Dealing with publication bias in a meta-analysis

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Publication bias

- Publication bias is the selective publication of studies and usually favoring statistically significant outcomes

- Consequences of publication bias:
  - False impression that an effect exists
  - Overestimation of effect size

- Publication bias is a problem for all synthesizing methods

- Meta-analysis actually enables us to assess publication bias by using meta-information

Publication bias: Evidence

- Coursol and Wagner (1986) [1] surveyed researchers on the effects of positive findings

Table 1
Relation Between Outcome (Positive vs. Neutral or Negative) and Decision to Submit Research for Publication

Direction of outcome	Submission decision: Yes	Submission decision: No	Total
Positive (Client improved)	106	23	129
Neutral or negative (Client did not improve)	28	37	65
Total	134	60	194

Publication bias: Evidence

- Coursol and Wagner (1986) [1] surveyed researchers on the effects of positive findings

Table 2
Relation Between Outcome (Positive vs. Neutral or Negative) and Acceptance of Research Submitted for Publication

Direction of outcome	Accepted	Not accepted	Total
Positive (Client improved)	85	21	106
Neutral or negative (Client did not improve)	14	14	28
Total	99	35	134

Publication bias methods

- There are very many different methods
- Methods can be split into *funnel plot-based* and *selection model approaches*
- An arbitrary selection of methods based on popularity and potential are discussed

Working example

- Example meta-analysis by McDaniel et al. (1994) [2] available in R package "metadat" [3]

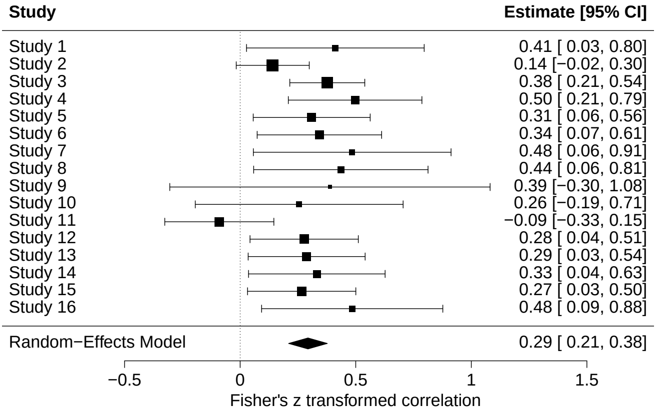
- Association between scores on employment interviews and job performance $\rightarrow k = 16$ correlations

- A positive correlation indicates a stronger association

- Fisher's z transformation is applied prior to the analysis

- Analyses are done with R packages `metafor` [4] and `puniform` [5]

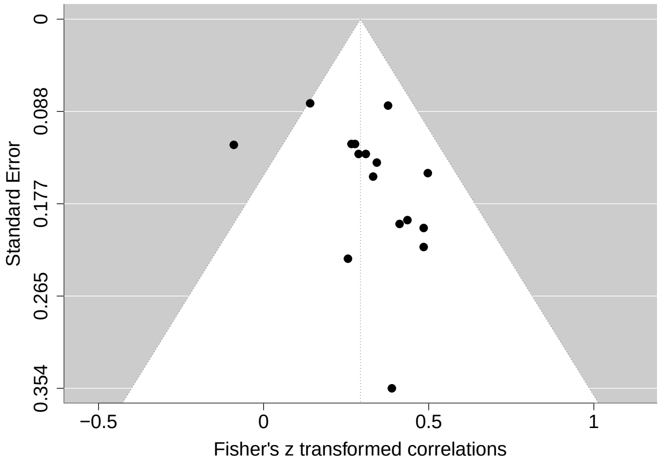
Working example: Forest plot



- **Interpretation:** The association between employment interviews and job performance is 0.29 (p<.001)

Funnel plot [6]

- Shows relationship between effect size and its precision



Funnel plot [6]

