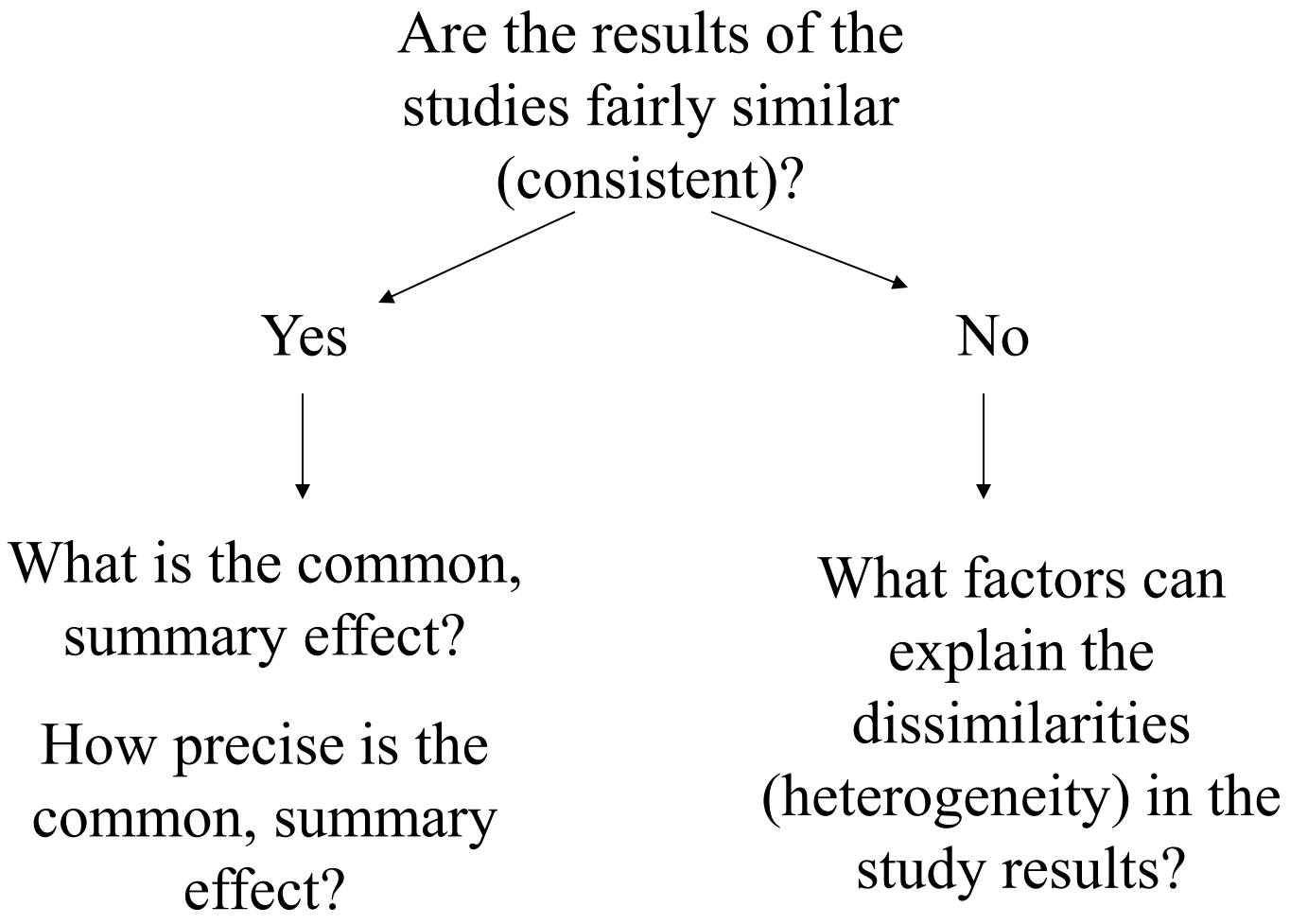
Data Analysis in Systematic Reviews

Madhukar Pai, MD, PhD
Associate Professor
McGill University
Montreal
Email: madhukar.pai@mcgill.ca

McGill

Central questions of interest



Steps in data analysis & presentation

1. Tabulate summary data
2. Graph data
3. Check for heterogeneity
4. Perform a meta-analysis if heterogeneity is not a major concern
5. If heterogeneity is found, identify factors that can explain it
6. Evaluate the impact of study quality on results
7. Explore the potential for publication bias

1. Tabulate summary data

- Prepare tables comparing studies with respect to:
  - Year
  - Setting
  - Patients
  - Intervention
  - Comparison
  - Outcome (results)
  - Quality
- Gives a 'first hand' feel for the data
- Can make some assessment of quality and heterogeneity

Tabulate summary data
Example: Cochrane albumin review

Study	Year	Patient population	Intervention	Comparison	Summary measure (RR)	Allocation concealment
Lucas et al.	1978	Trauma	Albumin	No albumin	13.9	Inadequate
Jelenko et al.	1979	Burns	Albumin	Ringer's lactate	0.50	Unclear
Rubin et al.	1997	Hypoalbuminemia	Albumin	No albumin	1.9	Adequate

Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systematic review of randomised controlled trials. BMJ 1998;317:235-40.

2. Graph summary data

- Efficient way of presenting summary results
- Forest plot:
  - Presents the point estimate and CI of each trial
  - Also presents the overall, summary estimate
  - Allows visual appraisal of heterogeneity
- Other graphs:
  - Cumulative meta-analysis
  - Sensitivity analysis
  - Funnel plot for publication bias
  - Galbraith, L'Abbe plots, etc [rarely used]

Forest Plot

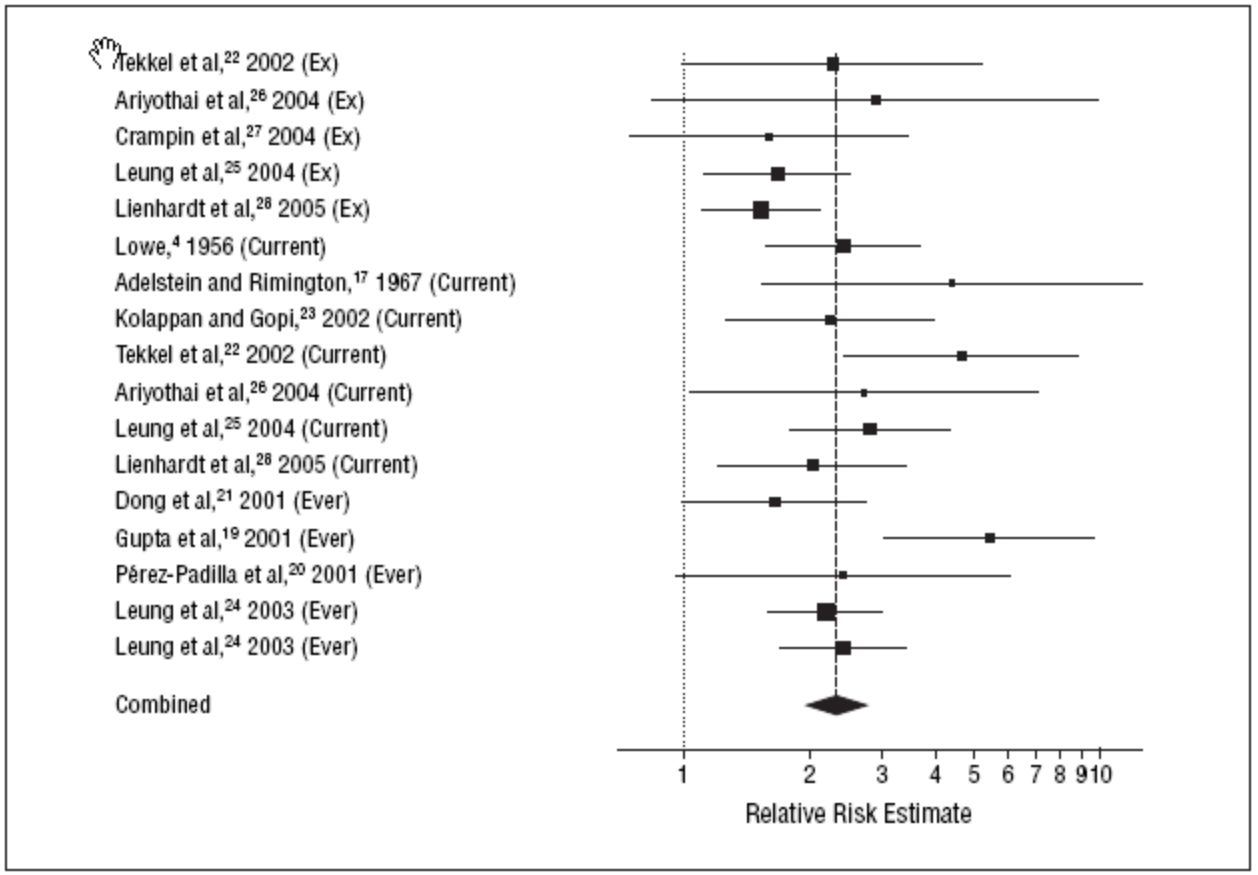


Figure 3. Forest plot of results for men only and for men and women combined in studies[4,17,19-28] that examined smoking and tuberculosis disease. The smoking type (ex-smokers [Ex], current smokers [Current], and ever smokers [Ever]) of the study population is shown on the y-axis.

Bates et al. Arch Intern Med 2007

Interpreting and understanding meta-analysis graphs

A practical guide

PROFESSIONAL PRACTICE

Research

Karin Ried

PhD, MSc, GDPH, is Research Fellow & PHCRED Program Manager, Discipline of General Practice, The University of Adelaide, South Australia.
karin.ried@adelaide.edu.au

Ideally, clinical decision making ought to be based on the latest evidence available. However, to keep abreast with the continuously increasing number of publications in health research, a primary health care professional would need to read an unsurmountable meta-analysis before diving into the fine points of the meta-analysis results and drawing conclusions on patient treatment. *Table 1* can guide the assessment.

