Meta-Research

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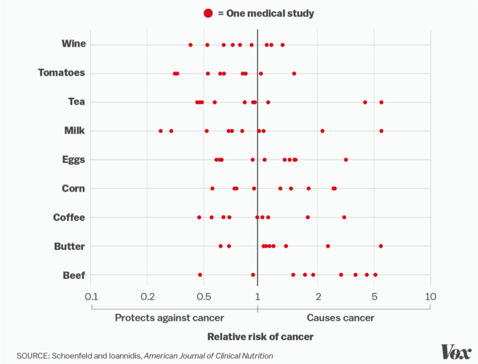
Road Map

- Why
- How to
- Fun things to do

Why Are Meta-Analyses Important?

- Any one given study is not all that informative.



Why Are Meta-Analyses Important?

- Research might be biased.

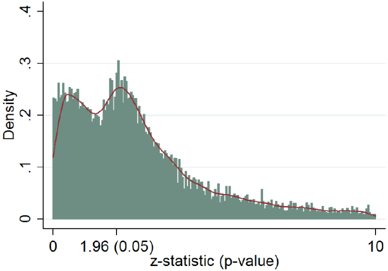


Figure: Brodeur *et al.*, 2016

Why Are Meta-Analyses Important?

- Studies are often underpowered.

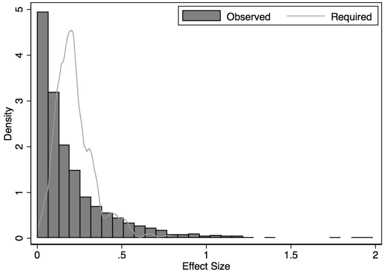


Figure: Vivalt, 2017

Why Are Meta-Analyses Important?

- Studies are partially informative about *each other*.

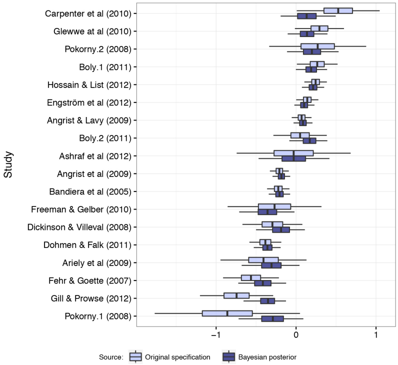


Figure: Fischer *et al.*, 2017

How To Do A Meta-Analysis

- Start by making a lot of decisions about what you will do.
  - Topic
  - Search
  - Screening
  - Data extraction
  - Analysis

Search and Screening: PICOS

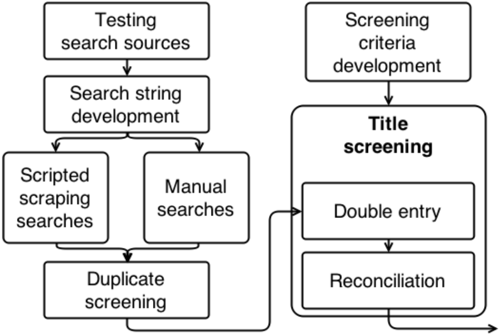
- Population
- Intervention
- Comparison
- Outcome
- Study design

Search and Screening: Quality Measures

- Was the study a randomized controlled trial?
- Was it blinded?
- Did it report attrition?
- Were the hypotheses pre-specified?
- Was it published in a good journal? (Bias?)
- *etc.*

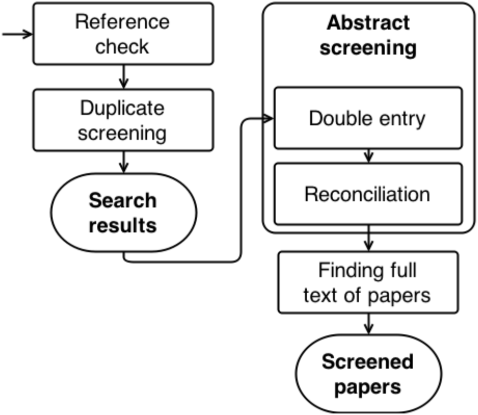
Sample Process Diagram

Figure: Search and Screening, Part 1



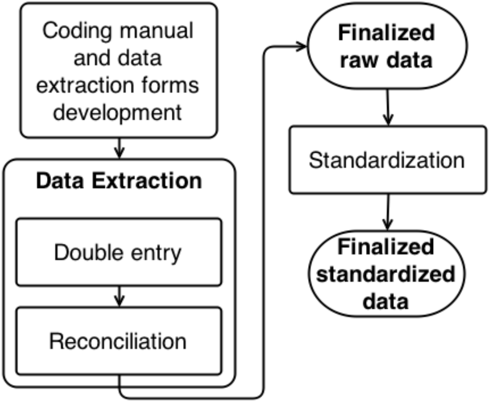
Sample Process Diagram

Figure: Search and Screening, Part 2



Sample Process Diagram

Figure: Data Extraction



Conversion Between Data Types

- Studies report results in all sorts of different ways
- Some of them can be converted to each other, e.g. binary 2x2 tables can become risk ratios or odds ratios
- Refer to Cochrane handbook for different combinations

