Meta-Analysis with R

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Contents of This Presentation

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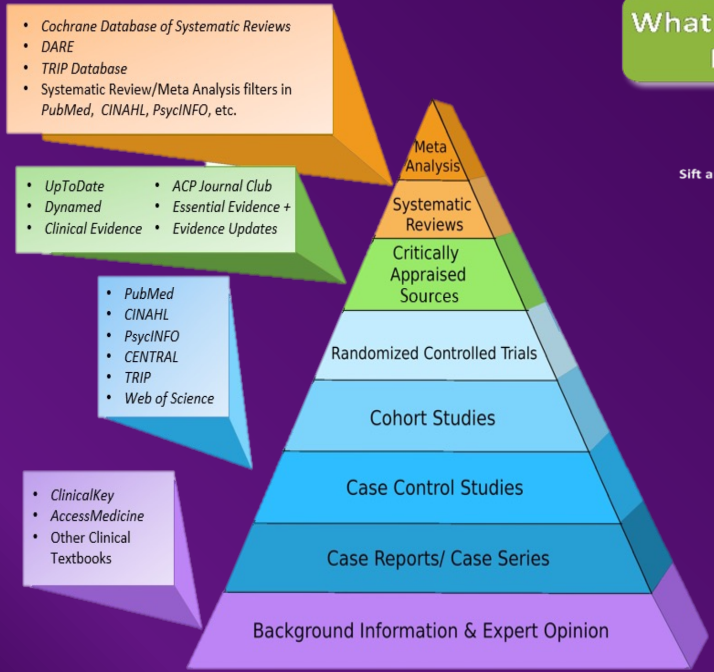
01 Systematic Review

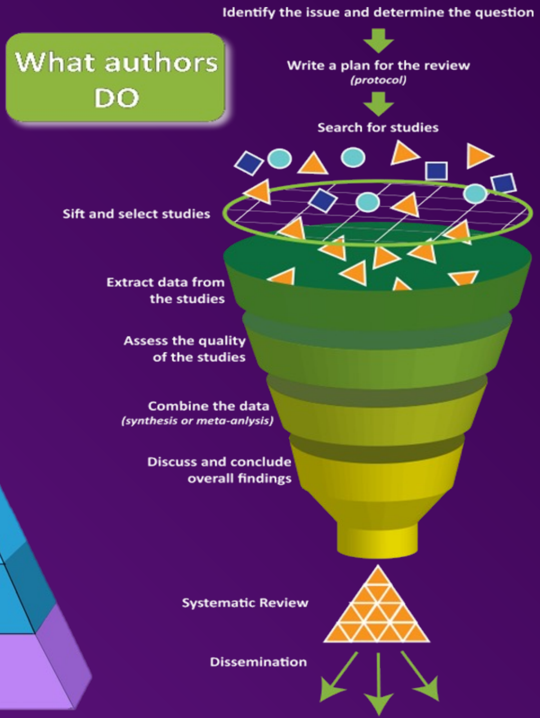
Introduction to Systematic Review and Meta-Analysis

“A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusions can be drawn and decisions made.”