Meta-analysis graphs

Ried K. Aus Fam Phys 2006

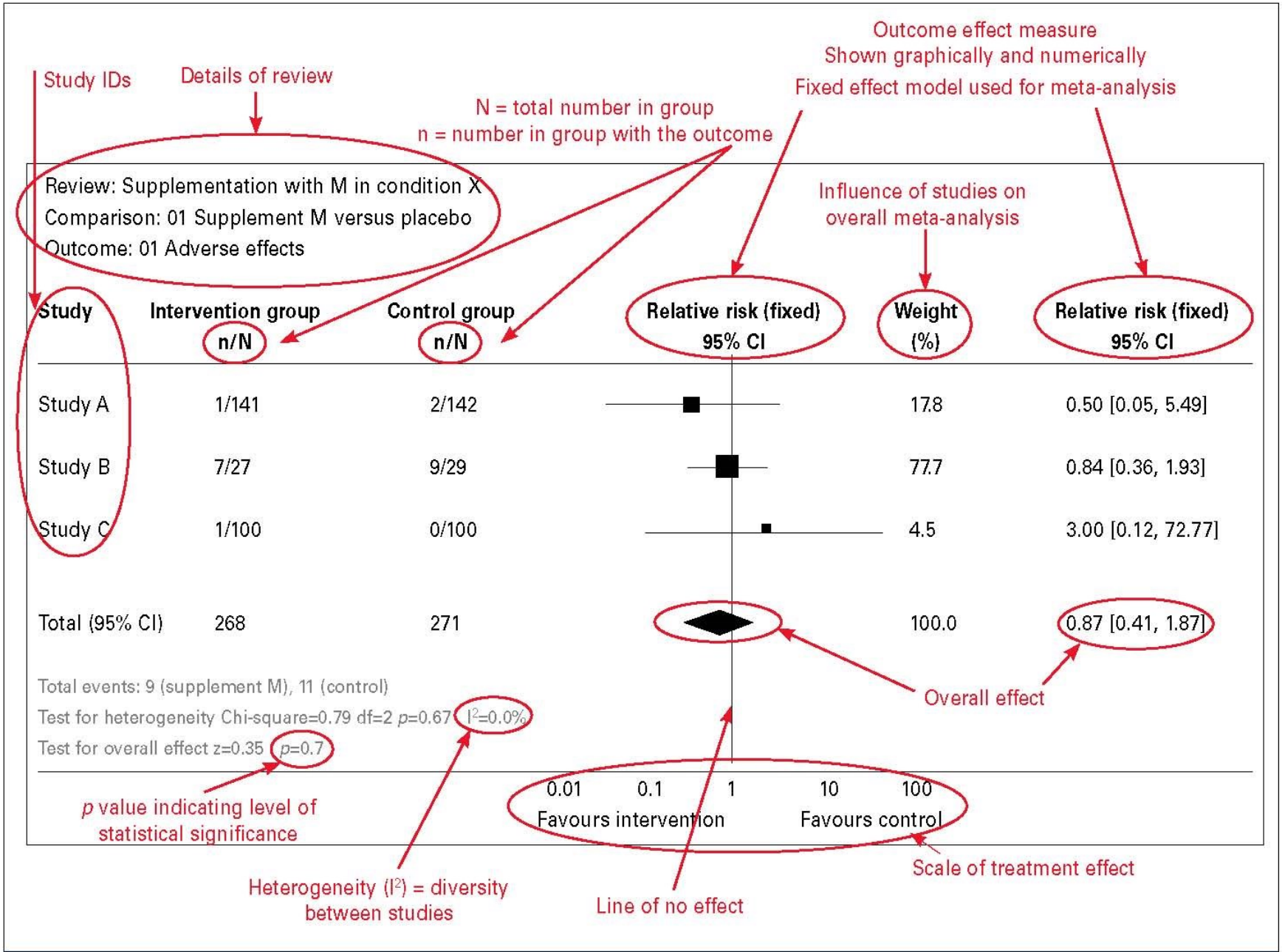


Figure 1. Meta-analysis of binary outcome measure

Ried K. Aus Fam Phys 2006

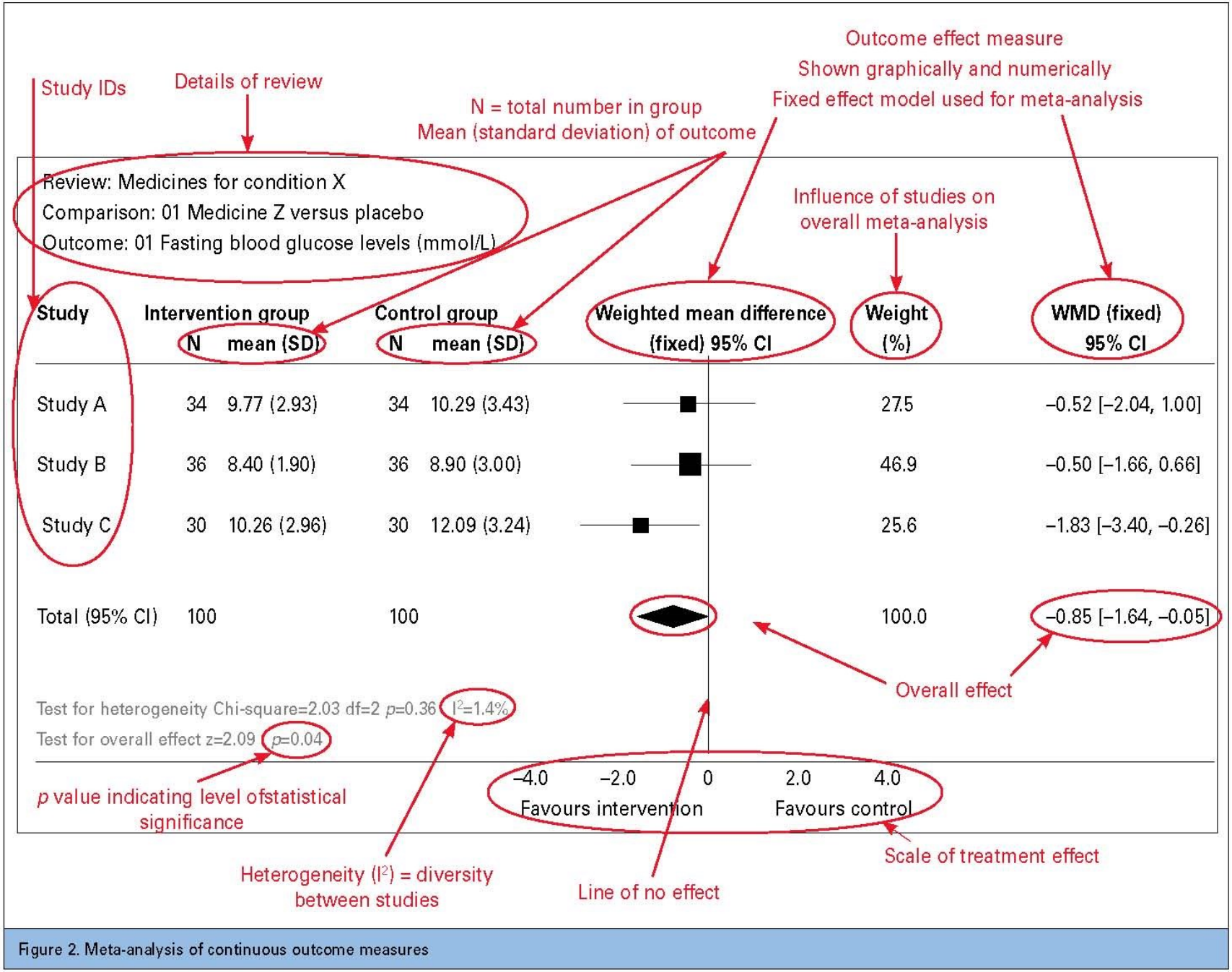
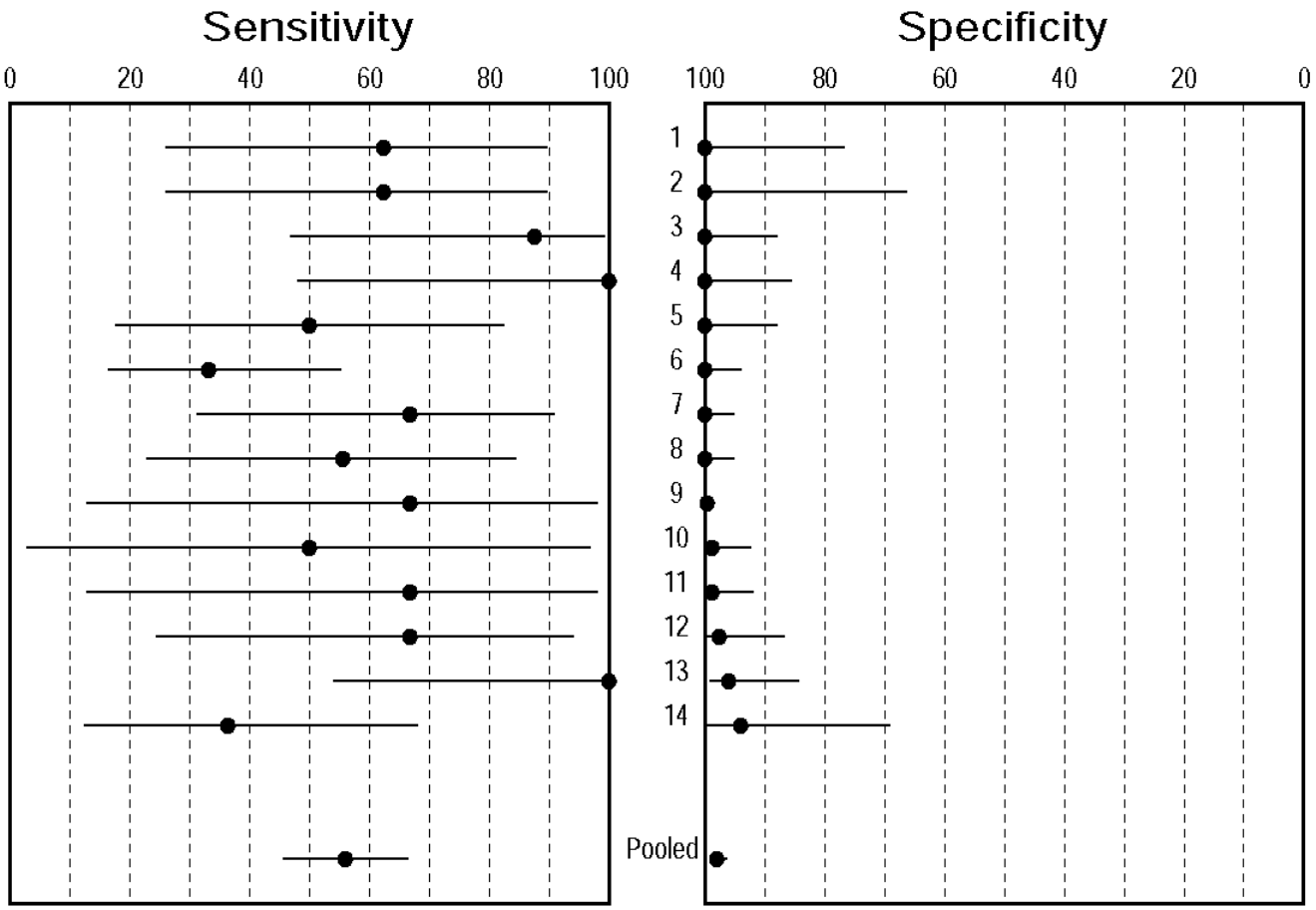


Figure 2. Meta-analysis of continuous outcome measures

Ried K. Aus Fam Phys 2006

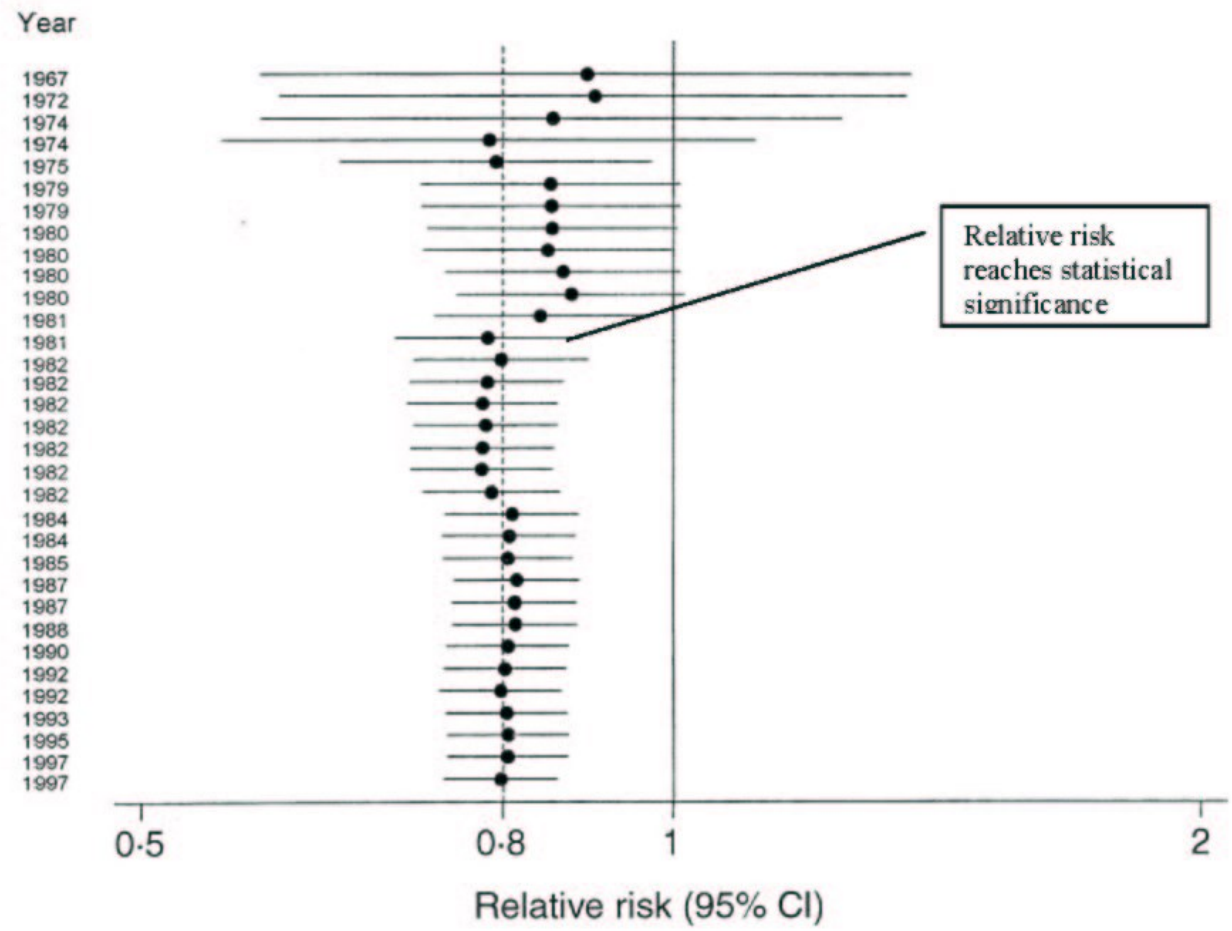
Forest Plot: diagnostic studies



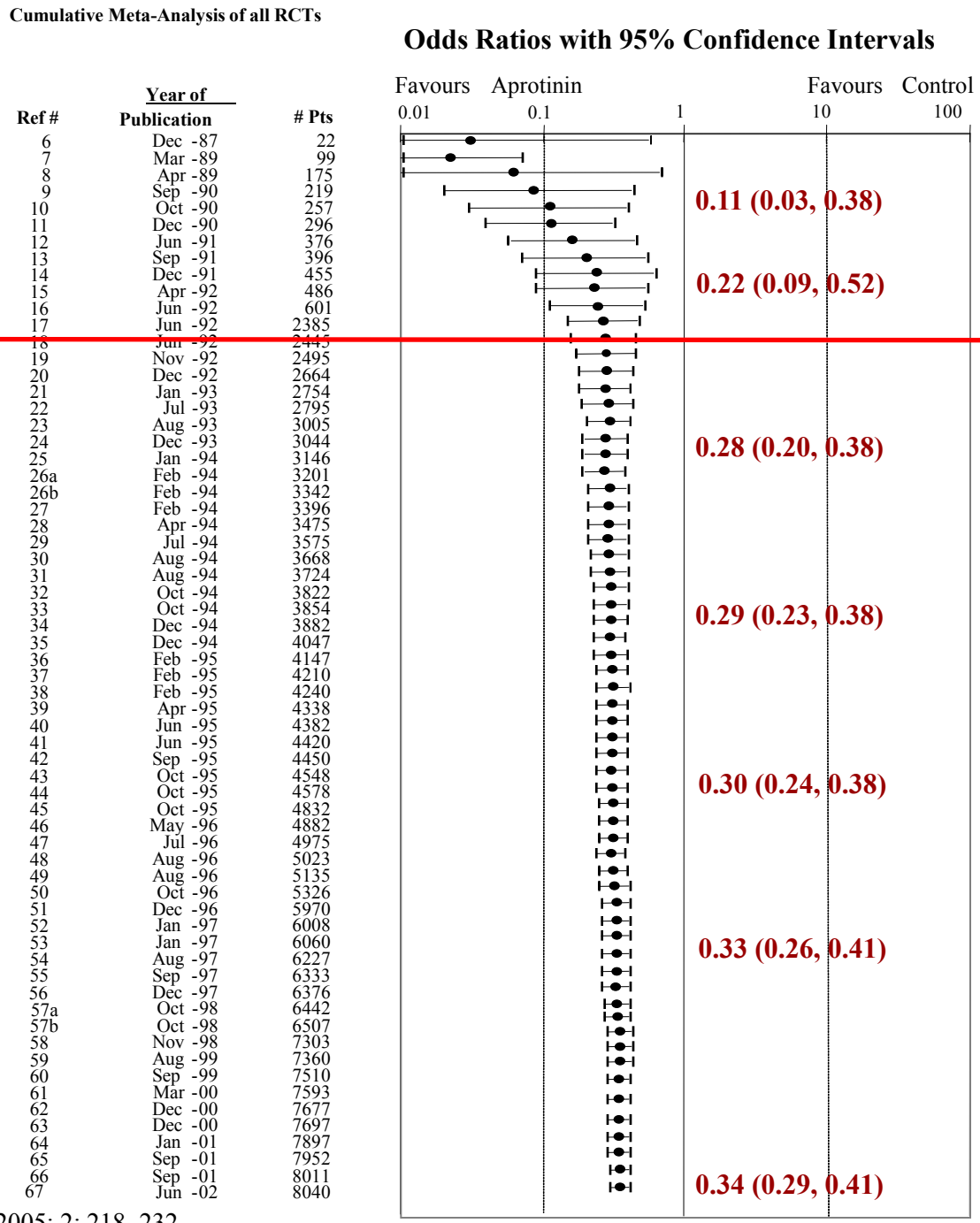
Commercial PCR tests for TB meningitis

Pai M, et al. Lancet Infect Dis 2003

Forest Plot: Cumulative Meta-analysis



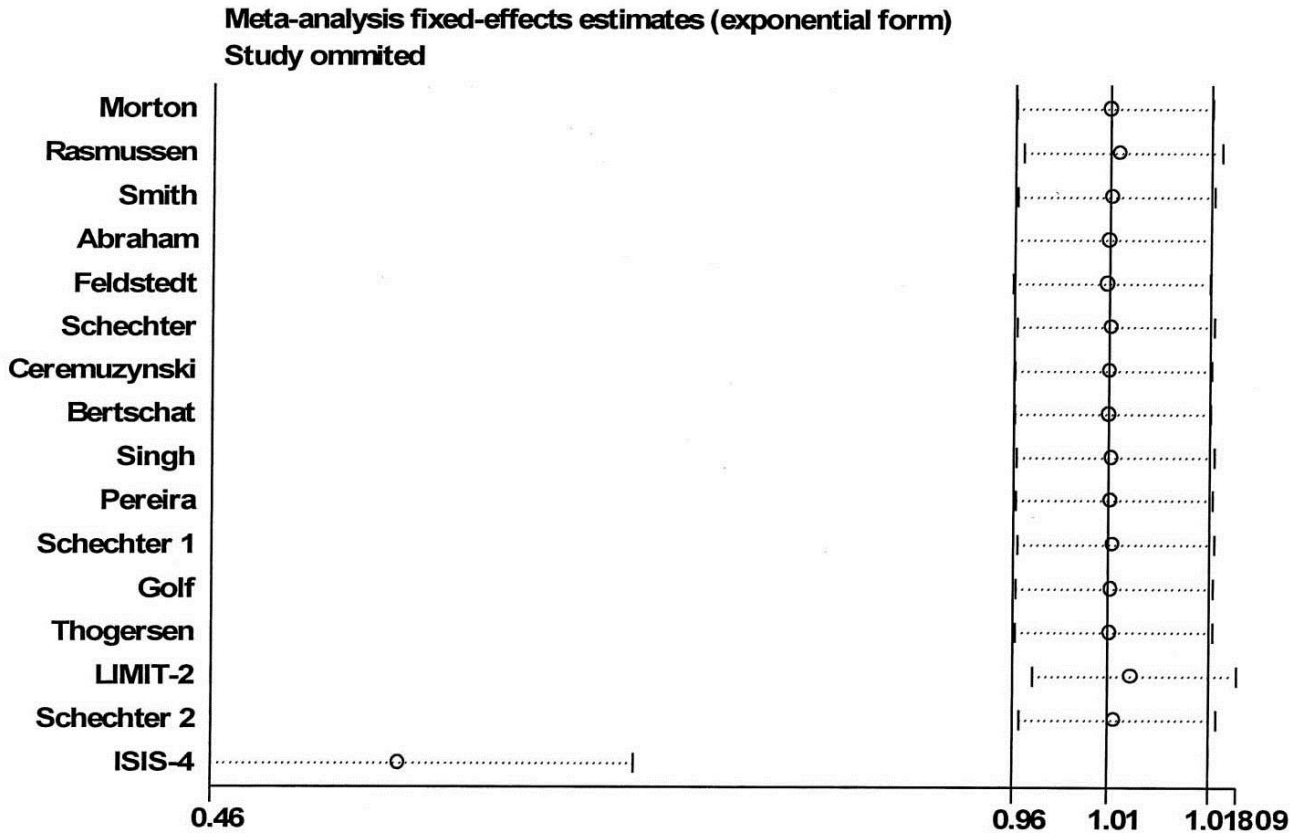
Beta-blockers after acute myocardial infarction



Aprotinin for cardiac surgery

Fergusson D et al. Clinical Trials 2005; 2: 218–232

Sensitivity analysis



IV magnesium for acute myocardial infarction

ISIS-4 trial had >50,000 patients! It showed no survival benefit from the addition of IV magnesium

3. Check for heterogeneity

- Indicates that effect varies a lot across studies
- If heterogeneity is present, a common, summary measure is hard to interpret
- Statistical vs clinical heterogeneity
- Can be due to due to differences in:
  - Patient populations studied
  - Interventions used
  - Co-interventions
  - Outcomes measured
  - Study design features (eg. length of follow-up)
  - Study quality
  - Random error

Two 'average' men having an 'average' meal.

