C	D	E	F	G	H	I
1	Sutton et a	author	year	g1.r1	g1.r0	g1.n	g0.r1	g0.r0	g0.n
2	1	author 1	1992	28	176	204	51	151	202
3	2	author 2	1962	70	215	285	38	109	147
4	3	author 3	1963	37	119	156	40	79	119
5	4	author 4	1981	2	86	88	3	27	30
6	5	author 5	1969	0	30	30	3	30	33

Example: Sutton-Smith (binary outcome)

Step 1: Import the data

These studies compare the mortality rates for Group 1 (intervention) and Group 0 (control).

The data is presented in counts where r1=event, r0=no event, n=total

				Group 1			Group 0		
	Sutton.et.al	author	year	g1.r1	g1.r0	g1.n	g0.r1	g0.r0	g0.n
1	1	author 1	1992	28	176	204	51	151	202
2	2	author 2	1962	70	215	285	38	109	147
3	3	author 3	1963	37	119	156	40	79	119
4	4	author 4	1981	2	86	88	3	27	30
5	5	author 5	1969	0	30	30	3	30	33
6	6	author 6	1988	61	218	279	82	194	276
7	7	author 7	1970	41	165	206	55	151	206
8	8	author 8	1965	20	103	123	24	105	129
9	9	author 9	1989	111	907	1018	113	902	1015
10	10	author 10	1968	81	346	427	27	116	143

What are the explanatory and response variables? Describe…

Example: Sutton-Smith (binary outcome)

Step 2: Calculate effect size (Odds Ratios)

We use the “escalc” function from metafor to create “yi” which is the log OR effect size and “vi” which is the variance of “yi”.

```
meta.es <- escalc(measure = "OR", g1.r1, g1.r0, g0.r1, g0.r0, data = metadata, slab = paste(author, year, sep = ", "))
```

	Sutton.et.al	author	year	g1.r1	g1.r0	g1.n	g0.r1	g0.r0	g0.n	yi	vi
1	1	author 1	1992	28	176	204	51	151	202	-0.752825281	0.067626464
2	2	author 2	1962	70	215	285	38	109	147	-0.068381064	0.054426978
3	3	author 3	1963	37	119	156	40	79	119	-0.487637182	0.073088616
4	4	author 4	1981	2	86	88	3	27	30	-1.563975538	0.881998277

Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

We use the “rma” function from metafor to create the meta-analysis summary statistics

Random effects is the default

```
meta.re <- rma(yi, vi, data = meta.es)
```

Fixed effect requires an optional argument

```
meta.fe <- rma(yi, vi, data = meta.es, method = "FE")
```

Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

Random-Effects model

```
Random-Effects Model (k = 34; tau^2 estimator: REML)

tau^2 (estimated amount of total heterogeneity): 0.0478 (SE = 0.0269)
tau (square root of estimated tau^2 value):      0.2186
I^2 (total heterogeneity / total variability):   53.87%
H^2 (total variability / sampling variability):  2.17

Test for Heterogeneity:
Q(df = 33) = 89.1065, p-val < .0001

Model Results:

estimate      se     zval    pval    ci.lb   ci.ub
 -0.1178  0.0628  -1.8750  0.0608  -0.2410  0.0053  .

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Note default REML estimation

Information on the summary effect size as log(OR)

Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

Fixed-Effect model

```
Fixed-Effects Model (k = 34)

I^2 (total heterogeneity / total variability):   62.97%
H^2 (total variability / sampling variability):  2.70

Test for Heterogeneity:
Q(df = 33) = 89.1065, p-val < .0001

Model Results:

estimate      se     zval    pval    ci.lb    ci.ub
 -0.1691  0.0324  -5.2258  <.0001  -0.2325  -0.1057  ***

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```



Information on the summary effect size as log(OR)

Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

Model comparison (convert log(OR) to OR first)

```
meta.re.or <- exp(c(meta.re$b, meta.re$ci.lb, meta.re$ci.ub))
meta.fe.or <- exp(c(meta.fe$b, meta.fe$ci.lb, meta.fe$ci.ub))
```