-Antman 1992, Oxman 1993

The EBM Pyramid





02

Meta-Analysis

When and How To Conduct Meta-Analysis

Why To Have a Meta-Analysis

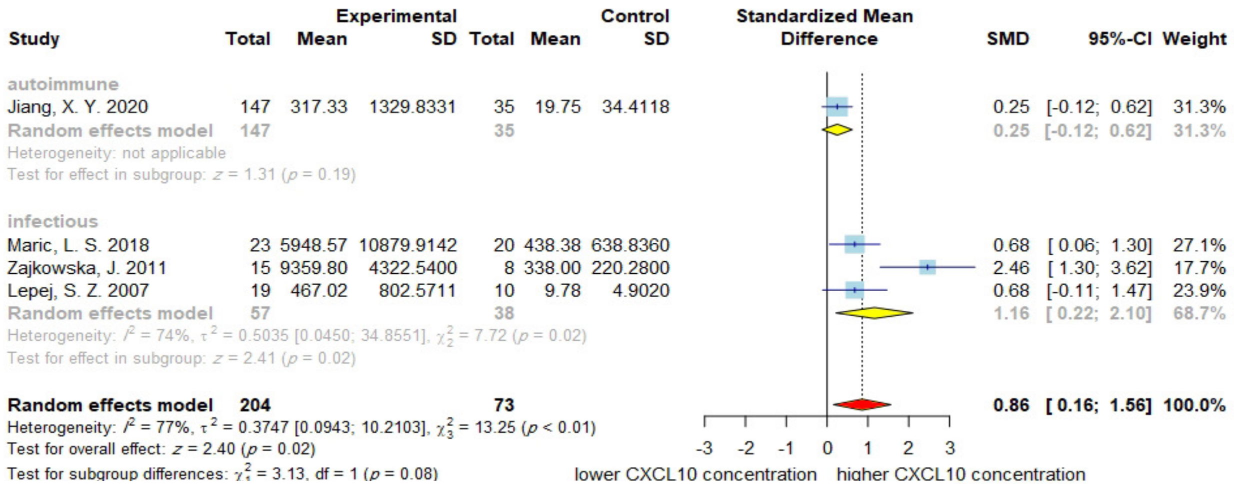
Inconsistency

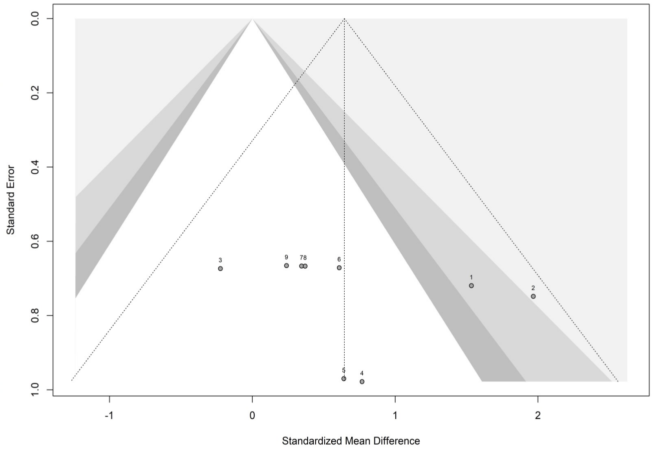
Inconsistent results between the previously conducted studies