3. Check for heterogeneity

- How to look for heterogeneity?
  - Visual
    - Forest plot: do confidence intervals of studies overlap with each other and the summary effect?
    - L'Abbe plot
  - Statistical tests:
    - Chi-square test for heterogeneity (Cochran Q test)
      - Tests whether the individual effects are farther away from the common effect, beyond what is expected by chance
      - Has poor power
      - P-value < 0.10 indicates significant heterogeneity
    - I-squared (newly introduced by Higgins et al): % of total variability in effect measure that is attributable to heterogeneity (i.e. not to chance)
      - Values of I-squared equal to 25%, 50%, and 75% representing low, moderate, and high heterogeneity, respectively.

Higgins JP, Thompson SG. Stat Med 2002;21:1539–58.

Visual appraisal of heterogeneity

Association between smoking and TB mortality

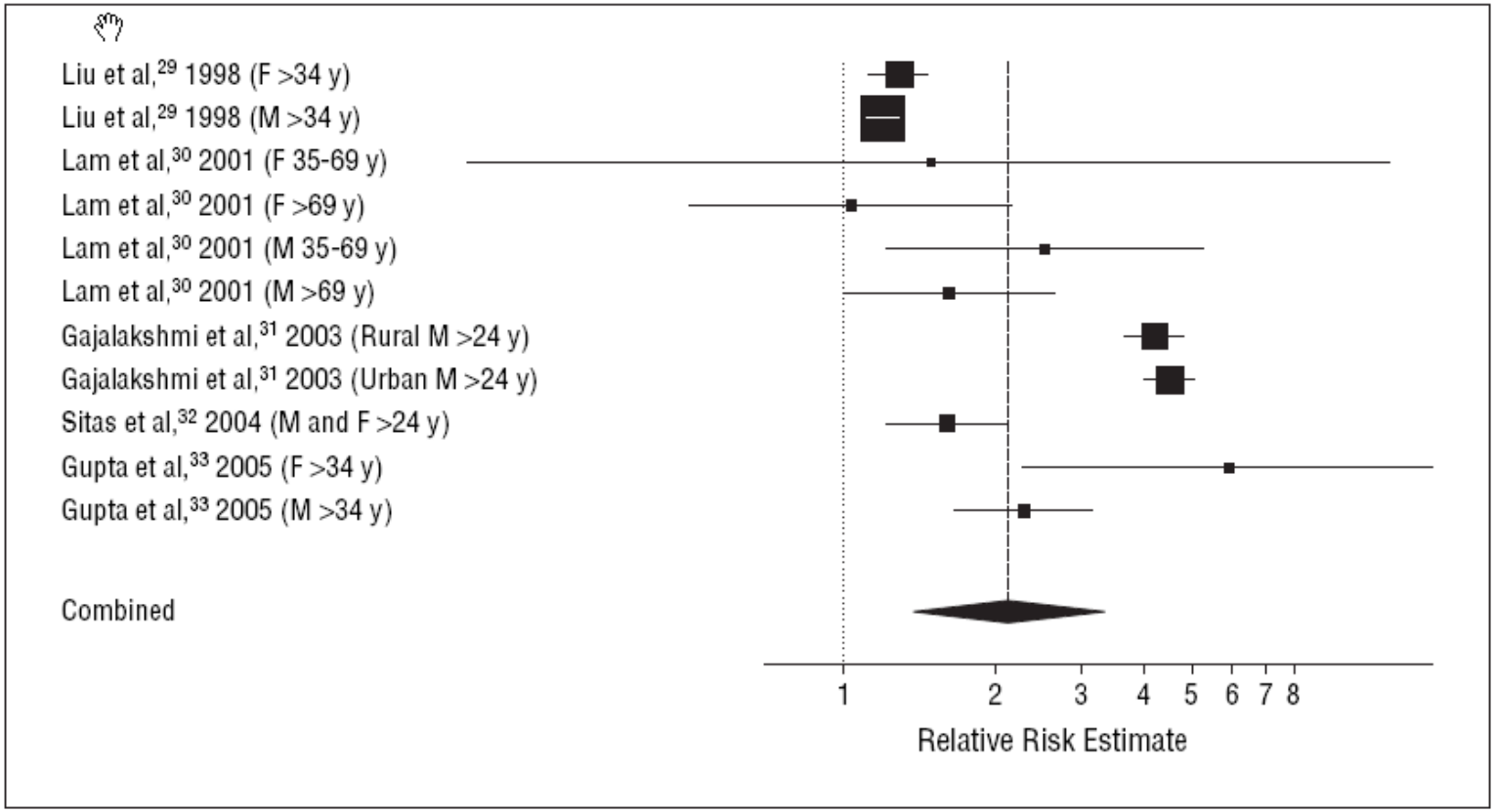
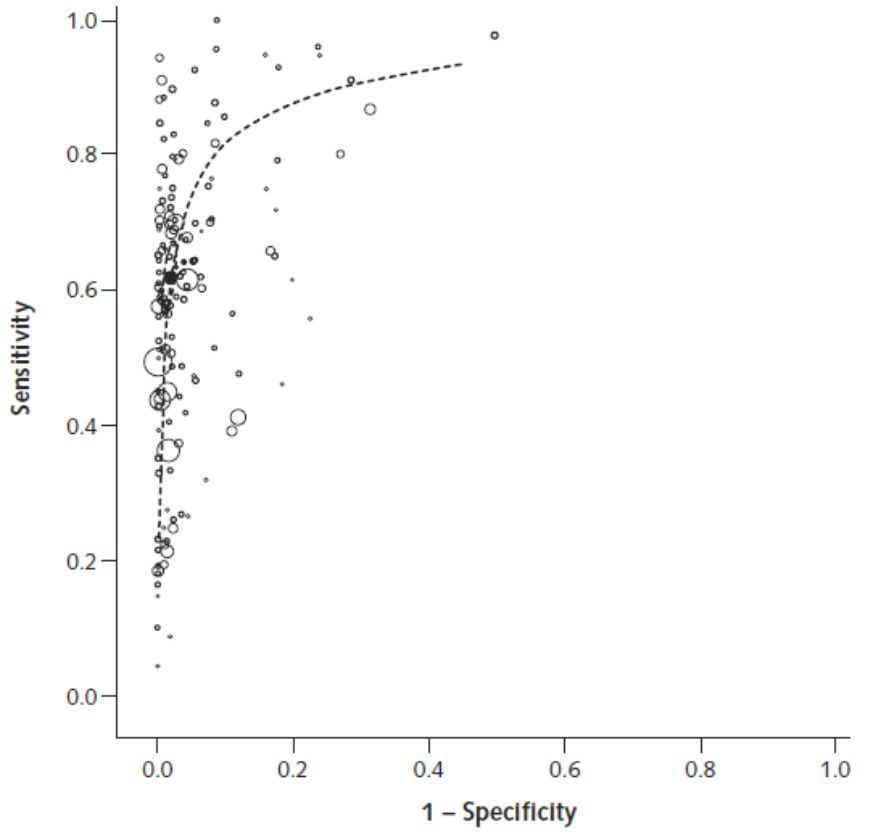


Figure 5. Forest plot of studies[29-33] that examined smoking and tuberculosis mortality. The sex and age of the study population are shown on the y-axis.

Bates et al. Arch Intern Med 2007

P-value for heterogeneity <0.001

Figure 2. **Hierarchical summary receiver-operating characteristic curve plot of rapid influenza diagnostic test studies.**

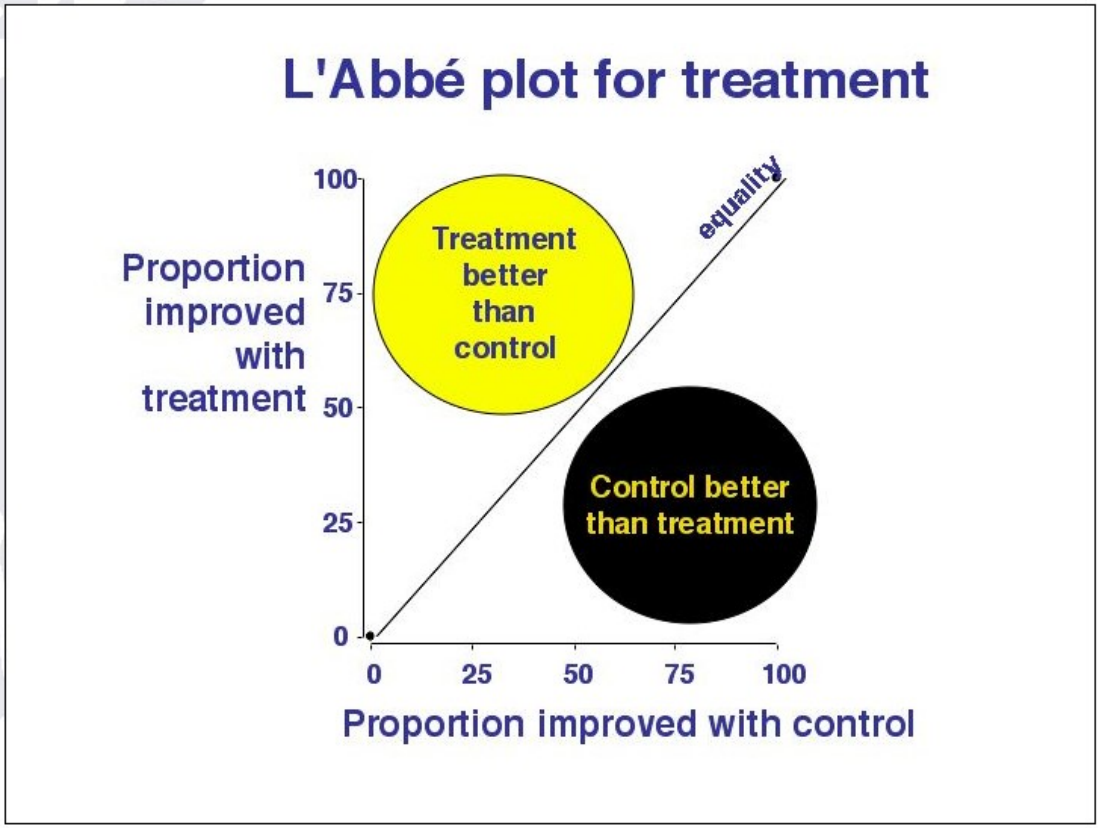


Individual studies (n = 159) are shown as open circles whose size is proportionate to the size of the study. Summary point is shown as a closed circle, representing sensitivity estimates pooled by using bivariate random-effects regression model. The hierarchical summary receiver-operating characteristic curve is shown as a dashed line and is truncated outside the area for which data exist.

Chartrand C et al. Annals 2012

L'Abbe plot for heterogeneity

- Trials in which the experimental treatment proves better than the control (EER > CER) will be in the upper left of the plot, between the y axis and the line of equality (Figure). If experimental is no better than control then the point will fall on the line of equality (EER = CER), and if control is better than experimental then the point will be in the lower right of the plot, between the x axis and the line of equality (EER < CER).



http://www.medicine.ox.ac.uk/bandolier/booth/glossary/labbe.html

3. Check for heterogeneity

- If significant heterogeneity is found:
  - Find out what factors might explain the heterogeneity
  - Can decide not to combine the data
- If no heterogeneity:
  - Can perform meta-analysis and generate a common, summary effect measure

Heterogeneity makes it hard to interpret pooled estimates

"We view the opposition of random-effects summaries and fixed-effects summaries as misleading and counterproductive, for the following reason: If the two summaries differ to a meaningful extent, there must be meaningful discrepancies (heterogeneity) among the study-specific effect estimates. In this situation, we contend that any summary will be inadequate."

Poole and Greenland (1999)

"[I]n drawing inferences from heterogeneous but logically related studies...the use of regression analysis to characterize differences in study outcomes may be more appropriate [than random-effects summarization]."