Analysis

Some references that might be useful:

- Borenstein *et al.* (2009). Introduction to Meta-Analysis
- Gelman *et al.* (2013). Bayesian Data Analysis
- Higgins and Green, *eds.* (2011). Cochrane Handbook for Systematic Reviews of Interventions

Coding references:

http://stats.idre.ucla.edu/stata/seminars/introduction-to-meta-analysis-in-stata/

http://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/

Analysis

- Fixed effect: there is one true effect
- Random-effects: true effects may vary by study
- Mixed model: true effects may vary by study, and we can explain some of that

Fixed Effect Model

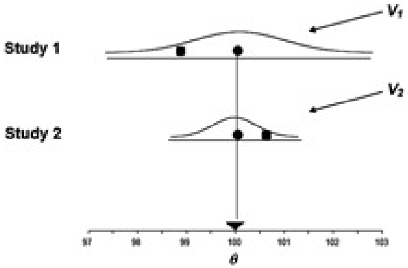


Figure: Borenstein *et al.*, 2009

Example Fixed Effect Model

$$Y_i = \theta + \epsilon_i$$

$$\epsilon_i \sim N(0, \sigma_i^2)$$

Y_i is the estimate of the effect in study i

θ is the true effect

ϵ_i is the error, normally distributed with some sampling variance σ_i^2

Fixed Effect Model

- Meta-analysis is a kind of weighted average
- Need to pick a weighting rule

Fixed Effect Model

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- Need to pick a weighting rule
    - Sample size?
    - Inverse variance?

Fixed Effect Model

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  - Inverse variance?

$$w_i = \frac{1}{v_i},\ M = \frac{\sum_i w_i Y_i}{\sum_i w_i},\ v_M = \frac{1}{\sum_i w_i}$$

Random-Effects Model

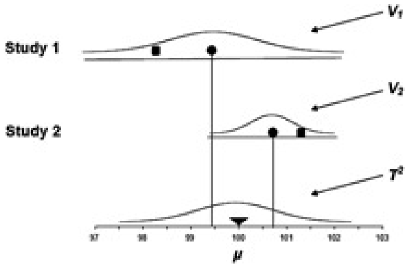

Figure: Borenstein *et al.*, 2009

Example Random-Effects Model

$$Y_i = \theta_i + \epsilon_i$$
$$\epsilon_i \sim N(0, \sigma_i^2)$$
$$\theta_i \sim N(\mu, \tau^2)$$

Y_i is the estimate of the effect in study i

θ_i is the true effect in study i

ϵ_i is the error, normally distributed with some sampling variance σ_i^2

μ is the grand mean

τ^2 is the inter-study variance

Random-Effects Model

- Now the variance has two components: $v_i = \sigma_i^2 + \tau^2$
- Most common way of estimating τ^2: DerSimonian-Laird estimator
- Better: Maximum likelihood, Empirical Bayes, Sidik-Jonkman (Sidik and Jonkman, 2007), Full Bayes
- Sensitivity analyses recommended, especially for small number of studies

Example Mixed Model

$$Y_i = \alpha + X_i\beta + \zeta_i + \epsilon_i$$
$$\theta_i = \alpha + X_i\beta + \zeta_i$$
$$\epsilon_i \sim N(0, \sigma_i^2)$$
$$\zeta_i \sim N(0, \tau^2)$$

Y_i is the estimate of the effect in study i

θ_i is the true effect in study i and is comprised of some component that can be explained ($X_i\beta$) and some component that cannot (ζ_i)

ϵ_i is the error, normally distributed with some sampling variance σ_i^2

τ^2 is the inter-study variance

Estimating in Stata

metan:

- metan TE lowerci upperci, fixedi
- metan TE lowerci upperci, randomi
- metan tdeath tnodeath cdeath cnodeath
- metan tsample tmean tsd csample cmean csd
- metan logor selogor, eform

Mantel-Haenszel method will be used if “fixed” or “random” is specified rather than “fixedi” or “randomi”. “fixed” is the default

Estimating in R

meta package:

- metagen for treatment effects:
  m.se< −metagen(TE, se, data=mydata, comb.fixed=TRUE, comb.random=FALSE, sm="SMD")
- metacont for raw data:
  m.raw< −metacont(NT, MT, ST, NC, MC, SC, data=mydata, comb.fixed=TRUE, comb.random=FALSE, sm="SMD")

Option method.tau governs how τ^2 is estimated. E.g. method.tau="DL", method.tau="ML", method.tau="EB", etc.