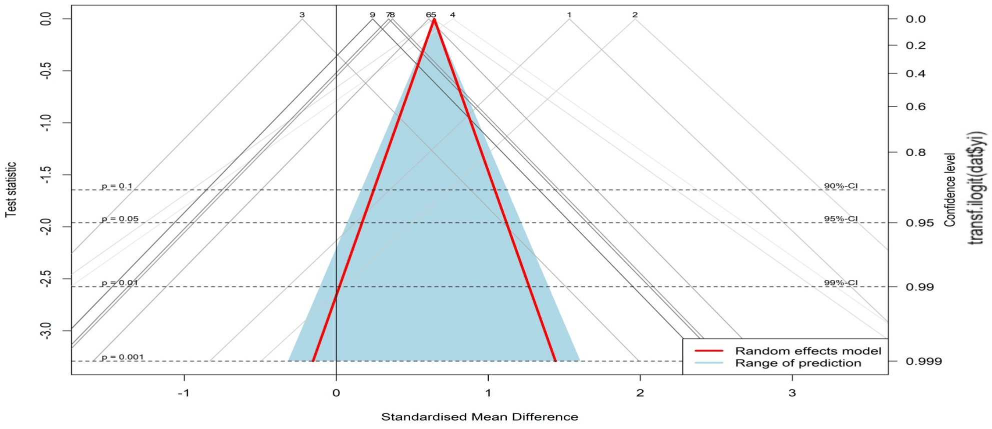
Better Presentation

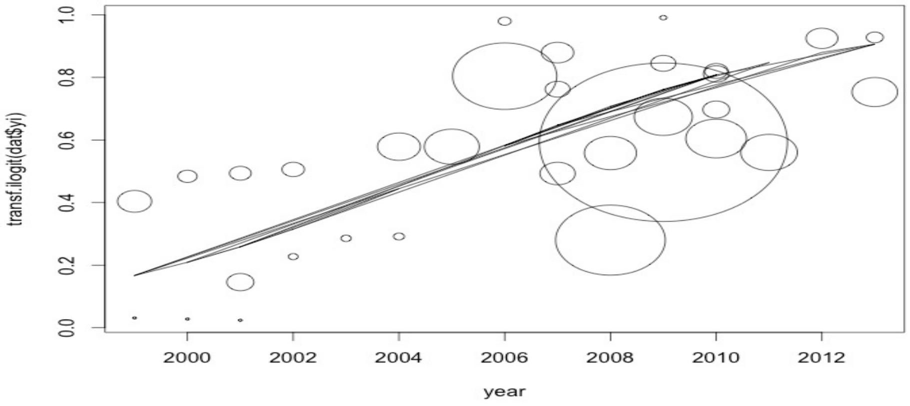
Quantitative data helps to present the result of the study in a more understandable way