Model	Effect size	lower CI	Upper CI	p value
Random-Effects	0.889	0.786	1.005	0.0608
Fixed-Effect	0.844	0.793	0.900	<.0001

Random-Effects model has

- Reduced OR Effect size from 0.84 to 0.89 (closer to 1)
- Increased width of CI from 0.79~0.90 to 0.79~1.01
- CI for effect size now traverses 1.00 (just)

Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

Forest Plot – R code

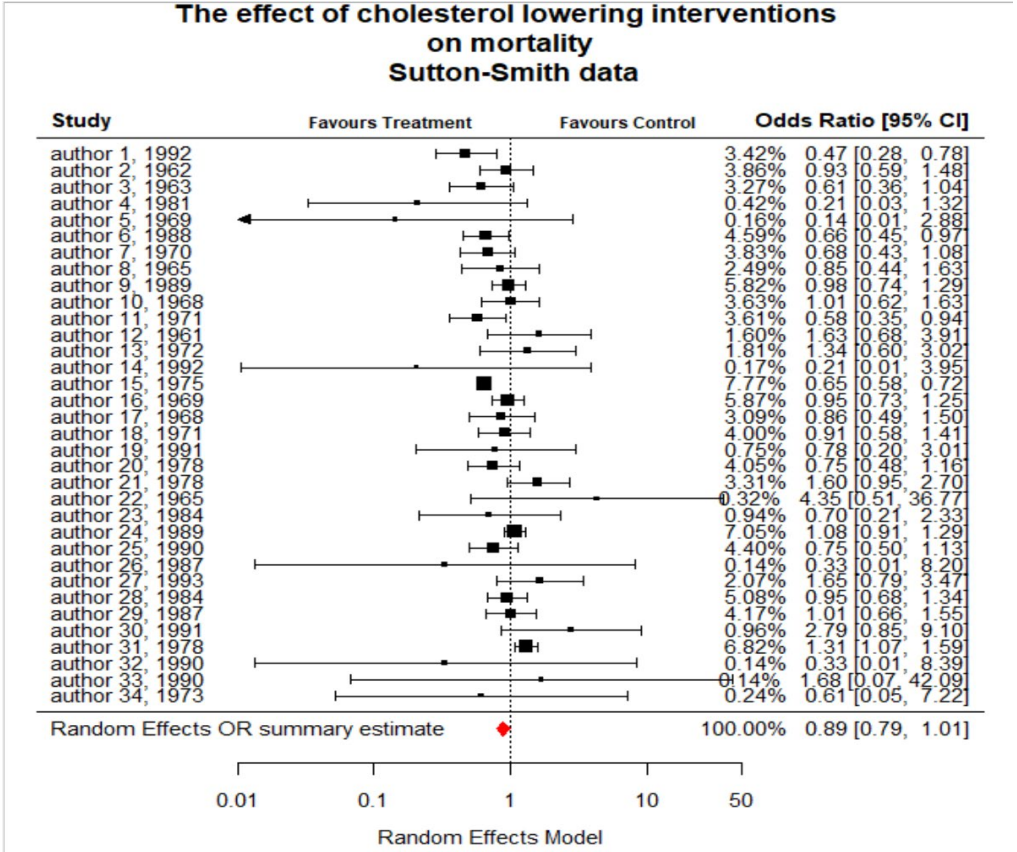
Use the forest() function to produce the plot. You may need to adjust quite a few plotting parameters to get it just the way you want. This is the code I used for the fixed-effect forest plot (code for random not shown).

```
forest(
  meta.fe,
  header = TRUE,
  atransf = exp, #display OR on x-axis log scale
  at = log(c(0.01, 0.1, 1, 10, 50)),
  xlim = c(-8, 8),
  xlab = "Fixed-Effect Model",
  mlab = "Fixed-Effect OR summary estimate",
  showweights = TRUE,
  pch = 15,
  border = "red",  #colour of summary diamond border
  col = "red",     #colour of summary diamond fill
  main = "The effect of cholesterol lowering interventions \n on mortality \n Sutton-Smith data"
)
op <- par(cex = 0.75, font = 2)
text(c(-2, 2), 36, c("Favours Treatment", "Favours Control"))
par(op)
```

Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

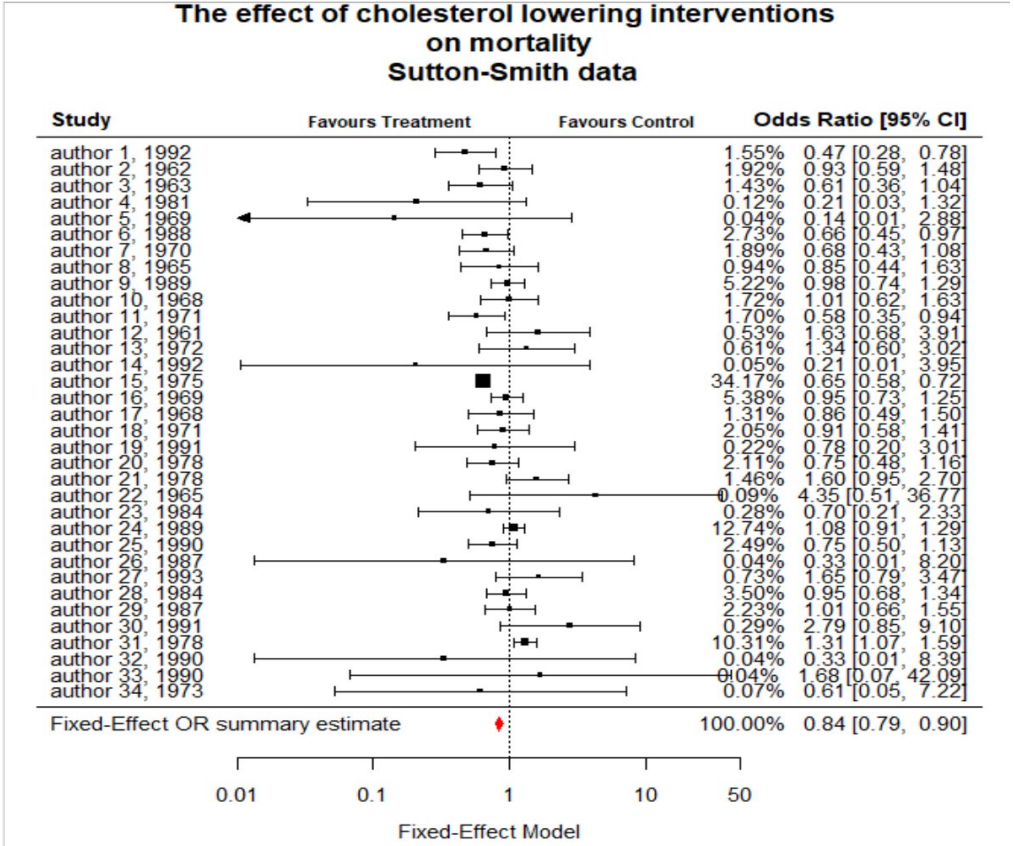
Forest Plot – Random-Effects



Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

Forest Plot – Fixed-Effect



Example: Sutton-Smith (binary outcome)

Step 3: Calculate meta-analysis summary

Forest Plot

Comments

- Note estimates and CI's for each study. Each study's weight designated by size of square.
- Graphical representation of (moderate) heterogeneity.
- Weightings are different between the two models

Example: Sutton-Smith (binary outcome)

Step 4: Explore heterogeneity

- Q statistic is significant $p<0.0001$ (heterogeneous studies)
- I squared (proportion of inconsistency) 54%~63% is moderate
- Tau squared estimate is > zero
- We expect studies to have underlying differences in effect size
- We should use random effects