Estimating in R

meta package [cont]:

- metabin for raw binary data:
  m.bin$<-$metabin(Et, Nt, Ec, Nc, data=mydata, comb.fixed=FALSE, comb.random=TRUE, sm="RR") (risk ratios)

metafor package:

- m $< -$ rma(yi = TE, sei = se, method = "FE", data = mydata)

Estimating in R

Bayesian hierarchical models:

- Priors over μ and τ, update using data, draw posterior distribution
- A long, hard way: coding up a Bayesian hierarchical model
- The short way: Rachael's new package using Stan
- Check: do you have the right functional form?
- Check: how sensitive are your results to the priors you selected?

Fun Things to Do

- Model and characterize heterogeneity
- Re-interpret study results in light of other studies
- Estimate biases
- Other ways to leverage Bayesian model

Characterizing Heterogeneity

- Some possible measures:
  - var(Y_i) or τ^2
  - coefficient of variation
  - $I^2 = \frac{\tau^2}{\tau^2+\sigma^2}$
- Each possible measure of heterogeneity is flawed

Studies are partially informative about *each other*

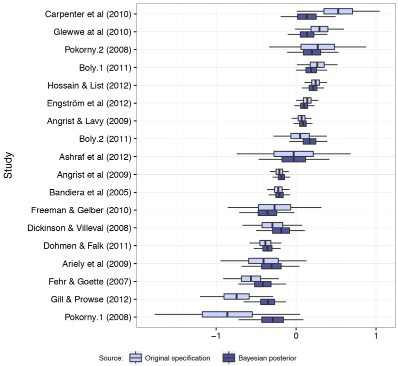

Figure: Fischer *et al.*, 2017

Model Heterogeneity

- Generally not enough data for meta-regression....

Estimate Biases

- Funnel plots:

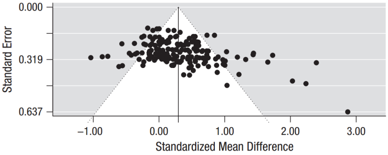

Fig. 2. Funnel plot of the meta-analysis of published studies. Each plotted point represents the standard error and standardized mean difference between bilinguals and monolinguals for a single study. The white triangle represents the region where 95% of the data points would lie in the absence of a publication bias. The vertical line represents the average standardized mean difference of 0.30 found in the meta-analysis.

Figure: de Bruin *et al.*, 2015

Examples in Stata

metafunnel:

- Plots funnel plots

metabias:

- Various tests for funnel-plot asymmetry

metatrim:

- "Trim and fill" method of adjusting meta-analysis to account for biases

These methods require heroic assumptions....

Examples in R

forest: part of the *meta* package

- forest(m.raw, raw) after m.raw

Why might a funnel plot not necessarily be a good way to gauge publication bias?

Estimate Biases

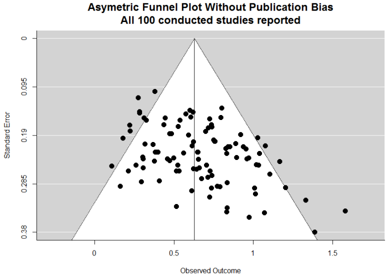

Figure: Simonsohn, Data Colada blog, 2017

Estimate Biases

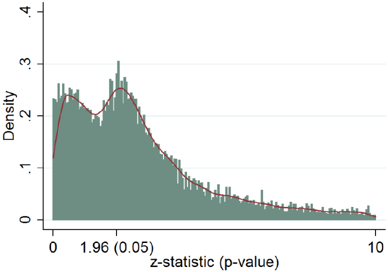

Figure: Brodeur *et al.*, 2016

Estimate Biases

- When can you use a caliper test?
- How should you use a caliper test?

Estimate Biases

- False positive and false negative report probability (FPRP/FNRP), "modified" FPRP/FNRP, Bayesian False Discovery Probability, or the conditional error probability (Wacholder *et al.*, 2004; Ioannidis, 2005; Wakefield, 2007; Wakefield, 2008; Lucke, 2009)
  - Need some kind of prior
  - Intuition: results that seem unlikely are either really novel and valuable or false positives

Estimate Biases

- In econ: Ioannidis, Stanley and Doucouliagos analyze power (2017). Use fixed effect meta-analysis result as true effect to try to avoid bias (but heterogeneity in treatment effects?)
- Type S and Type M errors (Gelman and Carlin, 2014)

Learn about Learning

- Can estimate how much we learn from an impact evaluation, e.g. given estimates of τ, σ
- Value of information

Cautions

- Like any study, meta-analyses are only as good as the methods used (and studies included)
- Meta-analyses can be biased
- Same best practices apply:
  - Pre-specify (register with Cochrane)
  - Document what is done in sufficient detail that it could be replicated
  - Version data