Some Figures You Usually See When Looking at Meta-Analyses

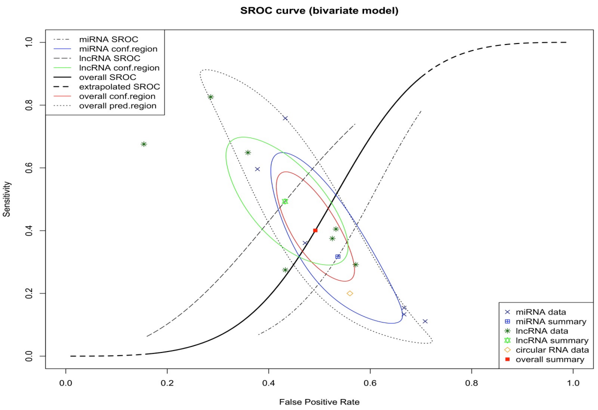


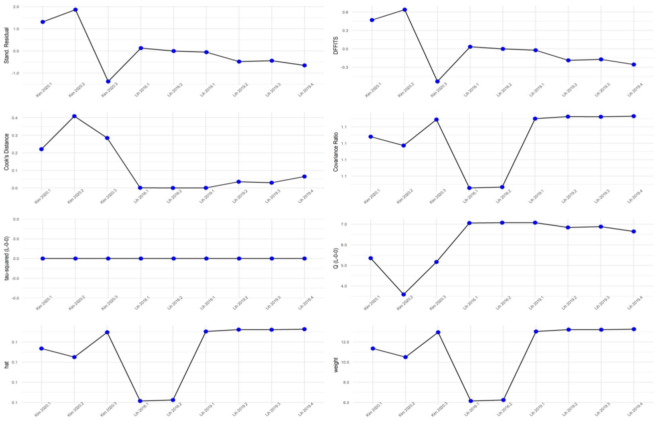


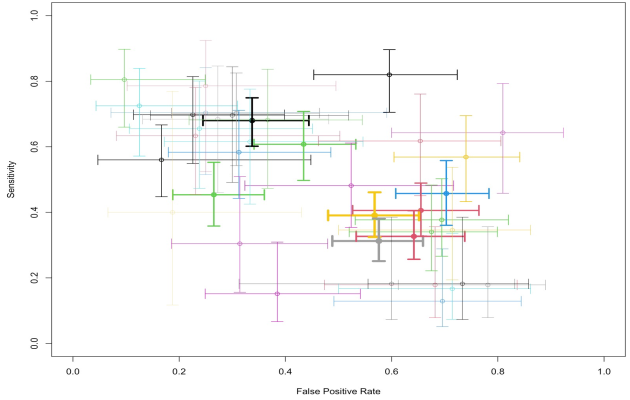


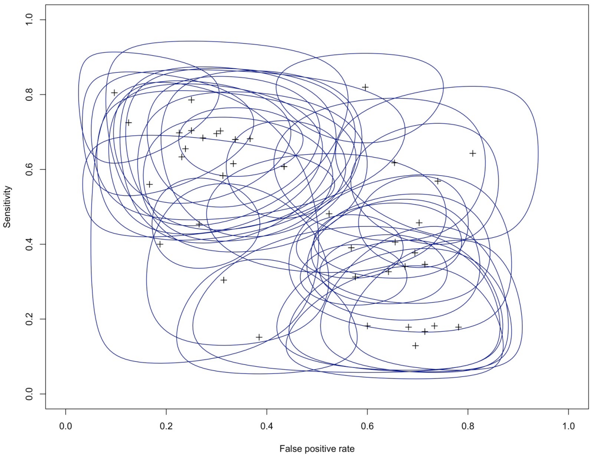


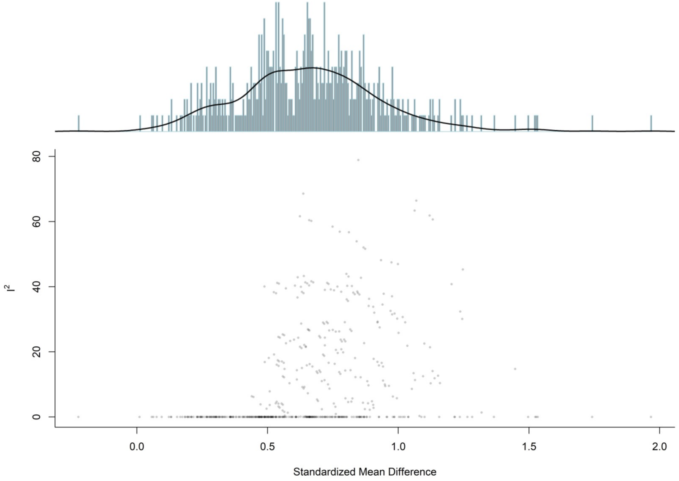
Some Figures You **Cannot** Usually See When Looking at Meta-Analyses

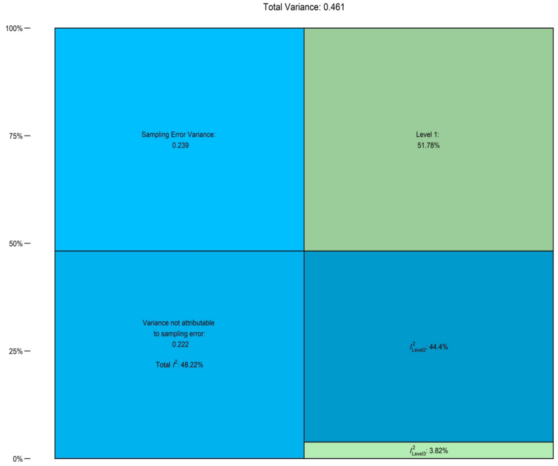












What is General Idea Behind Meta-Analysis?

It is Weighted Mean of Effect sizes

Effect Size

the effect size is a measure of the magnitude of the relationship or difference between two groups or conditions. It is used to quantitatively summarize the results of multiple studies and determine whether there is a consistent effect across studies.

Types of Effect Sizes

Mean

- Single Group Mean
- Standardized Mean difference
    - Cohen's d
    - Hedges' g
    - Etc.

Fractions

- Proportions
- Ratios
    - Odds
    - Risk
- Incidence Rate Ratio

Correlation

- Pearson Correlation
    - Usually is transformed into Fisher's Z

Brief Insight on Calculation of Effect sizes

Hedges's SMD

$d = (M1 - M2) / Sdpooled$
$SDpooled = sqrt((SD1^2 + SD2^2) / 2)$
$g = d * (1 - 3/(4*N-9))$

Log Odds Ratio

$Ln(OR)$

Fisher's Z-Transform

$r = \Sigma[(Xi - \bar{x})(Yi - \bar{y})] / [\sqrt{\Sigma}(Xi - \bar{x})^2 \sqrt{\Sigma}(Yi - \bar{y})^2]$
$SE(r) = [(1 - r^2) / \sqrt{(n - 2)}]$
$z = 0.5 * \ln[(1 + r) / (1 - r)]$
$SE(z) = 1/\sqrt{(n-3)}$

Types of Meta-Analysis

Fixed-Effect Model

A fixed-effect meta-analysis assumes that all studies included in the analysis share a common true effect size, and any variation in the observed effect sizes is due to sampling error or chance.