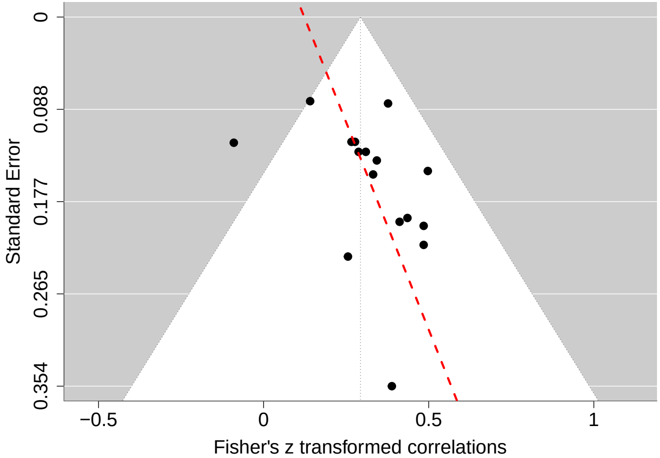
- An asymmetric funnel is often interpreted as evidence of publication bias

- However, it actually suggests the presence of so-called *small-study effects*

- Causes of small-study effects [7]:
  - Publication bias
  - Different designs and true effects in small vs. large studies
  - Power analysis to determine the required sample size in combination with heterogeneity
  - Chance
  - Etc.

Funnel plot asymmetry tests: Egger's test [8]

- Funnel plot asymmetry tests test for small-study effects
- Egger's test fits a regression line through the points in a funnel plot



Funnel plot asymmetry tests: Egger's test [8]

- Vertical line suggests a symmetric funnel
- If slope is significantly different from zero $\rightarrow$ funnel plot asymmetry
- Applied to our example: $z = 1.460$, $p = .144$
- **Conclusion:** We cannot reject the null hypothesis of no small-study effects

Funnel plot asymmetry tests: Egger's test [8]

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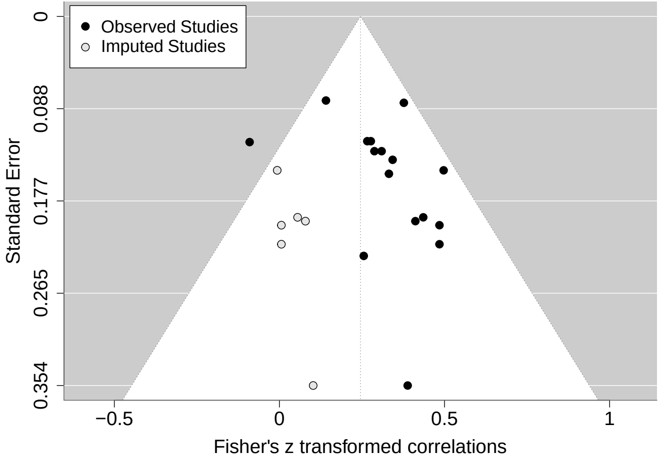
- Applied to our example: $z = 1.460$, $p = .144$
- **Conclusion:** We cannot reject the null hypothesis of no small-study effects
- Egger's test has low power in case of small k [9, 10] $\rightarrow$ recommended to be applied if $k > 10$ and use $\alpha = 0.1$ [8, 11]
- Variants have been proposed that use other measures of precision than the standard error

Trim-and-fill method [12, 13]

- Intuitive non-parametric method to correct effect size estimate
- Missing effect sizes from one side of funnel plot are *trimmed* and *filled* in other side



Trim-and-fill method [12, 13]