Example: Sutton-Smith (binary outcome)

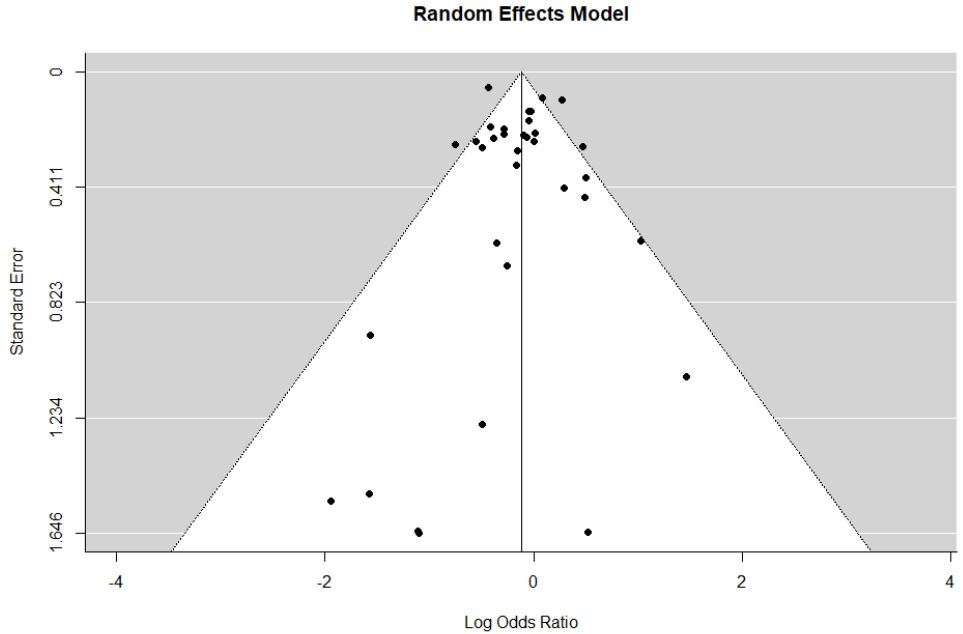
Step 5: Publication Bias -

Funnel Plot

funnel(meta.re, main = "Random Effects Model")

Check for asymmetry

- No of studies > 10
- Studies are of various sizes and precision
- Plot appears to be symmetrical (can use random effects model without problem)
- One more check



Example: Sutton-Smith (binary outcome)