Random-Effect Model

A random-effects meta-analysis, on the other hand, assumes that the true effect size may vary across studies, and any observed differences in effect sizes are due to both sampling error and true variation in the effect sizes across studies.

Questions

Whoa!

Let’s take a plunge into what we can practically do ...

03

Practice with R

Hands-on Practice on Doing Meta-Analysis with R

Four Sample Analyses

	Type	Data	Multiple Groups
Task 1	Percentage	dat.baker2009	✗
Task 2	SMD	SuicidePrevention	✓
Task 3	OR	DepressionMortality	✓
Task 4	Correlation	HealthWellbeing	✗

Usual Packages for the Meta-Analysis

- ❖ meta

A comprehensive package to conduct meta-analysis and present and visualize the results.

- ❖ metafor

A thorough package that provide tools to calculate various effect sizes, conduct meta-analysis, and visualize results.

- ❖ MAd

A comprehensive package for calculating and converting effect sizes.

- ❖ rmeta

A package that provide tools to visualize meta-analysis results.

- ❖ dmetar

Package guide of the “Doing Meta-Analysis in R” book.

- ❖ netameta

A package for conducting network meta-analysis.

</> How to Calculate Effect Sizes

- escalc() function from metafor package could be used for calculation of various effect sizes. This function gets the results statistics of studies and return the TE and seTE. Types of given data are:

  - Dichotomous data:
    - RR
    - OR
    - RD
    - AS (*arcsine square root transformed risk difference)*
    - PETO

  - If the data is not dichotomous, but it is a dichotomized version of quantative data:

    - "PBIT" for the *probit transformed risk difference* as an estimate of the standardized mean difference,
    - "OR2DN" for the *transformed odds ratio* as an estimate of the standardized mean difference (assuming normal distributions),
    - "OR2DL" for the *transformed odds ratio* as an estimate of the standardized mean difference (assuming logistic distributions).

- Quantitative Data:
  - MD
  - SMD
  - "SMDH" for the *standardized mean difference* with heteroscedastic population variances in the two groups (Bonett, 2008, 2009),
  - "SMD1" for the *standardized mean difference* where the mean difference is divided by the standard deviation of the second group (and "SMD1H" for the same but with heteroscedastic population variances),
  - "ROM" for the *log transformed ratio of means* (Hedges et al., 1999; Lajeunesse, 2011).

- Transformed Log odds ratio from SMD:
  - "D2ORN" for the *transformed standardized mean difference* as an estimate of the log odds ratio (assuming normal distributions),
  - "D2ORL" for the *transformed standardized mean difference* as an estimate of the log odds ratio (assuming logistic distributions).

- differences between the two groups with respect to their variability:
  - "CVR" for the *log transformed coefficient of variation ratio*,
  - "VR" for the *log transformed variability ratio*.

- Event Count:
  - "IRR" for the *log incidence rate ratio*,
  - "IRD" for the *incidence rate difference*,
  - "IRSD" for the *square root transformed incidence rate difference*.

- Variable Association:
  - "COR" for the *raw correlation coefficient*,
  - "UCOR" for the *raw correlation coefficient* corrected for its slight negative bias (based on equation 2.3 in Olkin & Pratt, 1958),
  - "ZCOR" for *Fisher's r-to-z transformed correlation coefficient* (Fisher, 1921).