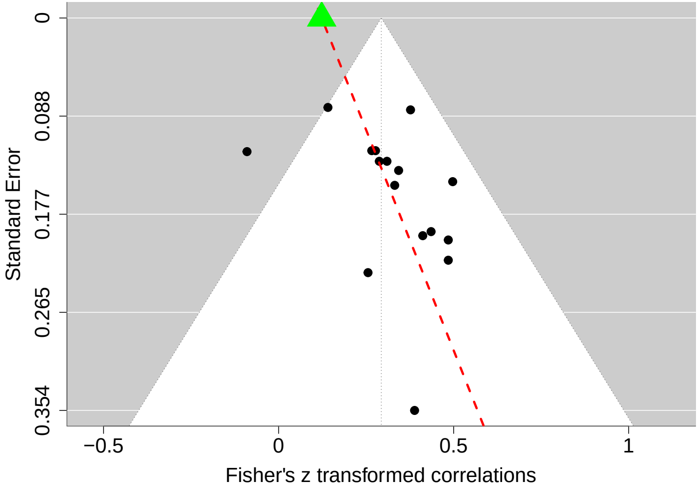
- Results of example (Pearson correlation coefficients):

	Est. 95% CI	Test results
RE model	0.285 (0.207;0.360)	z=6.875 (p<.001)
Trim-and-fill	0.241 (0.167;0.311)	z=6.271 (p<.001)

- Drawbacks:
  - Method based on funnel plot, so it corrects for small-study effects rather than publication bias
  - Simulation studies revealed that the method performs worse than other existing methods [e.g., 14, 15, 16]

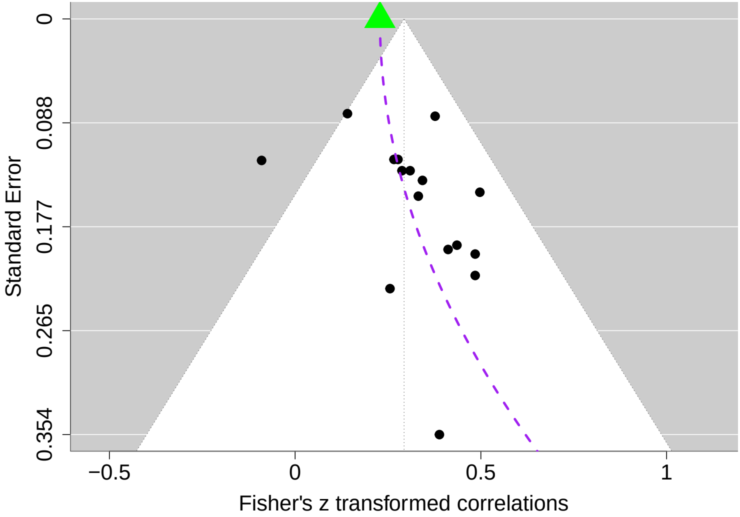
PET-PEESE [17]

- Estimate equals the effect size where standard error is zero (infinite sample size) $\rightarrow$ PET



PET-PEESE [17]

- PEESE → *sampling variance* as moderator



PET-PEESE [17]

- Results of example (Pearson correlation coefficients):

	Est. 95% CI	Test results
RE model	0.285 (0.207;0.360)	z=6.875 (p<.001)
PET	0.122 (-0.117;0.348)	z=1.003 (p=.316)
PEESE	0.224 (0.102;0.340)	z=3.558 (p<.001)

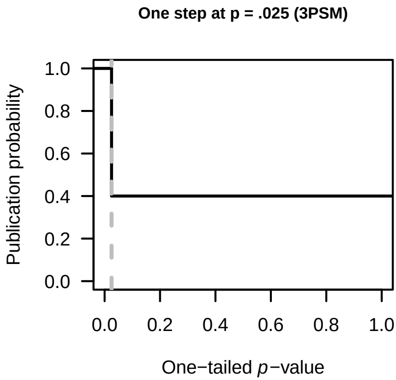
- Drawbacks:
  - Method corrects for small-study effects
  - 10 or more effect sizes are needed
  - Precision of effect sizes has to vary

Selection model approaches

- Generic term for methods combining effect size model with selection model
- *Effect size model:* distribution of effect sizes in the absence of publication bias
- *Selection model:* mechanism by which effect size estimates are selected to be observed
- Many different selection model approaches have been developed

Step function selection model [18]

- Intervals of p-values by setting "steps" $\rightarrow$ studies in an interval have the same probability of getting published



