

# Weight of Statistical Evidence

## Detection and Correction of Publication Bias

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Servan Grüninger

Écublens, July 9th

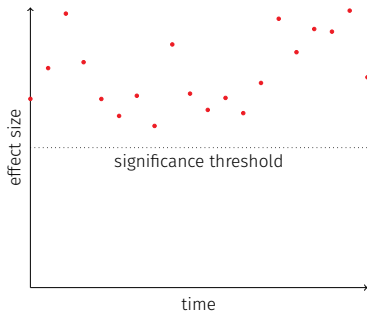
Master's Programme in Computational Science and Engineering

# The Woozle effect

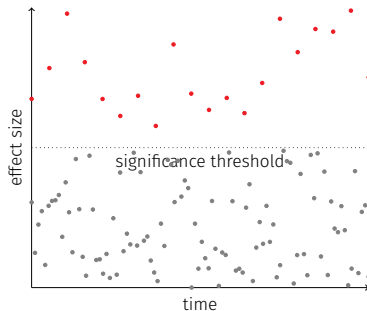
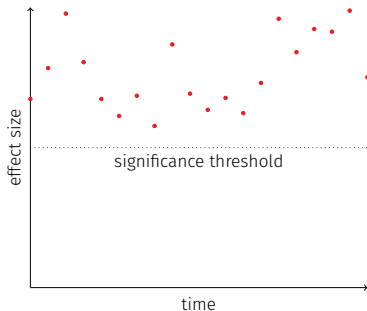


Pooh and Piglet tracking down the elusive Woozle (Image: Ernest H. Shepard)

# The Woozle effect—why care?



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# Table of Contents

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1. Analysing and Testing Evidence
2. Detecting Publication Bias
3. Correcting Publication Bias
4. Conclusion

# Analysing and Testing Evidence

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# Hypothesis Testing

$$H_0 : \mu \leq \mu_0$$

$$H_1 : \mu > \mu_0$$

# Making evidence comparable

To test hypotheses, we need a test statistic  $V_n$ .



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$E_2 : V_n \sim \mathcal{N}(\tau, 1)$ ;

$E_3 : \text{Var}[V_n] = 1$ ;

$E_4 : E_\mu[V_n] = \tau(\mu)$  is monotonically increasing in  $\mu$  from  $\tau(0) = 0$ .

## Example case: difference in means

Let  $X \sim \mathcal{N}(\mu, \sigma^2)$  with  $\mu$  and  $\sigma^2$  unknown.

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with

$$\hat{\mu} = \bar{X}_n = \frac{1}{n} \sum_{i=1}^n X_i; \quad \hat{\sigma}^2 = s_n^2 = \frac{1}{n-1} \sum_{i=1}^n (X_i - \bar{X}_N)^2$$



# Variance stabilising transformation

If  $n$  is large enough,  $T_n$  fulfills all properties  $E_1$  to  $E_4$  by virtue of the central limit theorem.

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For small  $n$ , however,  $E_2$  and  $E_3$  are violated.

Solution: Transform  $T_n$ !

# Variance stabilising transformation

$V_n = h_n(T_n) = \sqrt{2n} \sinh^{-1}(T_n/\sqrt{2n})$  yields improved approximation to standard normal distribution Kulinskaya, Morgenthaler, and Staudte (2008).

# Variance stabilising transformation

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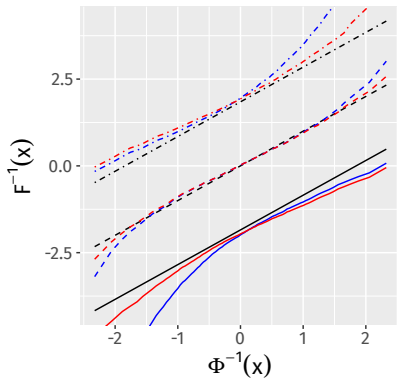
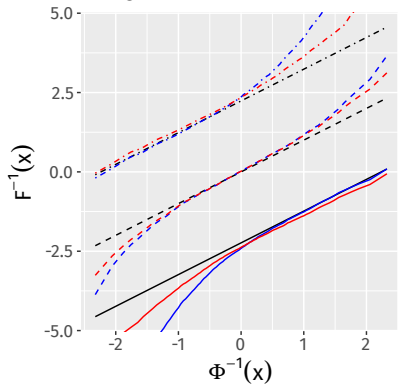
Further improvement by finite sample correction:

$$V_n^* = \frac{n - 1.7}{n - 1} \sqrt{2n} \sinh^{-1}(T_n/\sqrt{2n})$$

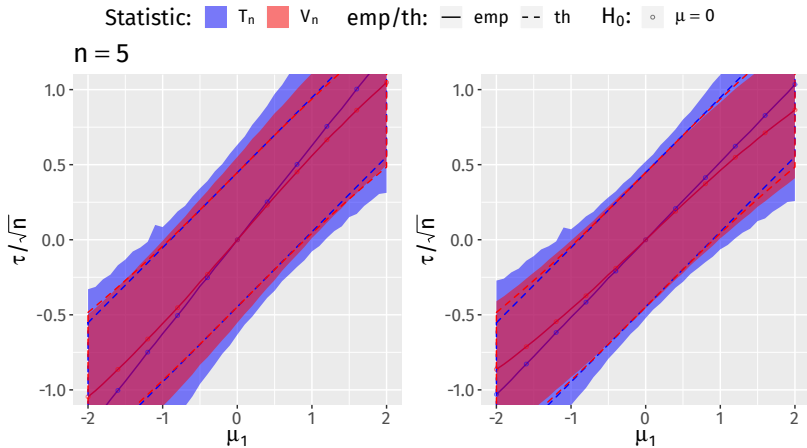
# $h_n$ improves normal fit

$H_1$ : —  $\mu = -2$  --  $\mu = 0$  -.-  $\mu = 2$   $F(x)$ : —  $\Phi(x - E[T_n])$  —  $T_n$  —  $V_n - E[V_n] + E[T_n]$

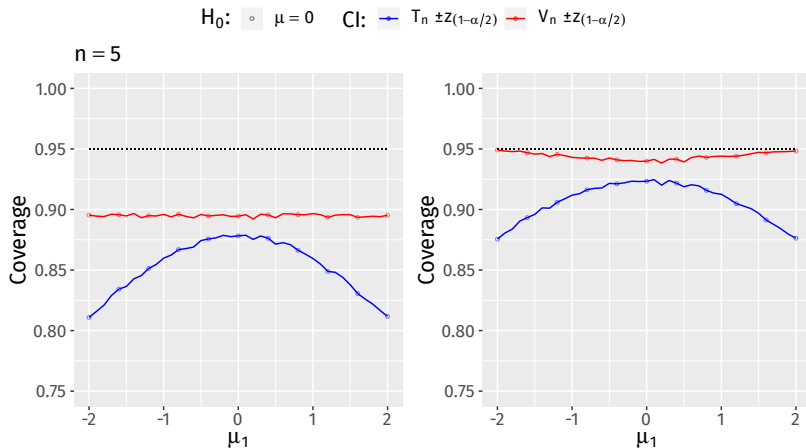
$n = 5$



# $h_n$ stabilises variance



# $h_n$ improves empirical coverage probability of confidence intervals





## Detecting Publication Bias

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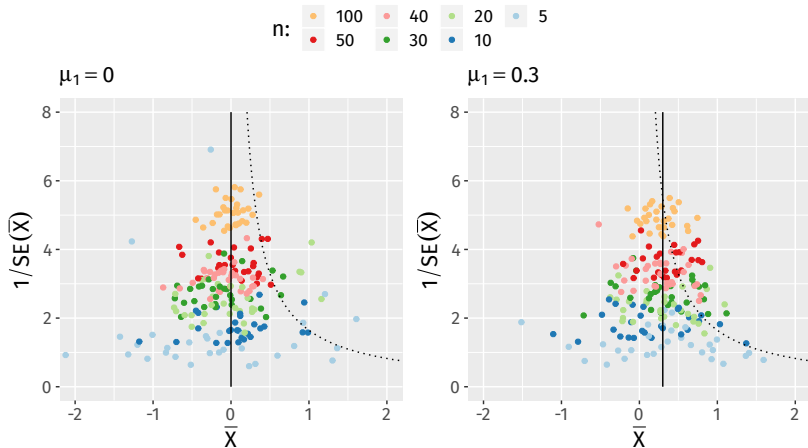
# Aggregate study effects in the absence of publication bias