*DerSimonian and Laird (1985)**

4. Perform meta-analysis

- Decide what data to combine
- Data types:
  - Continuous
  - Dichotomous
- Examples of measures that can be combined:
  - Risk ratio
  - Odds ratio
  - Risk difference
  - Effect size (Z statistic; standardized mean difference)
  - P-values
  - Correlation coefficient (R)
  - Sensitivity & Specificity of a diagnostic test

4. Perform meta-analysis

- Statistical models for combining data:
  - All methods are essentially compute weighted averages
  - Weighting factor is often the study size
  - Models:
    - Fixed effects model
      - Inverse-variance, Peto method, M-H method
    - Random effects model
      - DerSimonian & Laird method

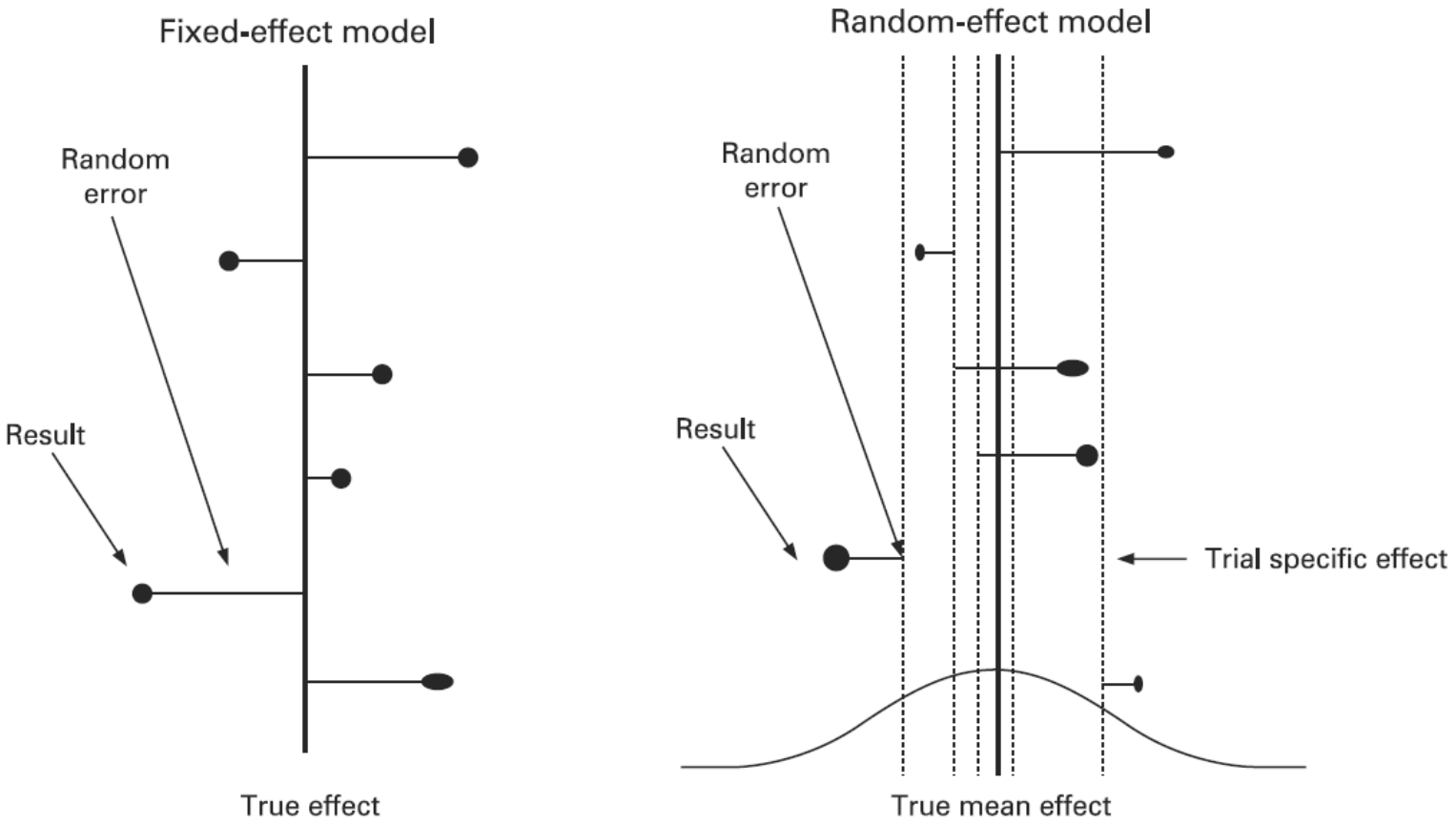
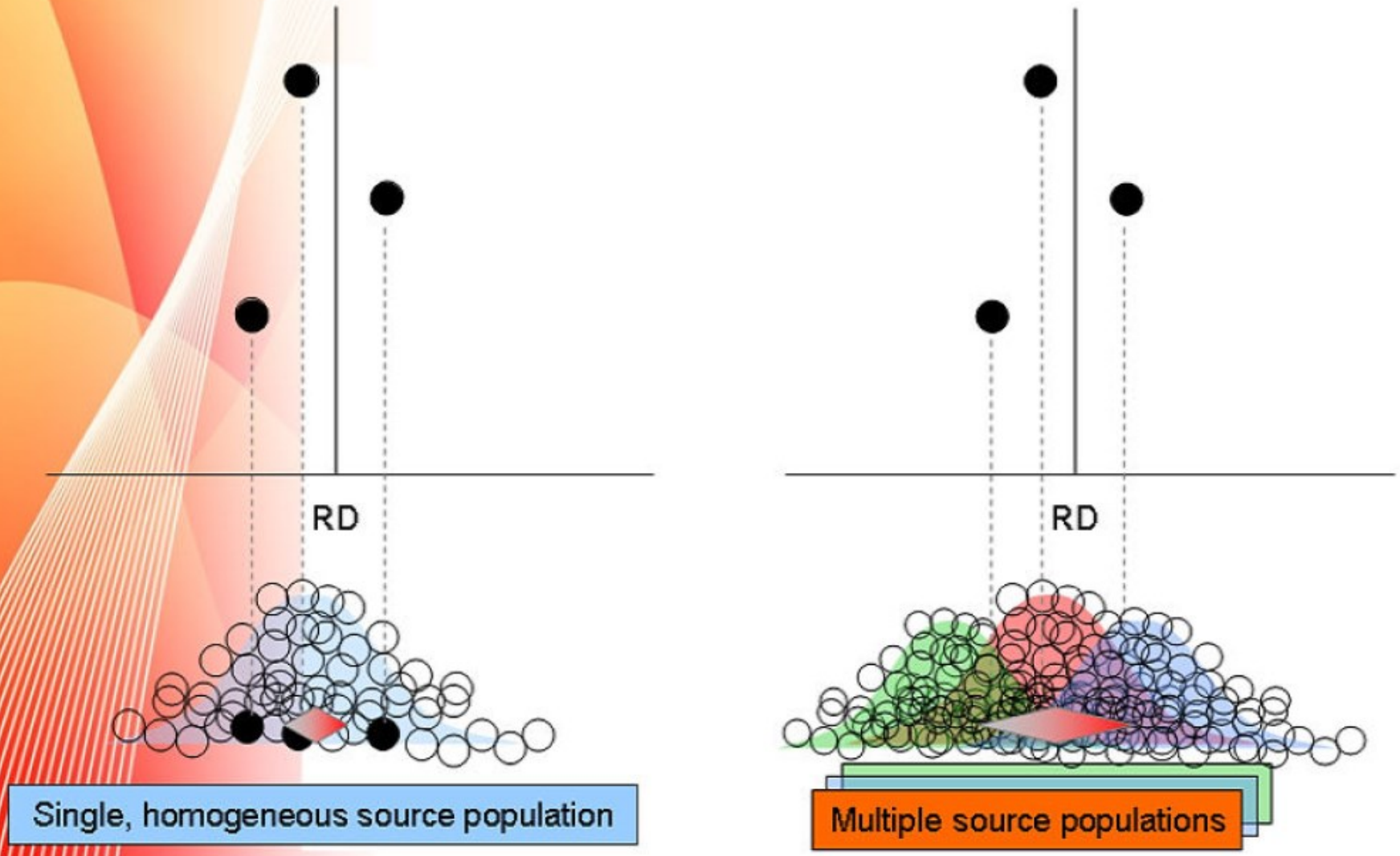


Figure 2. Graphical representation of the theoretical models used to combine data together.

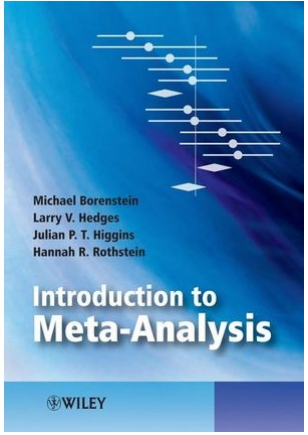
Fixed and random effects models



Courtesy: Leon Bax, http://www.mix-for-meta-analysis.info/index.html#

4. Perform meta-analysis

- Fixed effects model
  - based on the assumption that a single common (or 'fixed') effect underlies every study in the meta-analysis
  - For example, if we were doing a meta-analysis of ORs, we would assume that every study is estimating the same OR.
  - Under this assumption, if every study were infinitely large, every study would yield an identical result.
  - Same as assuming there is no statistical heterogeneity among the studies



	True effect	Observed effect
Study	●	■
Combined	▼	◆

Figure 10.1 Symbols for true and observed effects.

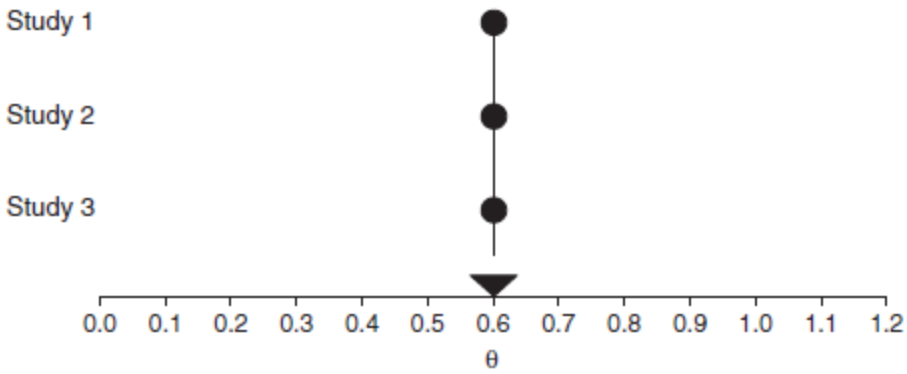


Figure 11.1 Fixed-effect model – true effects.

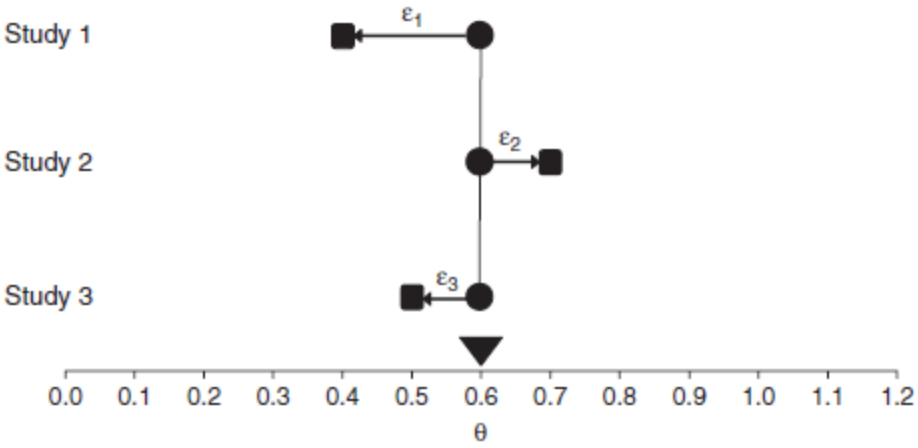


Figure 11.2 Fixed-effect model – true effects and sampling error.

Example of a fixed effects method (M-H)

Study 1

		Disease +	Disease -
Treatment	+	a	b
	-	c	d

Study 2

		Disease +	Disease -
Treatment	+	a	b
	-	c	d

$$OR_{MH} = \frac{\Sigma[a_i d_i / n_i]}{\Sigma[b_i c_i / n_i]}$$

Example of a fixed effects method (M-H)

Study 1: n1 = 200

		Disease +	Disease -
Treatment	+	10	90
	-	20	80

OR = 0.44

Study 2: n2 = 200

		Disease +	Disease -
Treatment	+	12	88
	-	16	84

OR = 0.72

$$OR_{MH} = \frac{\Sigma[a_i d_i / n_i]}{\Sigma[b_i c_i / n_i]} = (4+5.04) / (9+7.04) = OR_{MH} = 0.56$$

4. Perform meta-analysis

- Random effects model
  - Makes the assumption that individual studies are estimating different true effects
    - we assume they have a distribution with some central value and some degree of variability
    - the idea of a random effects MA is to learn about this distribution of effects across different studies
    - Random effects model:
      - Allows for random error plus inter-study variability
      - Results in wider confidence intervals (conservative)
      - Studies tend to be weighted more equally (relatively more weight is given to smaller studies)
      - Can be unpredictable (i.e. not stable)

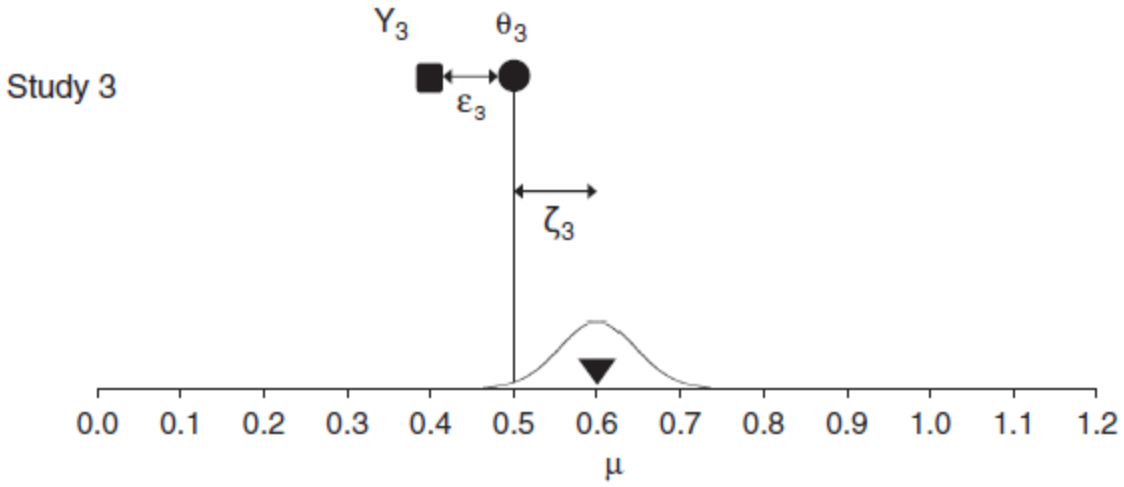


Figure 12.3 Random-effects model – true and observed effect in one study.

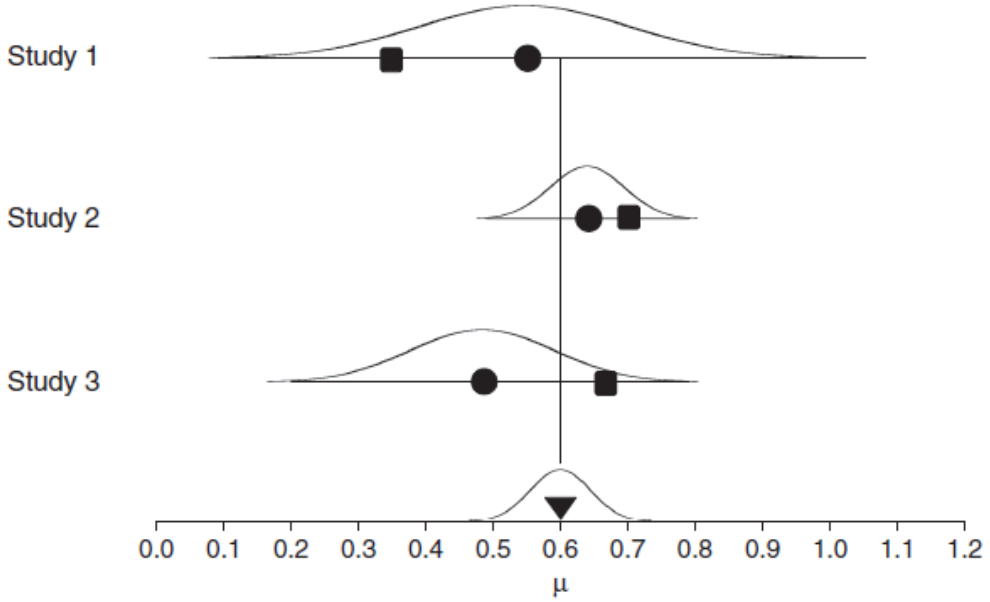
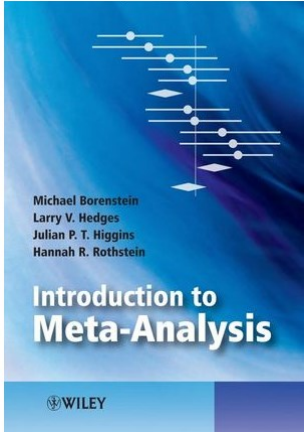


Figure 12.4 Random-effects model – between-study and within-study variance.