- Step at $p = 0.025 \rightarrow$ selected by the user
- Publication probabilities are 1 and 0.4 $\rightarrow$ estimated or specified by the user in a sensitivity analysis

Step function selection model approach [18]

- Results of fitting 3PSM with step at 0.025 (Pearson correlation coefficients):

	Est. 95% CI	Test results
RE model	0.285 (0.207;0.360)	z=6.875 (p<.001)
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- Drawbacks:
  - Complicated
  - Require substantial number of studies (but depends on selection model)

P-uniform* [19]

- [Robbie adds disclaimer]
- *P*-uniform* is an extension of *p*-uniform [15, 20], *p*-curve [21], and a method proposed in Hedges (1984) [22]
- *P*-uniform* can be seen as a selection model approach
- *P*-uniform*'s model is more parsimonious than 3PSM, because the publication probability does not have to be estimated
- *P*-uniform* and 3PSM show comparable performance in simulation studies [19]

P-uniform* [19]

- Results of example (Pearson correlation coefficients):

	Est. 95% CI	Test results
RE model	0.285 (0.207;0.360)	z=6.875 (p<.001)
P-uniform*	0.152 (-0.057;0.288)	LR=2.266 (p=.132)

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- Drawbacks:
  - Complicated
  - Unrealistic extreme effect sizes can be estimated if there are only significant studies in a meta-analysis

Summary results working example

- Funnel plot indicated that small-study effects might be present, but Egger's test was not significant

- Results estimating effect size:

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- **What to conclude?!**

Recommendations

- There is no uniformly best performing publication bias method
- Apply publication bias methods that are expected to perform well for the characteristics of the meta-analysis
- Simulation studies provide insights in the performance of the methods [e.g., 16, 20, 23, 24]
- Use triangulation [25, 26] and report all results
- Think about preregistering the planned publication bias analyses

Avenues for future research

- Model averaging can help summarizing the results of publication bias methods
  - Robust Bayes Model Averaging (RoBMA) [27]
  - Robust Frequentist Model Averaging (RoFMA)
- How to deal with dependent effect sizes in publication bias analyses?
  - Extend Egger's regression test [28, 29]
  - Apply methods that assume independence and follow up with cluster-robust inference [30]
  - Multivariate step function selection model
- What if only a subset of studies is susceptible to publication bias $\rightarrow$ Hybrid Extended Meta-Analysis method [31]
- Does publication bias also affects meta-regression analyses?

Closing remarks

- Mixed findings about the severity of publication bias in *meta*-meta-analyses [32–37]
- Comparing the results of published and unpublished studies can already be insightful
- *P*-hacking is known to distort many publication bias methods
- Hopefully, the uptake of preregistering primary studies mitigates the effect of publication bias

Thank you for your attention

Slides are available on my website:

www.robbievanaert.com

Our research group at Tilburg University:

www.metaresearch.nl

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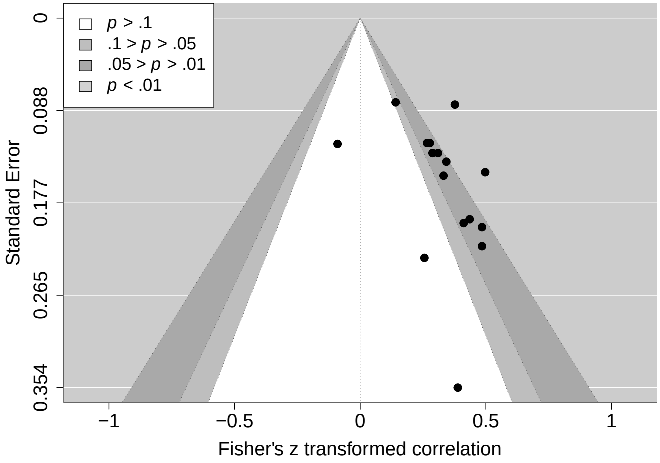
Contour-enhanced funnel plot [38]

- Eyeballing a funnel plot for asymmetry is difficult [39] $\rightarrow$ contour-enhanced funnel plot