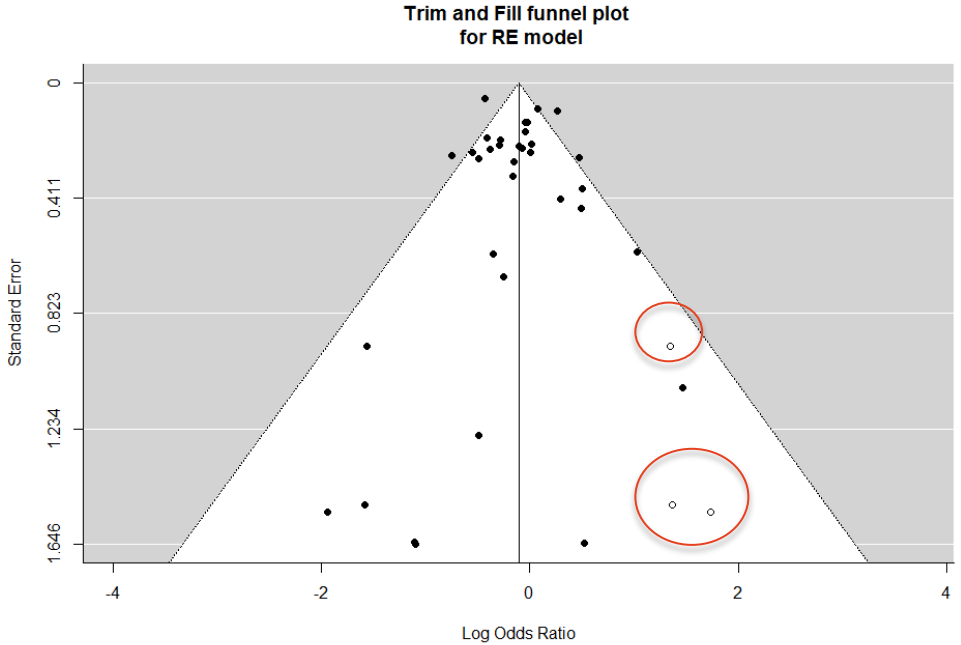
Step 5: Publication Bias

Funnel Plot

Use trimfill() function to add imputed studies to the funnel plot

```
meta.tf <- trimfill(meta.re)
funnel(meta.tf, main = "Trim and Fill funnel plot \n for RE model")
```

Note: 3 imputed studies (open circles)



Example: Sutton-Smith (binary outcome)

Step 6: Sub-group analysis

The original study looked at a sub-group analysis using the factor:

Coronary heart disease risk group – high, medium, low

Sub-group analysis found significant differences between these groups, with only the high risk CHD (treatment) group showing a benefit in terms of total mortality.

A meta-regression was also carried out showing a similar trend.

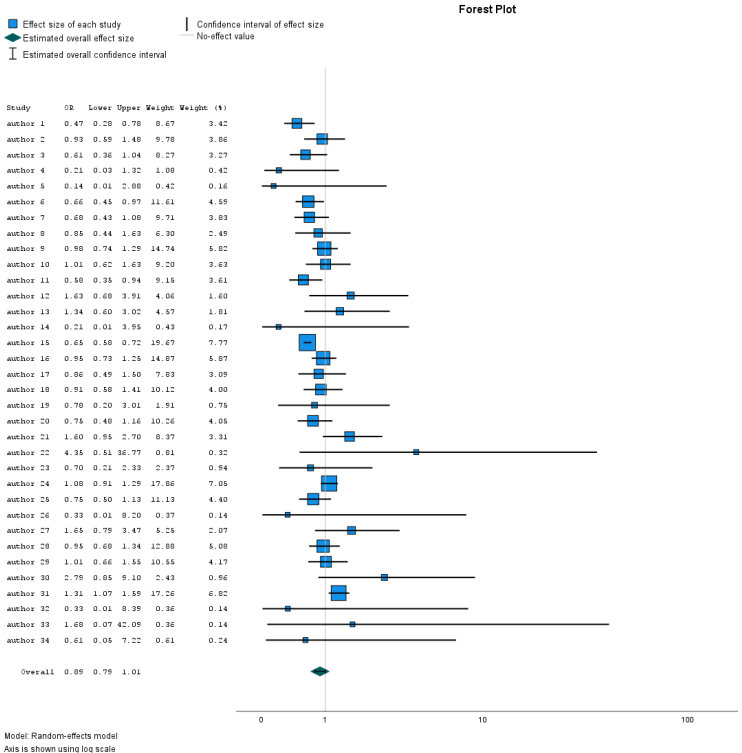
(This analysis is not included in this workshop)

Example: Sutton-Smith (binary outcome)