DerSimonian and Laird Model

$$Q = \sum_{i=1}^{n} w_i (y_i - \bar{y})^2,$$

where $w_i = \sigma_i^{-2}$, $\bar{y} = \sum_{i=1}^{n} w_i y_i / \sum_{i=1}^{n} w_i$ and n denotes the number of studies. Under the assumptions of the random effects model it can be shown that the expectation of Q is

$$E[Q] = (n-1) + \left(S_1 - \frac{S_2}{S_1}\right)\tau^2$$

where $S_r = \sum_{i=1}^{n} w_i^r$, which provides the DerSimonian and Laird estimate

$$\hat{\tau}^2_{DL} = \max\left(0, \frac{Q-(n-1)}{S_1 - \frac{S_2}{S_1}}\right).$$

The corresponding estimate of treatment effect is

$$\hat{\mu}_{DL} = \frac{\sum_{i=1}^{n} \frac{y_i}{\sigma_i^2 + \hat{\tau}^2_{DL}}}{\sum_{i=1}^{n} \frac{1}{\sigma_i^2 + \hat{\tau}^2_{DL}}}.$$

R. DerSimonian and N. Laird, Meta-analysis in clinical trials, *Controlled Clinical Trials* **7** (1986), pp. 177–188

RESEARCH METHODS & REPORTING

Interpretation of random effects meta-analyses

Richard D Riley,[1] Julian P T Higgins,[2] Jonathan J Deeks[1]

[1]Department of Public Health, Epidemiology and Biostatistics, Public Health Building, University of Birmingham, Birmingham B15 2TT, UK
[2]MRC Biostatistics Unit, Institute of Public Health, Cambridge CB2 0SR, UK
Correspondence to: R D Riley
r.d.riley@bham.ac.uk
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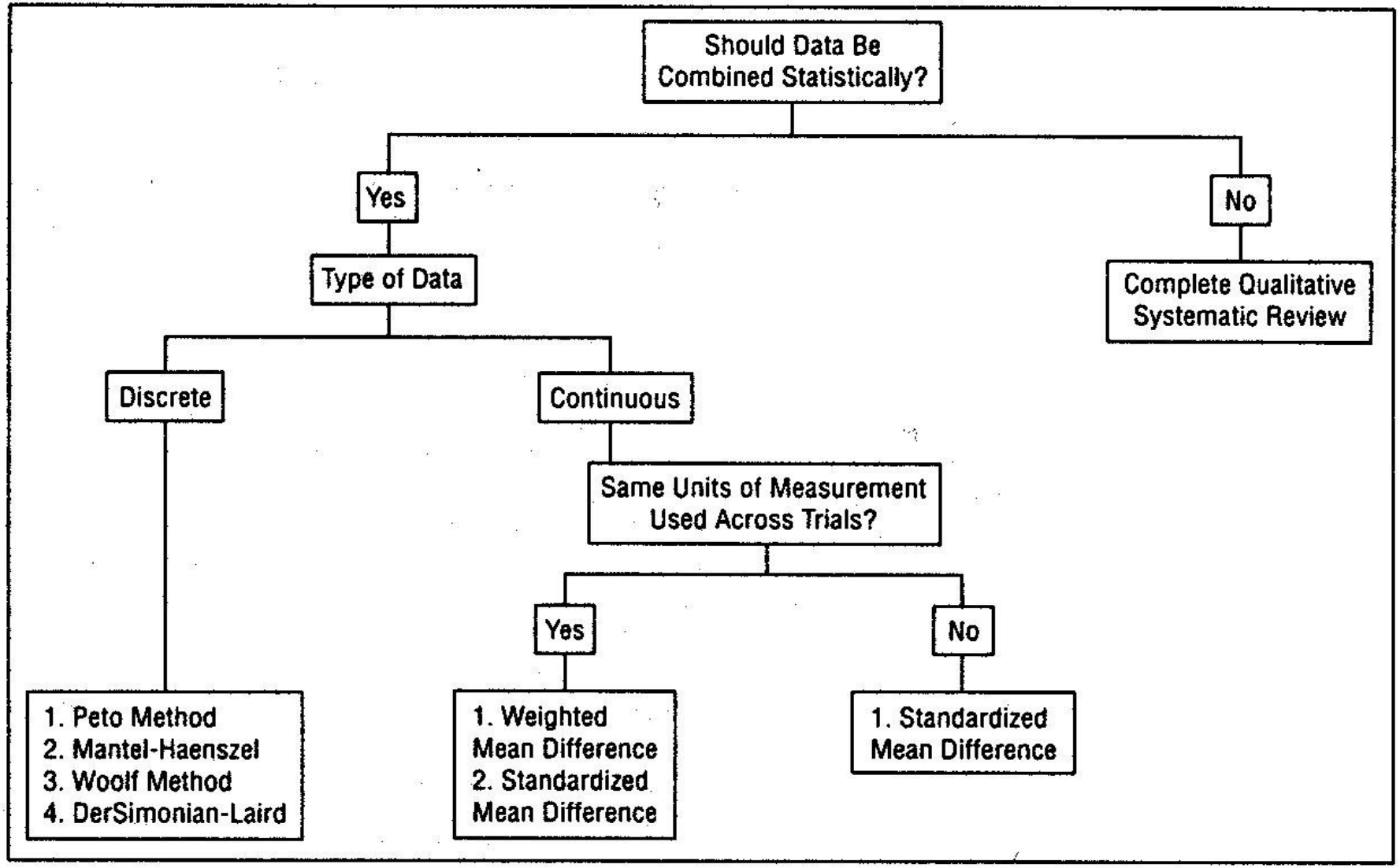
doi: 10.1136/bmj.d549

Summary estimates of treatment effect from random effects meta-analysis give only the average effect across all studies. Inclusion of prediction intervals, which estimate the likely effect in an individual setting, could make it easier to apply the results to clinical practice

mean difference in change in systolic blood pressure between the treatment group and the control group. Negative estimates indicate a greater blood pressure reduction for patients in the treatment group than the control group.

The two meta-analyses give identical summary estimates of treatment effect of −0.33 with a 95% confidence interval of −0.48 to −0.18, but the first uses a fixed effect model and the second a random effects model. In the following two sections we explain why the summary result should be interpreted differently in these two examples because of the different meta-analysis models they use.



Algorithm of statistical choices available to systematic reviewers.

Moher D et al. Arch Pediatr Adolesc Med 1998;152:915-20

5. Identify factors that can explain heterogeneity

- If heterogeneity is found, use these approaches to identify factors that can explain it:
  - Graphical methods
  - Subgroup analysis
  - Sensitivity analysis
  - Meta-regression
- Of all these approaches, subgroup analysis is easily done and interpreted

Graphical exploration

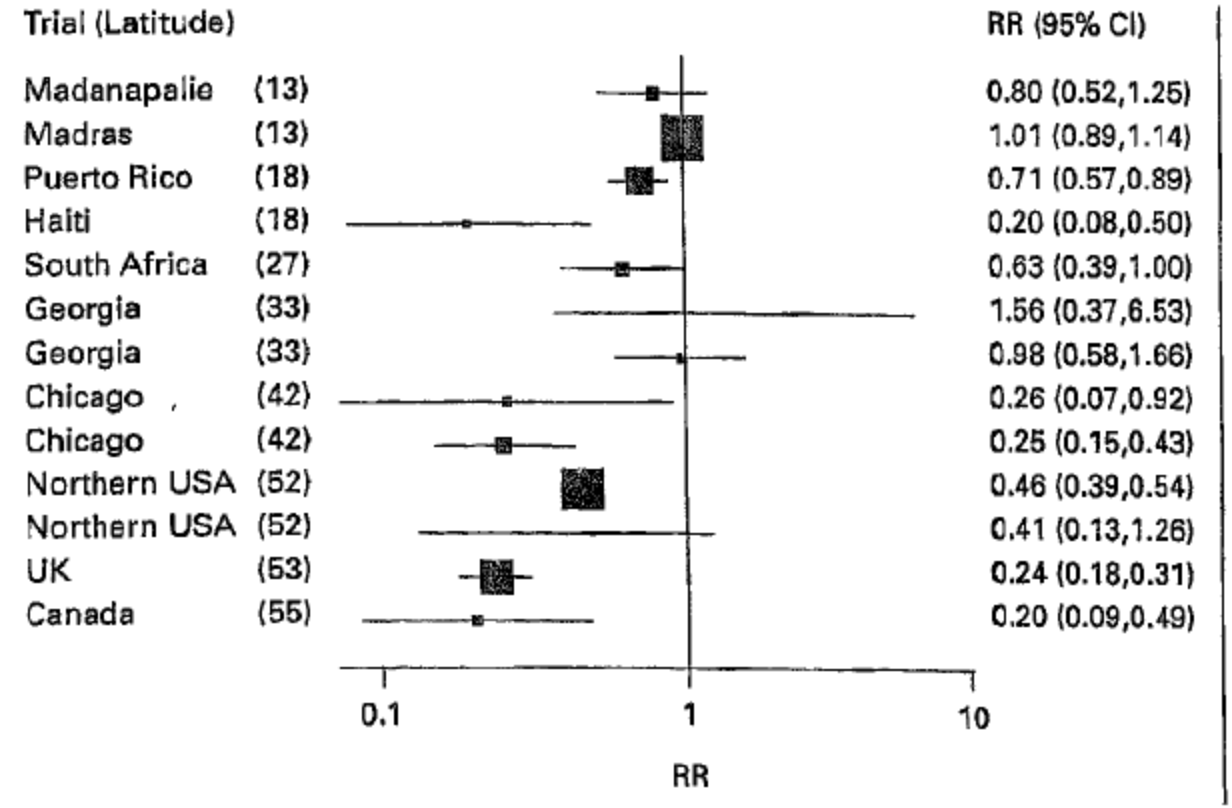


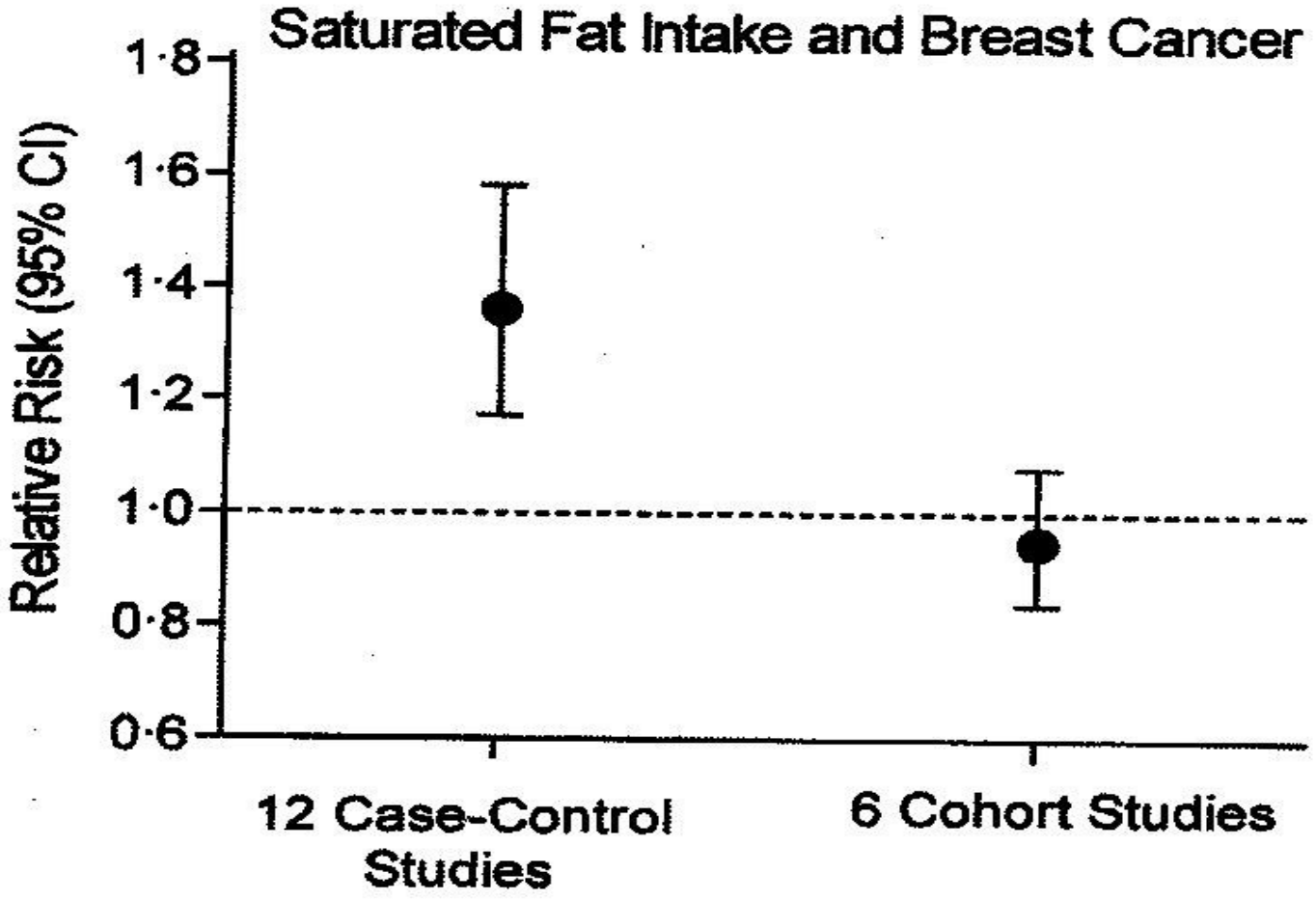
Fig 4. Forest plot of trials of BCG vaccine to prevent tuberculosis. Trials are ordered according to the latitude of the study location, expressed as degrees from the equator. No meta-analysis is shown (CI = confidence intervals, RR = relative risk) (adapted from Colditz *et al.*[47]).

I-squared = 92%

Meta-analysis on efficacy of BCG vaccination for TB

This photo is of a sign located on Interstate 89 in Vermont just south of the border with Quebec Province, Canada [source: Wikipedia]

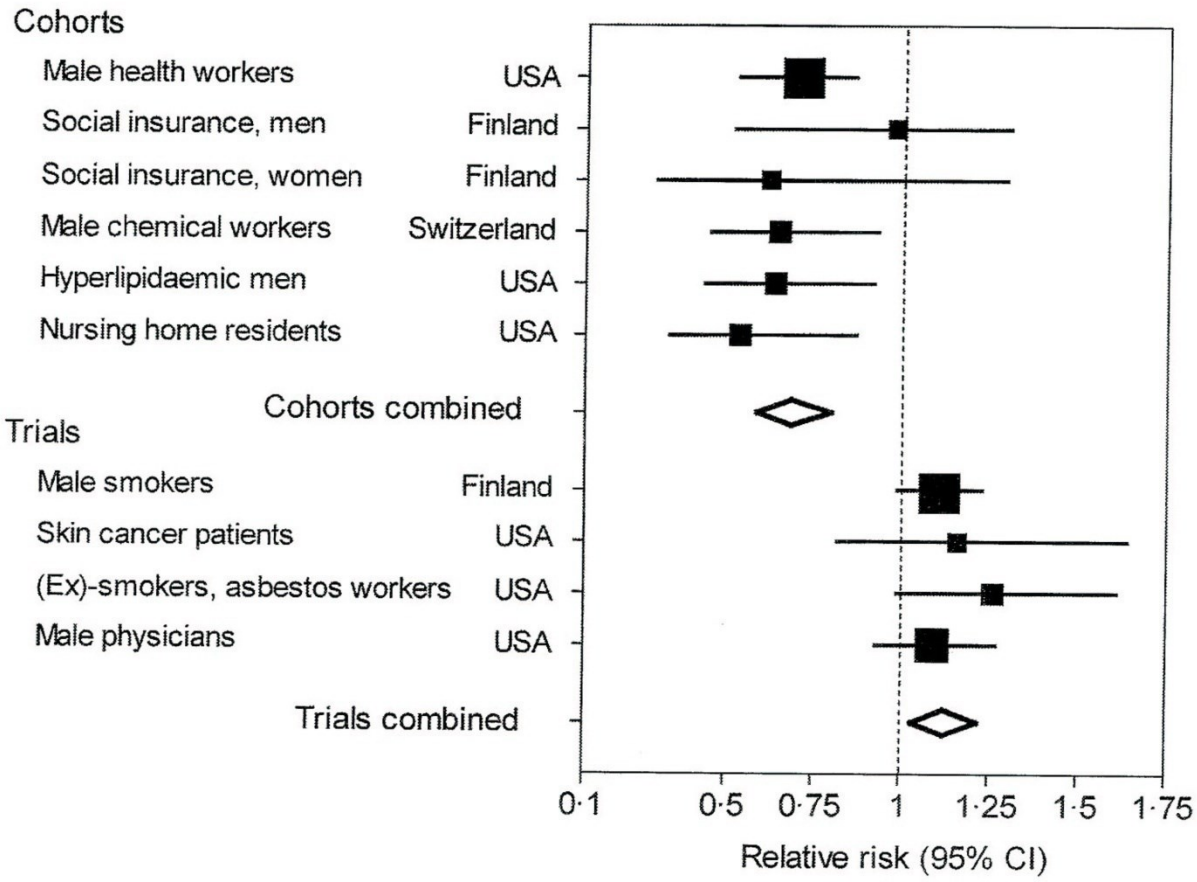
Subgroup analysis: example



Egger et al. Systematic reviews in health care. London: BMJ books, 2001.