PDF of the step function selection model

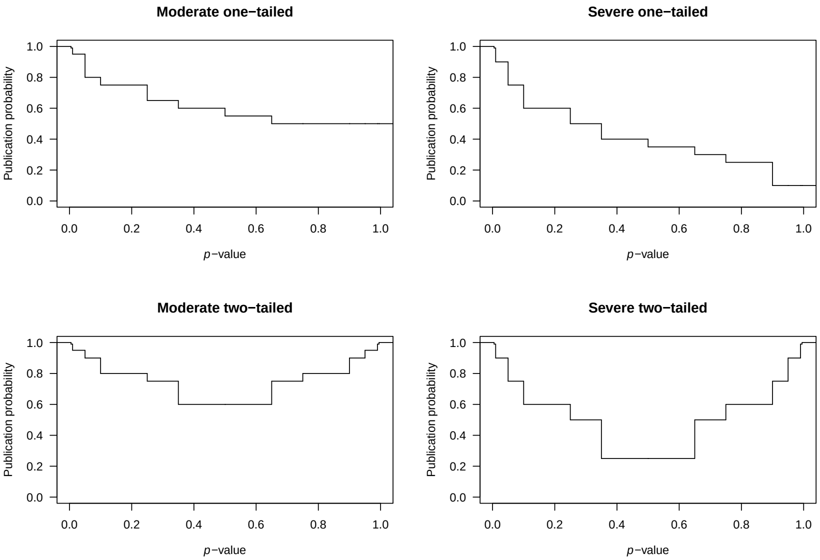
$$f(Y_i; \mu, \boldsymbol{\omega}, s_i, \sigma_i) = \frac{s_i^{-1} w(Y_i, \sigma_i) \phi\left(\frac{Y_i - \mu}{s_i}\right)}{\int s_i^{-1} w(Y_i, \sigma_i) \phi\left(\frac{Y_i - \mu}{s_i}\right) dY_i} \tag{1}$$

$$w(Y_i, \sigma_i) = \begin{cases} \omega_1 & \text{if } -\sigma_i \Phi^{-1}(a_1) < Y_i < \infty; \\ \omega_m & \text{if } -\sigma_i \Phi^{-1}(a_m) < Y_i \leq -\sigma_i \Phi^{-1}(a_{m-1}); \\ \omega_M & \text{if } -\infty < Y_i \leq -\sigma_i \Phi^{-1}(a_{M-1}) \end{cases} \tag{2}$$

- Y_i: observed effect size estimate
- σ_i: square root of the within-study sampling variance
- s_i: square root of the total variance
- ϕ: PDF of standard normal distribution
- m: index for the intervals
- M: total number of intervals
- $a_1, \cdots, a_M$: cut points on the p-value scale

Step function selection model

- Probabilities can also assumed to be known [40]



Likelihood function p-uniform*

$$L(\mu, \tau^2; y_i, \sigma_i^2, y_i^{cv}) = \begin{cases} \dfrac{\dfrac{1}{\sqrt{\sigma_i^2 + \tau^2}} \phi\left(\dfrac{y_i - \mu}{\sqrt{\sigma_i^2 + \tau^2}}\right)}{1 - \Phi\left(\dfrac{y_i^{cv} - \mu}{\sqrt{\sigma_i^2 + \tau^2}}\right)} & \text{if } p_i \leq \alpha \\ \dfrac{\dfrac{1}{\sqrt{\sigma_i^2 + \tau^2}} \phi\left(\dfrac{y_i - \mu}{\sqrt{\sigma_i^2 + \tau^2}}\right)}{\Phi\left(\dfrac{y_i^{cv} - \mu}{\sqrt{\sigma_i^2 + \tau^2}}\right)} & \text{if } p_i > \alpha \end{cases}$$

- y_i: observed effect size estimate
- σ_i^2: within-study sampling variance
- y_i^{CV}: critical value
- ϕ: PDF of standard normal distribution
- Φ: CDF of standard normal distribution
- p_i: right-tailed p-value