Without publication bias, the global effect size across  $k$  studies can be estimated by:

$$\bar{X}_N = \frac{\sum_{j=1}^k \bar{X}_{n_j} w_j}{\sum_{j=1}^k w_j} \sim \mathcal{N}(\mu, \sigma^2/N); \quad N = \sum_{j=1}^k n_j; \quad w_j = n_j/\sigma^2$$

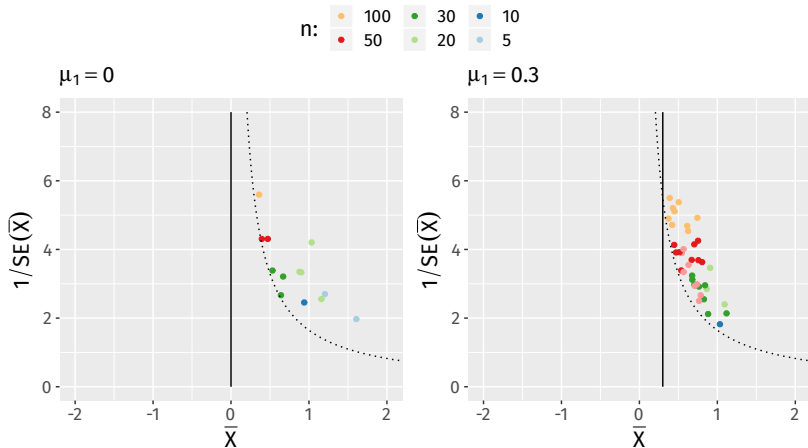
Funnel plots: draw effect size against precision, look for gaps.  
Idea proposed by Light and Pillemer (1984, p. 64–69).

# Funnelling statistical evidence



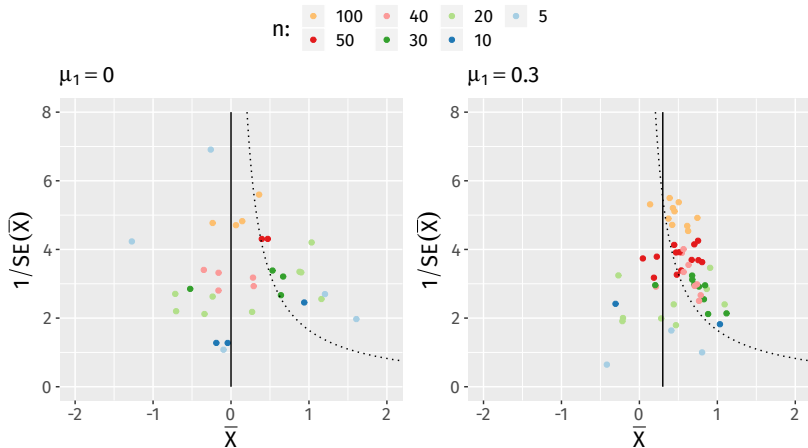
No publication bias

# Funnelling statistical evidence



Significant studies only

# Funnelling statistical evidence



Significant studies and 10% of non-significant studies

# The file drawer problem



Many studies land in the file drawer (Image: Geckoboard)

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Worst case assumption by Rosenthal (1979): Published results are Type I error only.