Subgroup analysis: example

Beta-carotene intake and cardiovascular mortality



Egger et al. Systematic reviews in health care. London: BMJ books, 2001.

Subgroup analysis: example

REVIEW | Annals of Internal Medicine

Accuracy of Rapid Influenza Diagnostic Tests

A Meta-analysis

Caroline Chartrand, MD, MSc; Mariska M.G. Leeflang, DVM, PhD; Jessica Minion, MD, MSc; Timothy Brewer, MD, MPH; and Madhukar Pai, MD, PhD

Table 2. Accuracy Estimates From Subgroup Analyses

Characteristic	Pooled Sensitivity (95% CI), %	*P* Value	Pooled Specificity (95% CI), %	*P* Value
Population				
Children (60 studies)	66.6 (61.6–71.7)	<0.001	98.2 (97.5–99.0)	0.135
Adults (33 studies)	53.9 (47.9–59.8)	Reference	98.6 (98.0–98.9)	Reference
Virus type				
Influenza A (72 studies)	64.6 (59.0–70.1)	0.62	99.1 (98.7–99.4)	<0.001
Influenza B (27 studies)	52.2 (45.0–59.3)	0.050	99.8 (99.7–99.9)	<0.001
Influenza A and B (47 studies)	62.3 (55.2–69.4)	Reference	96.1 (94.4–97.8)	Reference

"Considerable heterogeneity was found in the pooled estimates, as expected. Despite our attempts to explain it through the regression model, substantial heterogeneity remained unexplained."

Exploring heterogeneity using meta-regression

- A meta-regression can be either a linear or logistic regression model
  - Can be weighted or unweighted
- Unit of analysis is a study (similar to an ecological study).
- Outcome variable: effect (e.g. log odds ratio)
- Covariates: study-level variables (e.g. Study quality, mean age of participants, etc)

Model: $\log OR = a + b_1X_1 + b_2X_2 + b_3X_3$

where, X_1, X_2, etc are study level covariates

Exploring heterogeneity using meta-regression

- Limitations:
  - Need sufficient data points (studies)
  - Confounding is a concern
  - False positives are likely and therefore need to pre-specify covariates (same as subgroup analysis)
  - Need to limit the number of covariates (otherwise over-fitting is a problem)

STATISTICS IN MEDICINE
Statist. Med. 2002; **21**:1559–1573 (DOI: 10.1002/sim.1187)

How should meta-regression analyses be undertaken and interpreted?

Simon G. Thompson*,† and Julian P. T. Higgins

MRC Biostatistics Unit, Institute of Public Health, Robinson Way, Cambridge CB2 2SR, U.K.

6. Evaluate impact of study quality on results

- Narrative discussion of impact of quality on results
- Display study quality and results in a tabular format
- Weight the data by quality (not recommended)
- Subgroup analysis by quality
- Include quality as a covariate in meta-regression

"It's publish or perish, and he hasn't published."

New Yorker, 1966

7. Explore publication bias

- Studies with significant results are more likely
  - to be published
  - to be published in English
  - to be cited by others
  - to produce multiple publications
- Including only published studies can introduce publication bias
- Most reviews do not look for publication bias
- Methods for detecting publication bias:
  - Graphical: funnel plot asymmetry
  - Tests: Egger test, Rosenthal's Fail-safe N [all have low power]

Table 1. **Steps in the Publishing Process Where Publication Bias May Intrude**

Phases of research publication	Actions contributing to and/or resulting in publication bias
Preliminary and pilot studies	Small studies, more likely to be negative (discarded failed hypotheses), are unpublished—some under "industrial secret."
Trial design, organization, and funding	Proposal selectively cites positive studies.
Institutional/ethics review board approval	No registries are kept of approved trials.
Study completion	Interim analysis shows that study is likely to be negative and project is dropped.
Report completion	Authors decide reporting a negative study is worthless and uninteresting, and no time or effort is assigned.
Report submission	Authors decide to forgo the submission of the negative study.
Journal selection	Authors decide to submit the report to a nonindexed, non–English-language, limited-circulation journal.
Editorial consideration	Editor decides that the negative study is not worth peer review process and rejects manuscript. If editor decides it is worth reviewing, manuscript goes to lower priority list.
Peer review	Reviewers conclude that the negative study does not contribute to the field and recommend rejection of the manuscript.
Author revision and resubmission	Author of rejected manuscript decides to forgo the submission of the negative study or to do it again at a later time to another journal (see "Journal selection").
Report publication	Journal delays publication of the negative study.
Lay press report	The negative study is not considered newsworthy.
Electronic database indexing	Medline, EMBASE, Best Evidence do not scan or index articles in the journal/language of publication of the negative study.
Decision-maker retrieval	Health managers and policymakers do not retrieve the negative study to dictate policy.
Further trial evidence	New trial reports discuss their findings but do not cite the findings of the negative study.
Narrative review	Experts draft a review, but the negative study is never cited.
Systematic review	Reviewer goes to extremes to identify negative reports but misses the negative study. Industry-associated reviewer uses arbitrarily selected unpublished data "on file"; this further discredits incorporation of unpublished reports in systematic reviews.
Systematic review submission	Journal editors reject a meta-analysis because it included unpublished reports not exposed to the rigor of peer review. Review then follows the same path described here for the negative study.
Practice guidelines	Evidence-based guidelines are produced based on a systematic review that missed the negative study.
Funding opportunities	Further funding opportunities are identified without consideration of the negative study.

Montori et al. Mayo Clin Proc 2000

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PLoS one

Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias

Kerry Dwan[1]*, Douglas G. Altman[2], Juan A. Arnaiz[3], Jill Bloom[4], An-Wen Chan[5], Eugenia Cronin[6], Evelyne Decullier[7], Philippa J. Easterbrook[8], Erik Von Elm[9,10], Carrol Gamble[1], Davina Ghersi[11], John P. A. Ioannidis[12,13], John Simes[14], Paula R. Williamson[1]

1 Centre for Medical Statistics and Health Evaluation, University of Liverpool, Liverpool, United Kingdom, **2** Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom, **3** Clinical Pharmacology Unit, UASP Hospital Clínic, Barcelona, Spain, **4** Moorfields Eye Hospital, London, United Kingdom, **5** Randomized Controlled Trials Unit, Canadian Institutes of Health Research, Ottawa, Canada, **6** Healthier Communities/Public Health, Greenwich Council, London, England, **7** Clinical Epidemiology Unit, DIM-Hospices Civils de Lyon, Lyon, France, **8** Department of HIV/GUM, King's College London, London, United Kingdom, **9** Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, **10** German Cochrane Centre, Department of Medical Biometry and Medical Informatics, University Medical Centre Freiburg, Freiburg, Germany, **11** NHMRC Clinical Trials Centre, Camperdown, Australia, **12** Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece, **13** Institute for Clinical Research and Health Policy Studies, Department of Medicine, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, United States of America, **14** National Health and Medical Research Council (NHMRC) Clinical Trials Centre, University of Sydney, Sydney, Australia

Abstract

Background: The increased use of meta-analysis in systematic reviews of healthcare interventions has highlighted several types of bias that can arise during the completion of a randomised controlled trial. Study publication bias has been recognised as a potential threat to the validity of meta-analysis and can make the readily available evidence unreliable for decision making. Until recently, outcome reporting bias has received less attention.

Methodology/Principal Findings: We review and summarise the evidence from a series of cohort studies that have assessed study publication bias and outcome reporting bias in randomised controlled trials. Sixteen studies were eligible of which only two followed the cohort all the way through from protocol approval to information regarding publication of outcomes. Eleven of the studies investigated study publication bias and five investigated outcome reporting bias. Three studies have found that statistically significant outcomes had a higher odds of being fully reported compared to non-significant outcomes (range of odds ratios: 2.2 to 4.7). In comparing trial publications to protocols, we found that 40–62% of studies had at least one primary outcome that was changed, introduced, or omitted. We decided not to undertake meta-analysis due to the differences between studies.

Conclusions: Recent work provides direct empirical evidence for the existence of study publication bias and outcome reporting bias. There is strong evidence of an association between significant results and publication; studies that report positive or significant results are more likely to be published and outcomes that are statistically significant have higher odds of being fully reported. Publications have been found to be inconsistent with their protocols. Researchers need to be aware of the problems of both types of bias and efforts should be concentrated on improving the reporting of trials.

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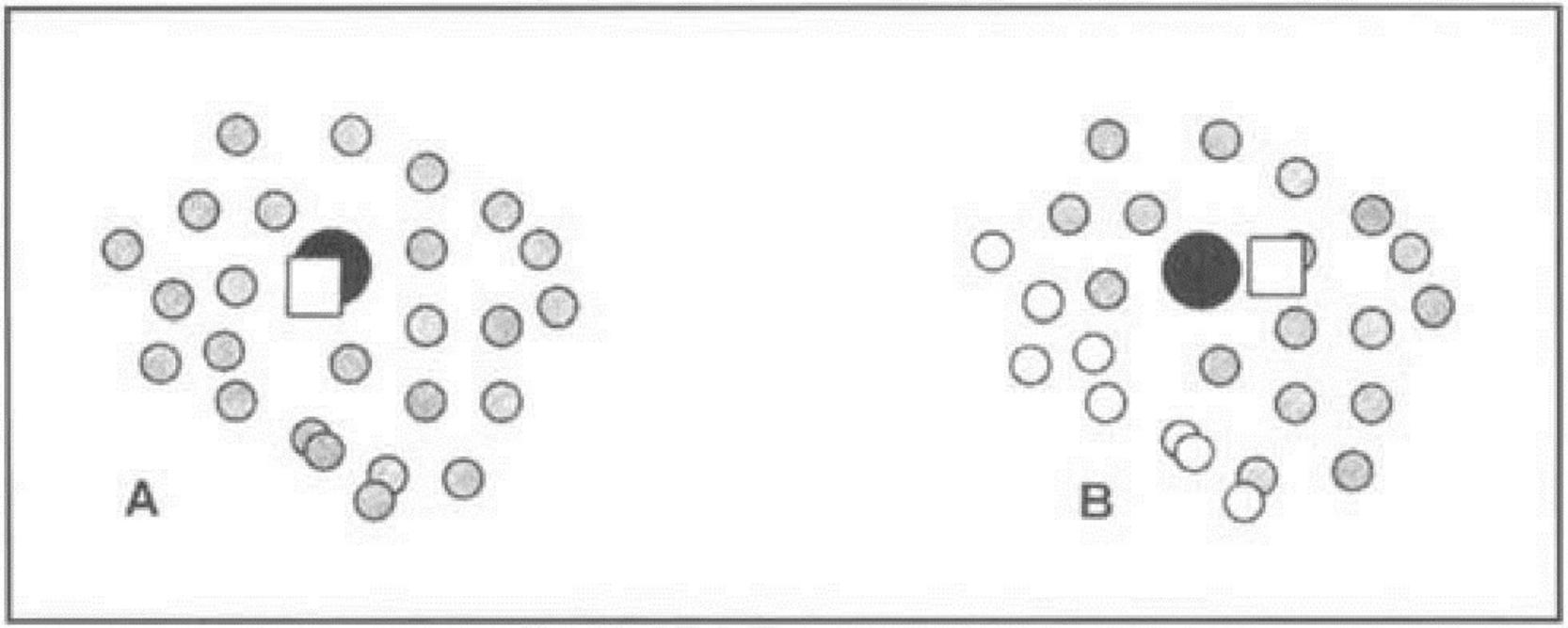
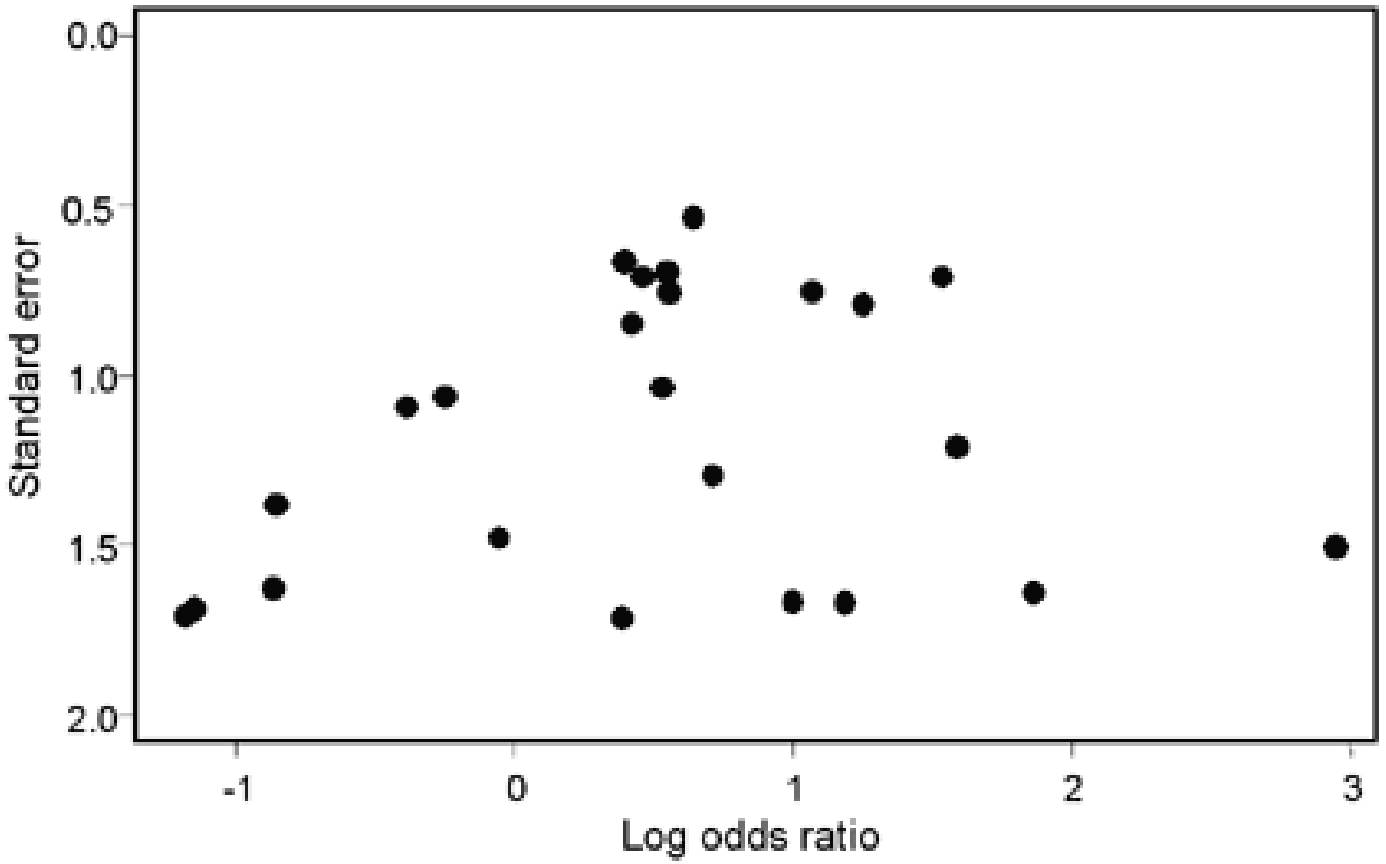


Figure 1. Publication bias. A, The black circle represents the underlying truth. The white square represents the pooled estimate from a systematic review of all the evidence (small shaded circles). B, The white circles represent evidence that was not identified by the reviewers because it was not published. Note the error in the pooled estimate (publication bias).