SPSS (Version 28) Meta-Analysis

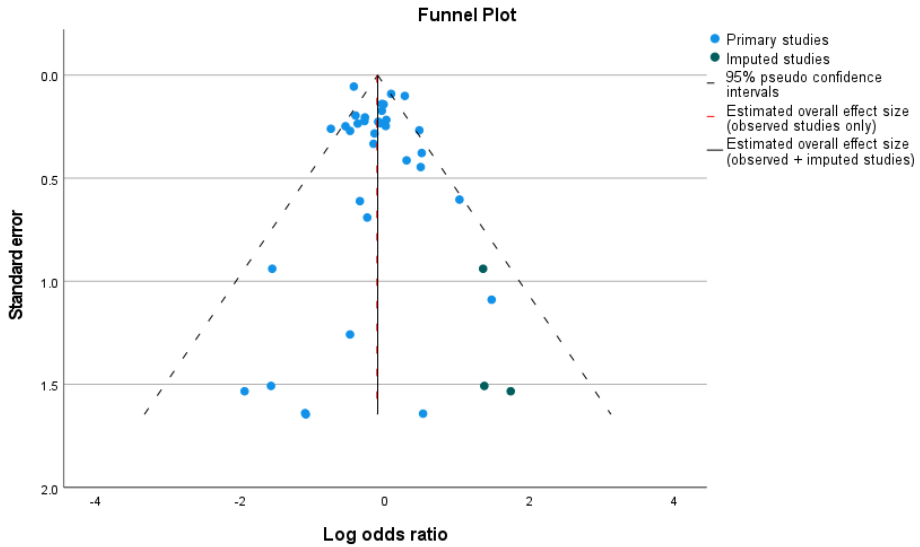
SPSS will produce the same output (although there are fewer formatting options)

Random Effects estimate



Effect Size Estimates

	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval Lower	95% Confidence Interval Upper	Exp. Effect Size	Exp. 95% Confidence Interval Lower	Exp. 95% Confidence Interval Upper
Overall	-.118	.0628	-1.875	.061	-.241	.005	.889	.786	1.005



End of workshop

Final comments



THE UNIVERSITY OF SYDNEY

Further Assistance at Sydney University

SIH

- Statistical Consulting website: containing our workshop slides and our favourite external resources (including links for learning R and SPSS)
- Hacky Hour an informal monthly meetup for getting help with coding or using statistics software
- 1on1 Consults can be requested on our website (click on the big red 'contact us' link)

SIH Workshops

- Create your own custom programmes tailored to your research needs by attending more of our Statistical Consulting workshops. Look for the statistics workshops on our training page.
- Other SIH workshops
- Sign up to our mailing list to be notified of upcoming training

Other

- Open Learning Environment (OLE) courses
- Linkedin Learning

A reminder: Acknowledging SIH



All University of Sydney resources are available to Sydney researchers **free of charge**. The use of the SIH services including the Artemis HPC and associated support and training warrants acknowledgement in any publications, conference proceedings or posters describing work facilitated by these services.

The continued acknowledgment of the use of SIH facilities ensures the sustainability of our services.

Suggested wording for use of workshops and workflows:

"The authors acknowledge the Statistical workshops and workflows provided by the Sydney Informatics Hub, a Core Research Facility of the University of Sydney."

Appendices

additional resources



Published Meta-analysis examples

1. When publication bias is present – from Experimental Psychology (inspect the funnel plot)

Shanks, David R et al. "Romance, Risk, and Replication: Can Consumer Choices and Risk-Taking Be Primed by Mating Motives?" Journal of experimental psychology. General 144.6 (2015): e142–e158. Web.

https://sydney.primo.exlibrisgroup.com/permalink/61USYD_INST/1367smt/cdi_gale_infotracacademiconefile_A444328766

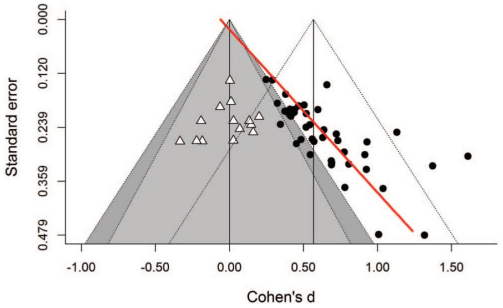


Figure 2. Funnel plot from the meta-analysis. Black circles represent the

2. Good example of tabulation of study data (Tables 1,2,3) but bad example of plotting meta-regression (figures 2 and 4)

Rong, Chen. "Egg Consumption and Risk of Coronary Heart Disease and Stroke: Dose-Response Meta-Analysis of Prospective Cohort Studies." BMJ : British Medical Journal 346.7890 (2013): 12–12. Web.