Meta-Analysis Using meta package

1. Importing the data
2. Inspecting the data and choosing the effect size
3. Doing the meta-analysis
4. Drawing the forest plot
5. Drawing funnel plot
6. Checking publication bias
7. Sensitivity and influence analysis
8. Trim and fill
9. Gosh plot (metafor)

Meta-Analysis Using meta package

1. Importing the data
2. Inspecting the data

```r
effect <- escalc(measure = "SMD", m1i = mean.e, m2i = mean.c,
                 sd1i = sd.e, sd2i = sd.c,
                 n1i = n.e, n2i = n.c, data = df_SMD)

head(effect)
```

```
> head(df_meta)
# A tibble: 6 × 10
  author             n.e mean.e  sd.e   n.c mean.c  sd.c pubyear age_group control
  <chr>            <dbl>  <dbl> <dbl> <dbl>  <dbl> <dbl>   <dbl> <chr>     <chr>
1 Berry et al.        90  15.0   3.29    95  15.5   4.41    2006 gen       WLC
2 DeVries et al.      77  16.2   5.35    69  20.1   7.43    2019 older     no intervention
3 Fleming et al.      30   3.01  0.87    30   3.13  1.23    2006 gen       no intervention
4 Hunt & Burke        64  19.3   6.41    65  20.2   7.62    2011 gen       WLC
5 McCarthy et al.     50   4.54  2.75    50   5.61  2.66    1997 gen       WLC
6 Meijer et al.      109  15.1   4.63   111  16.5   5.39    2000 gen       no intervention
```

Meta-Analysis Using meta package

3. Doing Meta-Analysis

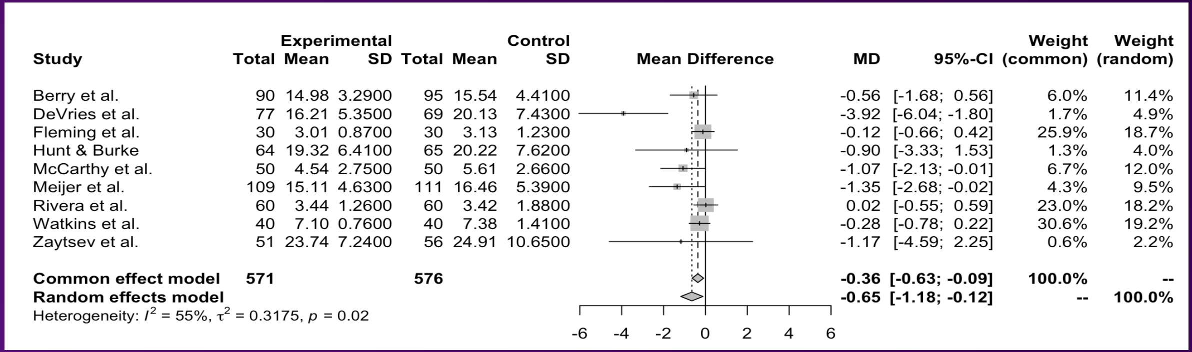
```r
meta_model_1 <- metacont(n.e = n.e, mean.e = mean.e, sd.e = sd.e,
                         n.c = n.c, mean.c = mean.c, sd.c = sd.c,
                         studlab = author, data = df_meta)

summary(meta_model_1)
```

```
> summary(meta_model_1)
                       MD             95%-CI %W(common) %W(random)
Berry et al.      -0.5600 [-1.6773;  0.5573]        6.0       11.4
DeVries et al.    -3.9200 [-6.0416; -1.7984]        1.7        4.9
Fleming et al.    -0.1200 [-0.6591;  0.4191]       25.9       18.7
Hunt & Burke      -0.9000 [-3.3285;  1.5285]        1.3        4.0
McCarthy et al.   -1.0700 [-2.1305; -0.0095]        6.7       12.0
Meijer et al.     -1.3500 [-2.6770; -0.0230]        4.3        9.5
Rivera et al.      0.0200 [-0.5527;  0.5927]       23.0       18.2
Watkins et al.    -0.2800 [-0.7764;  0.2164]       30.6       19.2
Zaytsev et al.    -1.1700 [-4.5947;  2.2547]        0.6        2.2

Number of studies combined: k = 9
Number of observations: o = 1147

                          MD             95%-CI     z  p-value
Common effect model  -0.3597 [-0.6341; -0.0853] -2.57   0.0102
Random effects model -0.6467 [-1.1774; -0.1159] -2.39   0.0169

Quantifying heterogeneity:
 tau^2 = 0.3175 [0.0044; 4.2610]; tau = 0.5635 [0.0662; 2.0642]
 I^2 = 54.9% [4.7%; 78.7%]; H = 1.49 [1.02; 2.17]

Test of heterogeneity:
     Q d.f. p-value
 17.76    8  0.0231

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
```