Montori et al. Mayo Clin Proc 2000

Funnel plot to detect publication bias



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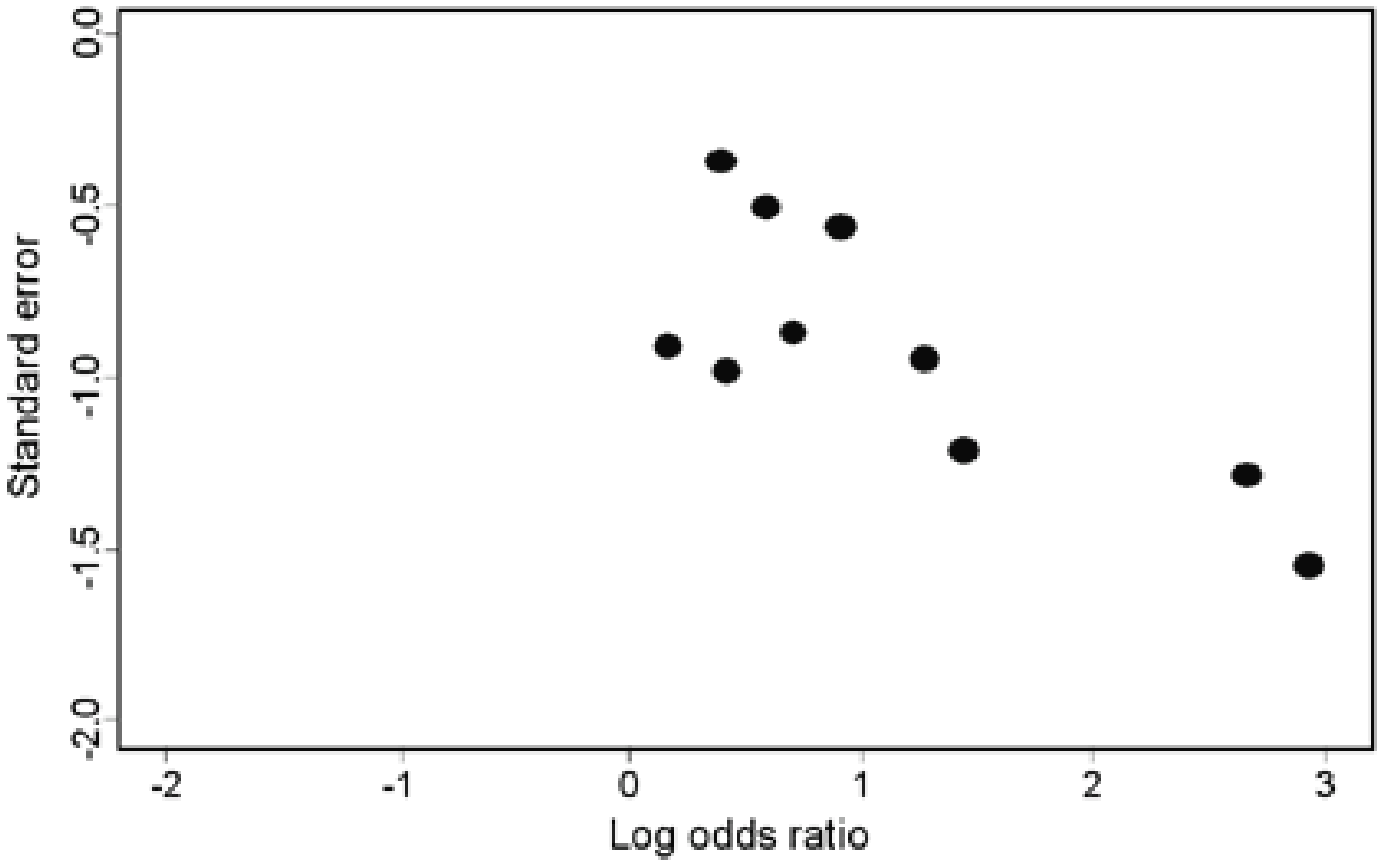
Funnel plot to detect publication bias



http://www.cochrane-net.org/openlearning/index.htm

Testing for funnel plot asymmetry

Reference	Basis of test
(Begg 1994)	Rank correlation between standardized intervention effect and its standard error.
(Egger 1997a)	Linear regression of intervention effect estimate against its standard error, weighted by the inverse of the variance of the intervention effect estimate.
(Tang 2000)	Linear regression of intervention effect estimate on $1/\sqrt{N_{tot}}$, with weights N_{tot}.
(Macaskill 2001)*	Linear regression of intervention effect estimate on N_{tot}, with weights $S \times F/N_{tot}$.
(Deeks 2005)*	Linear regression of log odds ratio on $1/\sqrt{ESS}$ with weights ESS, where effective sample size $ESS = 4N_E \times N_C / N_{tot}$.
(Harbord 2006)*	Modified version of the test proposed by Egger et al., based on the 'score' (O –E) and 'score variance' (V) of the log odds ratio.
(Peters 2006)*	Linear regression of intervention effect estimate on $1/N_{tot}$, with weights $S \times F/N_{tot}$.
(Schwarzer 2007)*	Rank correlation test, using mean and variance of the non-central hypergeometric distribution.
(Rücker 2008)	Test based on arcsine transformation of observed risks, with explicit modelling of between-study heterogeneity.

* Test formulated in terms of odds ratios, but may be applicable to other measures of intervention effect.

N_{tot} is the total sample size, N_E and N_C are the sizes of the experimental and control intervention groups, S is the total number of events across both groups and $F = N_{tot} - S$. Note that only the first three of these tests (Begg 1994, Egger 1997a, Tang 2000) can be used for continuous outcomes.

http://handbook.cochrane.org/

Recommendations by Cochrane

- As a rule of thumb, tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is too low to distinguish chance from real asymmetry.
- Tests for funnel plot asymmetry should not be used if all studies are of similar sizes (similar standard errors of intervention effect estimates).
- Results of tests for funnel plot asymmetry should be interpreted in the light of visual inspection of the funnel plot. For example, do small studies tend to lead to more or less beneficial intervention effect estimates? Are there studies with markedly different intervention effect estimates (outliers), or studies that are highly influential in the meta-analysis?
- When there is evidence of small-study effects, publication bias should be considered as only one of a number of possible explanations.
- Although funnel plots, and tests for funnel plot asymmetry, may alert review authors to a problem which needs considering, they do not provide a solution to this problem.
- Finally, review authors should remember that, because the tests typically have relatively low power, even when a test does not provide evidence of funnel plot asymmetry, bias (including publication bias) cannot be excluded.

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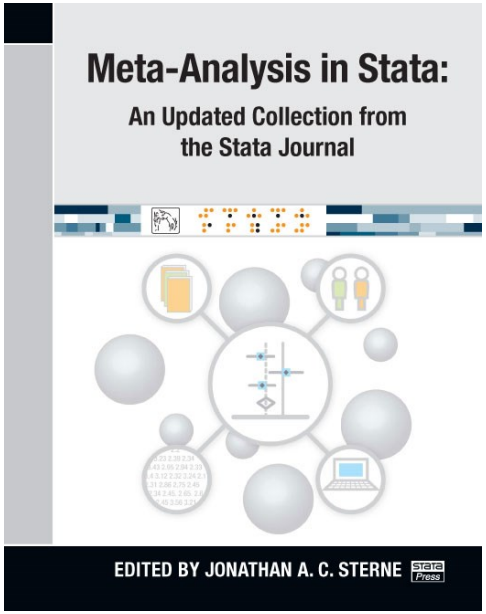
Meta-analysis Software



- Free
  - RevMan 5 [Review Manager]
  - Meta-Analyst
  - Epi Meta
  - Easy MA
  - Meta-DiSc
  - Meta-Stat
- Commercial
  - Comprehensive Meta-analysis Version 2
  - MIX 2.0 Pro
  - Meta-Win
  - WEasy MA
- General stats packages (commercial)
  - Stata
  - SAS
  - R

Meta-analysis software

BMC Medical Research Methodology

BioMed Central

Correspondence

Open Access

A systematic comparison of software dedicated to meta-analysis of causal studies

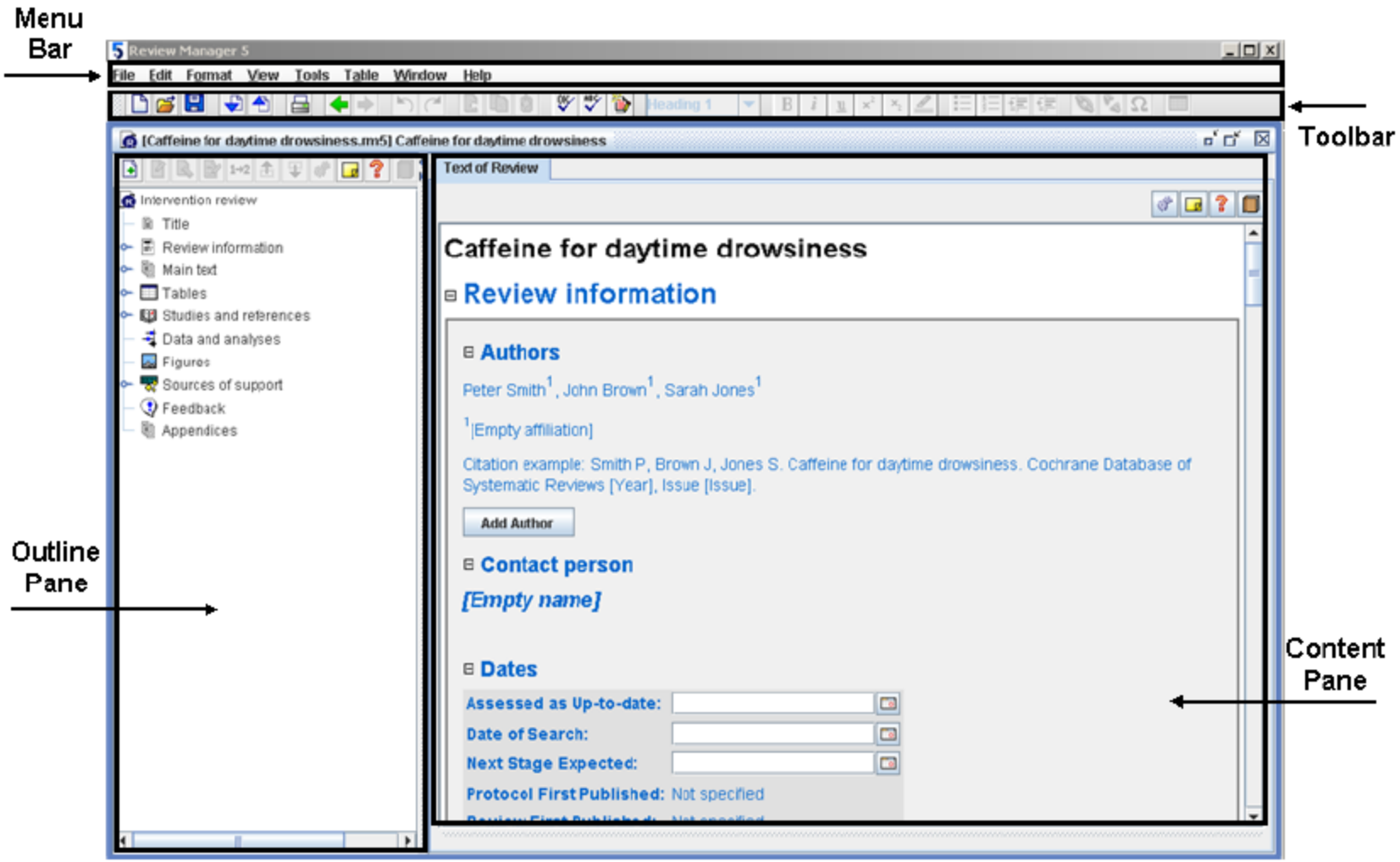
Leon Bax*[1,2], Ly-Mee Yu[3], Noriaki Ikeda[2] and Karel GM Moons[1]

Table 3: Meta-analysis software – basic feature comparison

	CMA	MetAnalysis	MetaWin	MIX	RevMan	WEasyMA
General						
URL	*meta-analysis.com*	-	*metawinsoft.com*	*mix-for-meta-analysis.info*	*cc-ims.net/RevMan*	*weasyma.com*
Corporate single user price	~$1295.00	~$75.00	~$150.00	Free	$650	~$490.00
Student single user price	~$395.00	~$75.00	~$75.00	Free	Free	~$280.00
Download/program size	30 Mb	5 Mb	9 Mb	20 Mb/50 Mb	9 Mb	3 Mb
Compatibility	Windows	Windows	Windows	Windows	Windows	Windows
Last update	2006	2005	2002	2006	2005	2002
License	Single user	Single user	Single user	Open	Open	Single user
Input options						
Manual input	✓	✓	✓	✓	✓	✓
Copy & paste	✓		✓	✓	(✓)	
Text file import			✓	✓		
File import (Excel, other software)			✓	✓		
Descriptive dichotomous, e.g. n(total), n(y = 1)	✓	✓	✓	✓	✓	✓
Descriptive continuous, e.g. n, m, sd	✓		✓	✓	✓	
Comparative, e.g. theta, se/var	✓		✓	✓	✓	
Multi-format (mixed in one data set)	✓					
Single data input/selection	✓	✓		✓	✓	✓
Maximum number of studies	Unlimited	Unlimited	Unlimited	100	Unlimited	Unlimited
Information sources						
Within-program HTML help			✓	(✓)	✓	(✓)
Printable manual	✓	✓	✓		✓	
Description of methods/calculations		(✓)	✓	(✓)	✓	
Additional information sources (PDFs/tutorials)	✓		✓	✓		
Up-to-date website	✓		✓	✓	✓	×

Bax et al. BMC 2007

RevMan 5


Menu Bar
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Toolbar
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Text of Review
Intervention review
Title
Review information
Main text
Tables
Studies and references
Data and analyses
Figures
Sources of support
Feedback
Appendices
Outline Pane
Caffeine for daytime drowsiness
Review information
Authors
Peter Smith[1], John Brown[1], Sarah Jones[1]
[1]Empty affiliation]
Citation example: Smith P, Brown J, Jones S. Caffeine for daytime drowsiness. Cochrane Database of Systematic Reviews [Year], Issue [Issue].
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Dates
Assessed as Up-to-date:
Date of Search:
Next Stage Expected:
Protocol First Published: Not specified
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File Edit Data Graphics Statistics User Window Help