https://sydney.primo.exlibrisgroup.com/permalink/61USYD_INST/1367smt/cdi_proquest_miscellaneous_1273301943

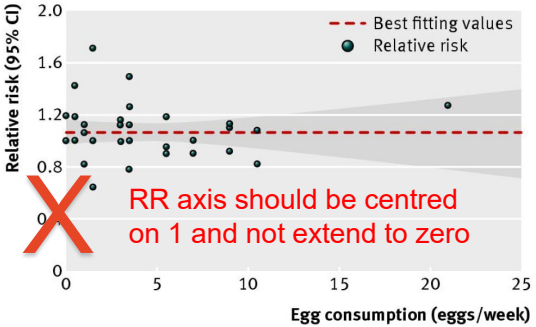


Fig 2 Dose-response analyses of egg consumption and

Published Meta-analysis examples

3. Scientific fraud and retracted papers examined by sub-group analysis

Zarychanski, Ryan et al. “Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically Ill Patients Requiring Volume Resuscitation: A Systematic Review and Meta-Analysis.” JAMA : the journal of the American Medical Association 309.7 (2013): 678–688. Web.

https://sydney.primo.exlibrisgroup.com/permalink/61USYD_INST/1367smt/cdi_proquest_miscellaneous_1291608126

Retraction Watch

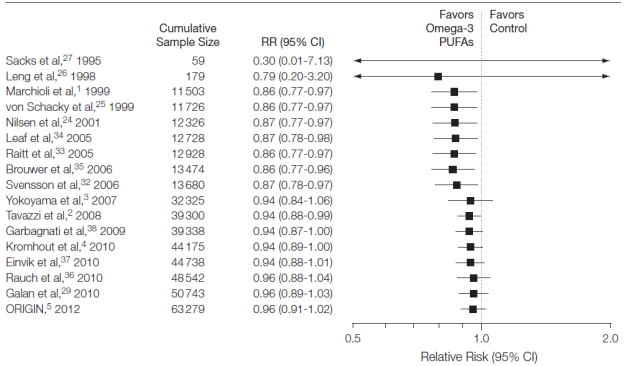
Tracking retractions as a window into the scientific process

4. Good example of Cumulative meta-analysis over 17yr

Rizos, Ntzani. “Association Between Omega-3 Fatty Acid Supplementation and Risk of Major Cardiovascular Disease Events: A Systematic Review and Meta-Analysis.” JAMA : the journal of the American Medical Association 308.10 (2012): 1024–1033. Web.

https://sydney.primo.exlibrisgroup.com/permalink/61USYD_INST/1367smt/cdi_proquest_miscellaneous_1039344012

Figure 5. Cumulative Meta-analysis of the Omega-3 Supplements for All-Cause Mortality



Error bars indicate the 95% CI of the cumulative meta-analysis estimates as randomized patients accumulate through time. PUFAs indicates polyunsaturated fatty acids; RR, relative risk.

Additional Resources



For Systematic Review:

- University Library – Support for Systematic Review
- University Library – Workshops, Canvas modules and Consultations
- Cochrane Handbook for Systematic Reviews of Interventions Online version

For Meta-Analysis:

- Borenstein, Michael. Introduction to Meta-Analysis. Chichester, U.K: John Wiley & Sons, 2009. Print.
- Cochrane Handbook Chapter 10: Meta-Analyses Online version
- Cochrane online learning http://training.cochrane.org/online-learning
- Hartung, Joachim, Guido Knapp, and Bimal K Sinha. Statistical Meta-Analysis with Applications. 1. Aufl. Hoboken, N.J: Wiley-Interscience, 2008. Web.
- Schwarzer, Guido., James R. Carpenter, and Gerta. Rücker. Meta-Analysis with R. 1st ed. 2015. Cham: Springer International Publishing, 2015. Web.
- A guide to Prospective Meta-analysis (from USyd NHMRC CTC) https://www.bmj.com/content/367/bmj.l5342.short