Meta-Analysis Using meta package

4. Forest Plot

```r
meta::forest(meta_model_1)
```



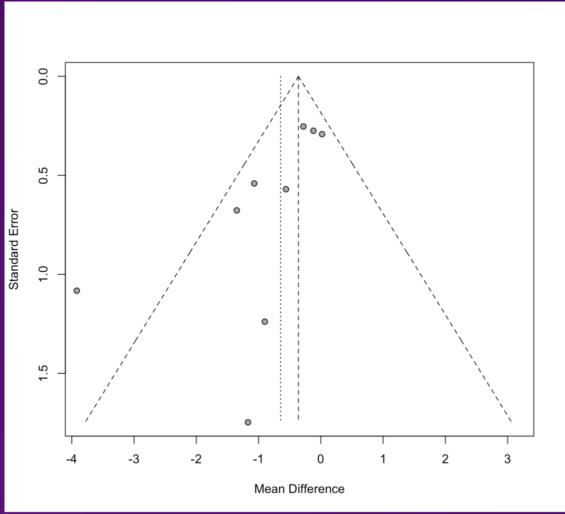
Study	Experimental Total	Experimental Mean	Experimental SD	Control Total	Control Mean	Control SD	MD	95%-CI	Weight (common)	Weight (random)
Berry et al.	90	14.98	3.2900	95	15.54	4.4100	-0.56	[-1.68; 0.56]	6.0%	11.4%
DeVries et al.	77	16.21	5.3500	69	20.13	7.4300	-3.92	[-6.04; -1.80]	1.7%	4.9%
Fleming et al.	30	3.01	0.8700	30	3.13	1.2300	-0.12	[-0.66; 0.42]	25.9%	18.7%
Hunt & Burke	64	19.32	6.4100	65	20.22	7.6200	-0.90	[-3.33; 1.53]	1.3%	4.0%
McCarthy et al.	50	4.54	2.7500	50	5.61	2.6600	-1.07	[-2.13; -0.01]	6.7%	12.0%
Meijer et al.	109	15.11	4.6300	111	16.46	5.3900	-1.35	[-2.68; -0.02]	4.3%	9.5%
Rivera et al.	60	3.44	1.2600	60	3.42	1.8800	0.02	[-0.55; 0.59]	23.0%	18.2%
Watkins et al.	40	7.10	0.7600	40	7.38	1.4100	-0.28	[-0.78; 0.22]	30.6%	19.2%
Zaytsev et al.	51	23.74	7.2400	56	24.91	10.6500	-1.17	[-4.59; 2.25]	0.6%	2.2%
Common effect model	**571**			**576**			**-0.36**	**[-0.63; -0.09]**	**100.0%**	**--**
Random effects model							**-0.65**	**[-1.18; -0.12]**	**--**	**100.0%**