Review

	Command
1	use "C:\Documents and S
2	metan deaths1 deaths0
3	metan deaths1 deaths0
4	metan deaths1 alive1 de

Variables

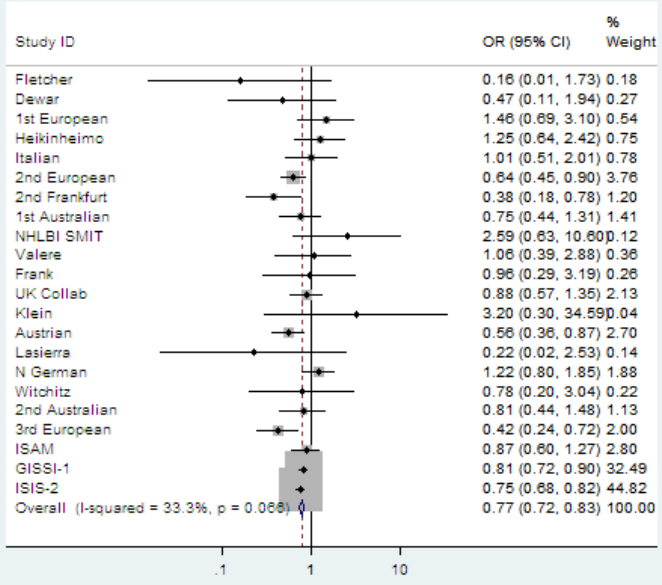
Name	Label
trial	Trial number
trialnam	Trial name
year	Year of publication
deaths1	Treated deaths
deaths0	Control deaths
alive1	
alive0	
logor	
selogor	
_SS	Sample size
_ES	OR
_selogES	se(logOR)
_LCI	Lower CI (OR)
_UCI	Upper CI (OR)
_WT	M-H weight

```
16                |   1.096        0.903      1.331        2.34
17                |   0.889        0.456      1.734        0.25
18                |   0.893        0.644      1.239        1.13
19                |   0.611        0.435      0.858        1.66
20                |   0.931        0.761      1.139        2.88
21                |   0.894        0.841      0.950       32.99
22                |   0.856        0.811      0.904       44.01
------------------+------------------------------------------------
M-H pooled RR     |   0.874        0.844      0.906      100.00
------------------+------------------------------------------------

  Heterogeneity chi-squared =   34.6
  I-squared (variation in RR attrib

  Test of RR=1 : z=   7.41 p = 0.00
option plot not allowed
r(198);

. metan deaths1 alive1 deaths0 aliv

          Study           |     OR    [9
--------------------------+------------
Fletcher                  |   0.159
Dewar                     |   0.471
1st European              |   1.460
Heikinheimo               |   1.248
Italian                   |   1.012
2nd European              |   0.635
2nd Frankfurt             |   0.378
1st Australian            |   0.754
NHLBI SMIT                |   2.587
Valere                    |   1.061
Frank                     |   0.959
UK Collab                 |   0.876
Klein                     |   3.200
Austrian                  |   0.562
Lasierra                  |   0.222
N German                  |   1.215
Witchitz                  |   0.778
2nd Australian            |   0.806
3rd European              |   0.416
ISAM                      |   0.872
GISSI-1                   |   0.807
ISIS-2                    |   0.746
--------------------------+------------
M-H pooled OR             |   0.774
--------------------------+------------

  Heterogeneity chi-squared =   31.5
  I-squared (variation in OR attrib

  Test of OR=1 : z=   7.76 p = 0.00

.
```

Stata Graph - Graph

File Edit Object Graph Tools Help

Graph



Command

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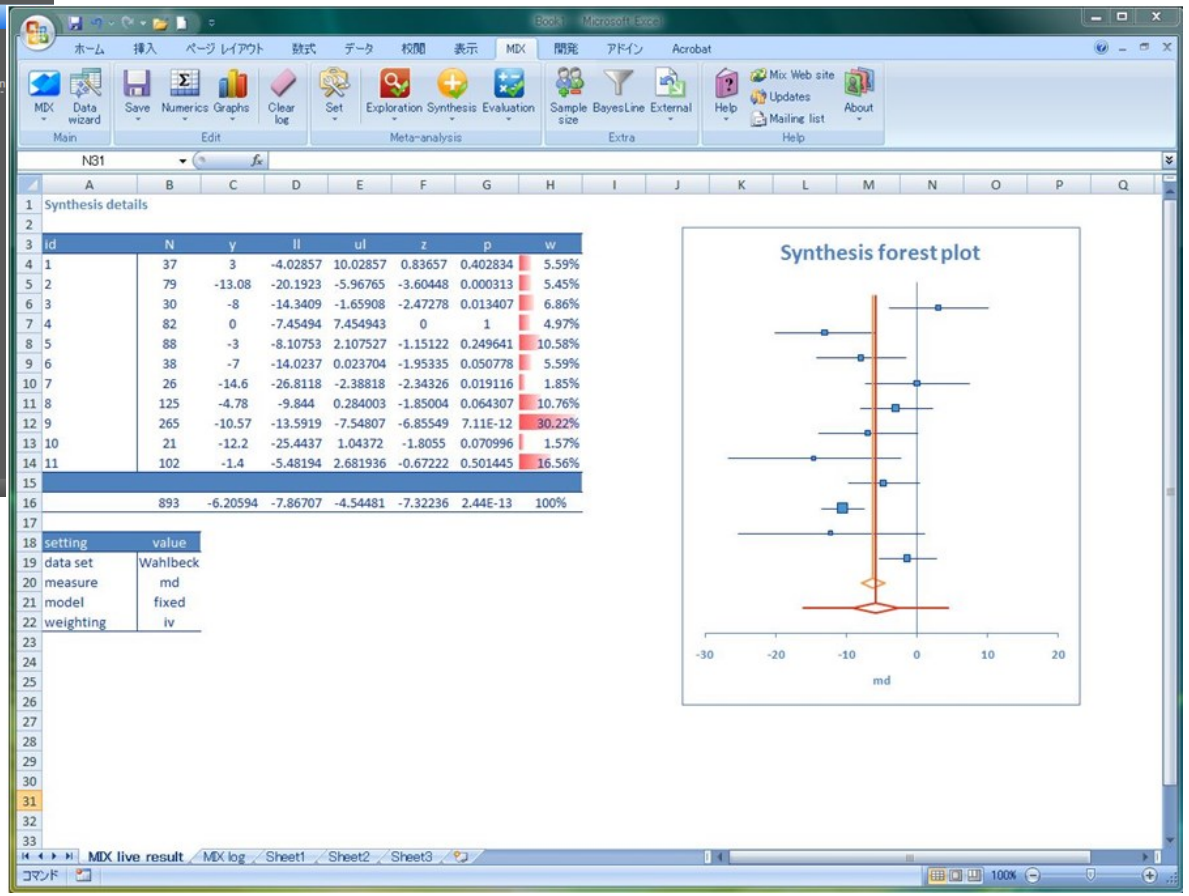

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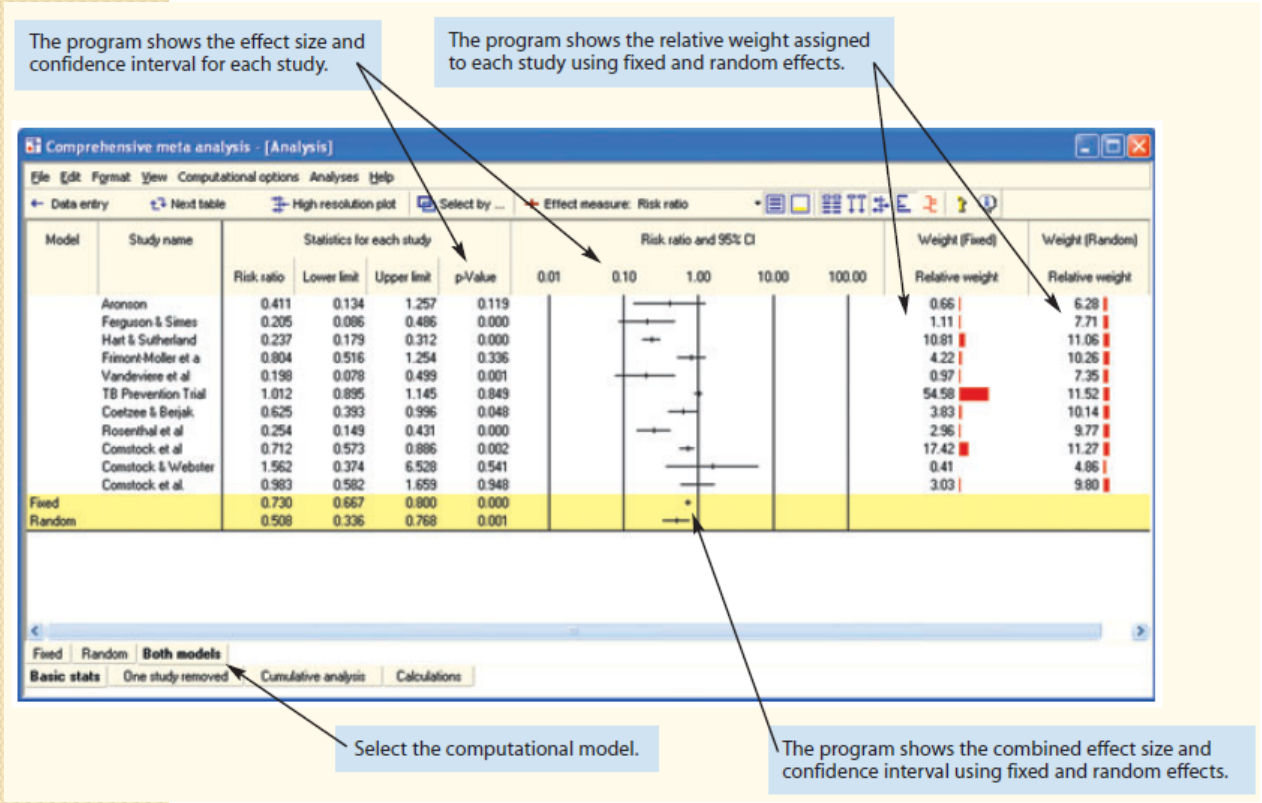
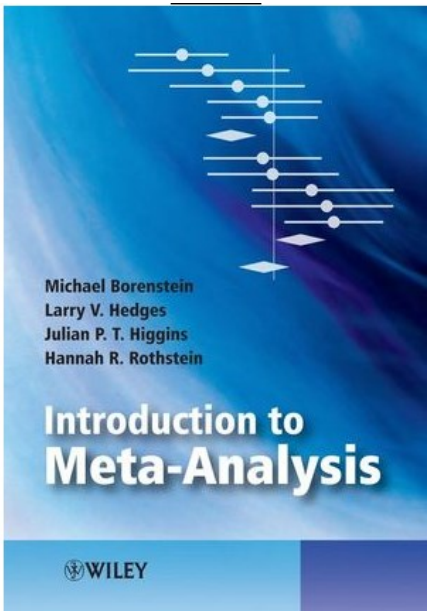
A computer program for meta-analysis

Version 2

http://www.meta-analysis.com/





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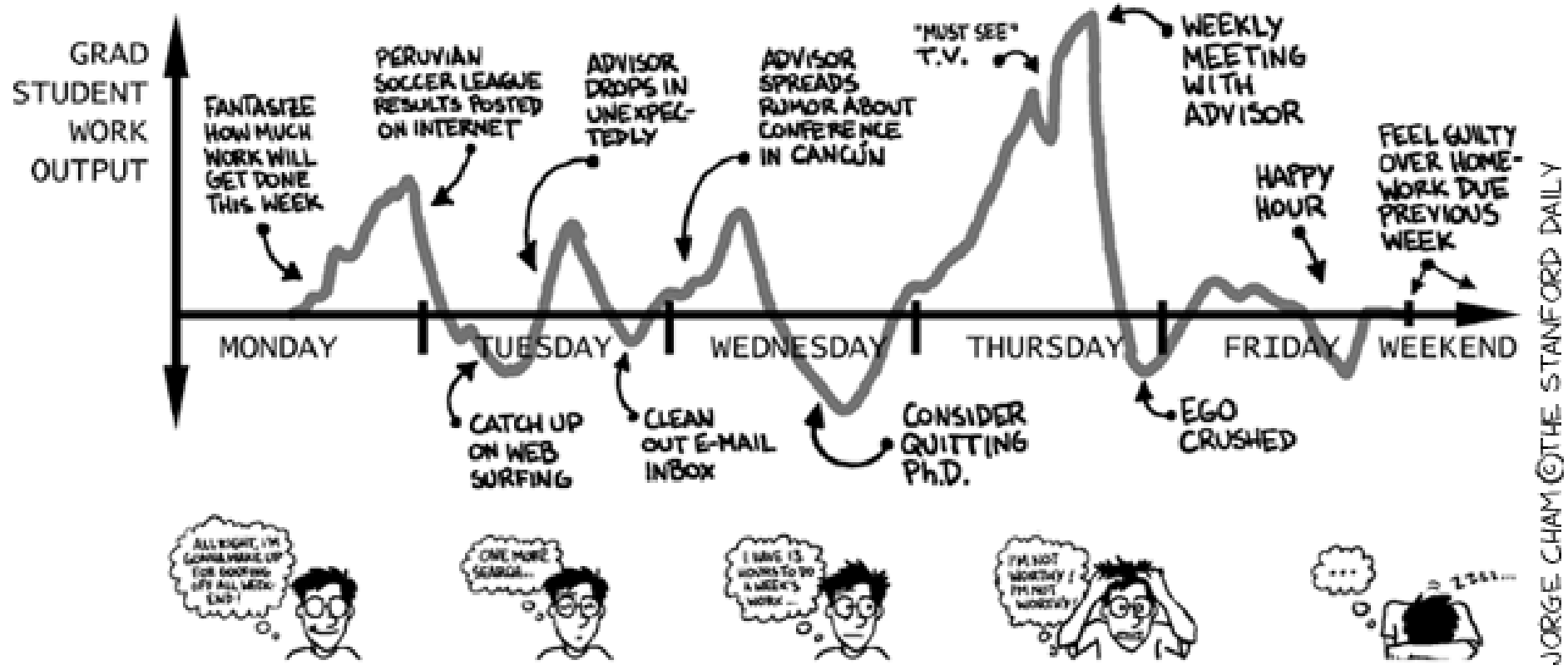
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FANTASIZE HOW MUCH WORK WILL GET DONE THIS WEEK
PERUVIAN SOCCER LEAGUE RESULTS POSTED ON INTERNET
ADVISOR DROPS IN UNEXPECTEDLY
ADVISOR SPREADS RUMOR ABOUT CONFERENCE IN CANCUN
"MUST SEE" T.V.
WEEKLY MEETING WITH ADVISOR
HAPPY HOUR
FEEL GUILTY OVER HOMEWORK DUE PREVIOUS WEEK
MONDAY
TUESDAY
WEDNESDAY
THURSDAY
FRIDAY
WEEKEND
CATCH UP ON WEB SURFING
CLEAN OUT E-MAIL INBOX
CONSIDER QUITTING Ph.D.
EGO CRUSHED
ALL RIGHT, I'M GONNA MAKE UP FOR SLACKING OFF ALL WEEK. END!
ONE MORE SEARCH...
I HAVE 15 HOURS TO DO A WEEK'S WORK...
I'M LOST WORTHLESS! I'M NOT WORTHY!
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