Heterogeneity: $I^2 = 55\%$, $\tau^2 = 0.3175$, $p = 0.02$

Meta-Analysis Using meta package

4. Funnel Plot

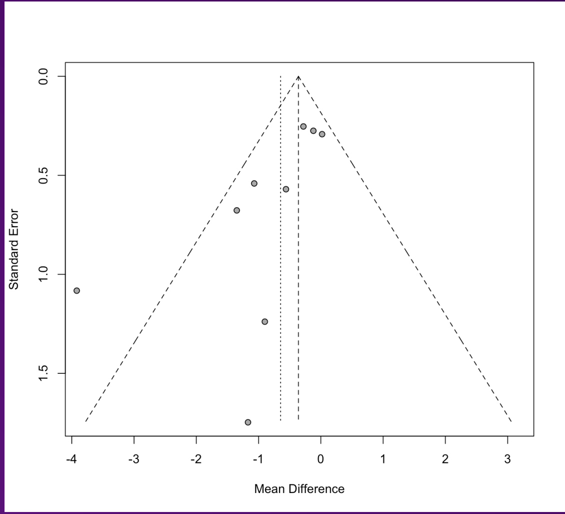
```
141 meta::funnel(meta_model_1)
```



Meta-Analysis Using meta package

5. Funnel Plot

```
meta::funnel(meta_model_1)
```



Meta-Analysis Using meta package

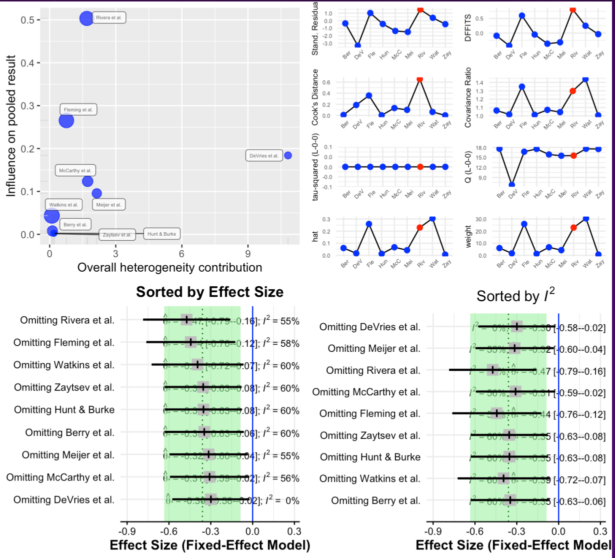
6. Publication Bias

```
> meta::metabias(meta_model_1)
Warning message:
Number of studies (k=9) too small to test for small study effects (k.min=10). Change argument 'k.min' if appropriate.
145   meta::metabias(meta_model_1, k.min = 3)
> meta::metabias(meta_model_1, k.min = 3)
Linear regression test of funnel plot asymmetry

Test result: t = -2.95, df = 7, p-value = 0.0215

Sample estimates:
    bias se.bias intercept se.intercept
 -2.0352  0.6908    0.3737       0.2901

Details:
- multiplicative residual heterogeneity variance (tau^2 = 1.1323)
- predictor: standard error
- weight:    inverse variance
- reference: Egger et al. (1997), BMJ
```

Meta-Analysis Using meta package

7. Influence Analysis

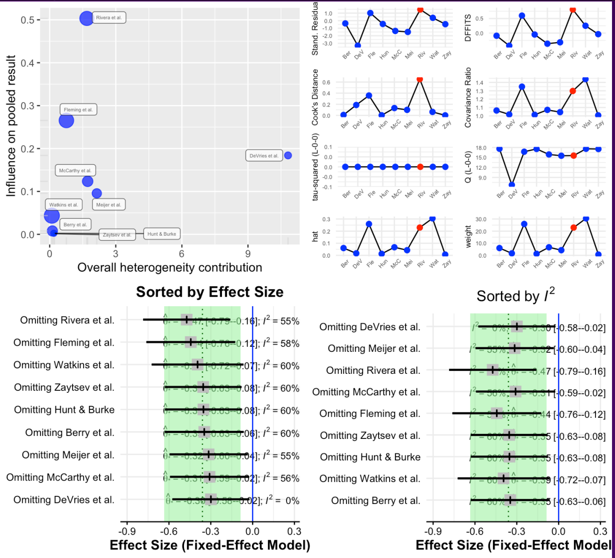
```r
influence <- InfluenceAnalysis(meta_model_1)
summary(influence)
plot(influence)
```



Meta-Analysis Using meta package

7. Influence Analysis

```r
influence <- InfluenceAnalysis(meta_model_1)
summary(influence)
plot(influence)
```



04

Advanced Methods

When and How To Conduct Meta-Analysis

Advanced Methods

References

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- Meta-analysis with r, Gerta Rücker, Guido Schwarzer, and James Carpenter
- How to perform a meta-analysis with R: a practical tutorial, Evidence-Based Mental Health, Balduzzi S, Rücker G, Schwarzer G
- onducting meta-analyses in R with the metafor package, Viechtbauer, W.

THANKS!

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