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Calculate number of omitted studies needed to make findings non-significant:

$$z_{(1-\alpha)} = \frac{k\bar{z}_k + o\bar{z}_o}{\sqrt{k + o}}$$

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Calculate number of omitted studies needed to make findings non-significant:

$$z_{(1-\alpha)} = \frac{k\bar{z}_k + o\bar{z}_o}{\sqrt{k + o}}$$
$$\iff o = \frac{(k\bar{z}_k + o\bar{z}_o)^2}{z_{(1-\alpha)}^2} - k.$$

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Assume that  $\bar{z}_o = 0$ :

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Assume that  $\bar{z}_o = 0$ :

$$o = \frac{(k\bar{z}_k)^2}{z_{(1-\alpha)}^2} - k.$$

More accurate is  $\bar{z}_o = E[Z \mid Z < z_{(1-\alpha)}]$ :

$$o^* = \frac{-2k\bar{z}_k\bar{z}_o + z_{(1-\alpha)}^2 - z_{(1-\alpha)}\sqrt{4k\bar{z}_o^2 - 4k\bar{z}_k\bar{z}_o + z_{(1-\alpha)}^2}}{2\bar{z}_o^2}.$$

Check whether  $o^* < 5k + 10$ .

# The file drawer problem

	$k$	$\mu_1$	$o$	$o^*$	bias detected?
full sample (no bias)	200	0	-141	-181	$o$ : no $o^*$ : no
	200	0.3	8123	884	$o$ : no $o^*$ : no

Critical value:  $5k + 10$

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full sample (no bias)	200	0	-141	-181	$o$ : no
	200	0.3	8123	884	$o^*$ : no $o$ : no $o^*$ : no
significant studies	13	0	320	109	$o$ : no $o^*$ : no
	38	0.3	2705	457	$o$ : no $o^*$ : no

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significant studies	13	0	320	109	$o$ : no
	38	0.3	2705	457	$o^*$ : no $o$ : no $o^*$ : no
significant studies and 10% of non-significant studies	32	0	99	43	$o$ : yes
	55	0.3	3086	494	$o^*$ : yes $o$ : no $o^*$ : no

Critical value:  $5k + 10$



## How many significant studies ought to be expected?

Assuming  $\sigma^2$  to be known, the (overestimated) power of the  $j$ th study is:

$$1 - \beta_j = \Phi\left(\sqrt{n_j} \frac{\bar{X}_N}{\sigma} - z_{(1-\alpha)}\right)$$

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Expected number of significant studies in the absence of publication bias (Ioannidis and Trikalinos, 2007):

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$$E = \sum_{j=1}^k (1 - \beta_j).$$

Compare to observed number of studies  $O$  via  $\chi^2$ -test:

$$A = [(O - E)^2/E + (O - E)^2/(k - E)] \sim \chi_1^2.$$

## How many significant studies ought to be expected?

	$k$	$\mu_1$	$\bar{x}_N$	$A$	bias detected?
full sample (no bias, A)	200	0	-0.02	1.70	no
	200	0.3	0.27	0.08	no

Critical value: 3.84 (95%-quantile of  $\chi^2_1$ -distribution)

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significant studies (B)	13	0	0.69	11.67	yes
	38	0.3	0.61	19.94	yes

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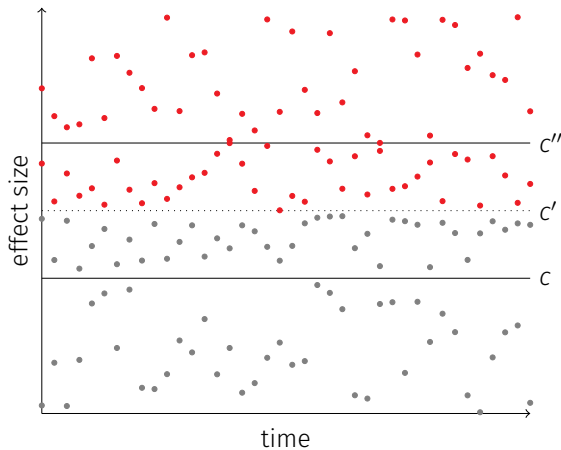
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significant studies (B)	13	0	0.69	11.67	yes
	38	0.3	0.61	19.94	yes
significant studies and 10% of non-significant studies (C)	32	0	0.15	28.64	yes
	55	0.3	0.51	8.21	yes

Critical value: 3.84 (95%-quantile of  $\chi_1^2$ -distribution)

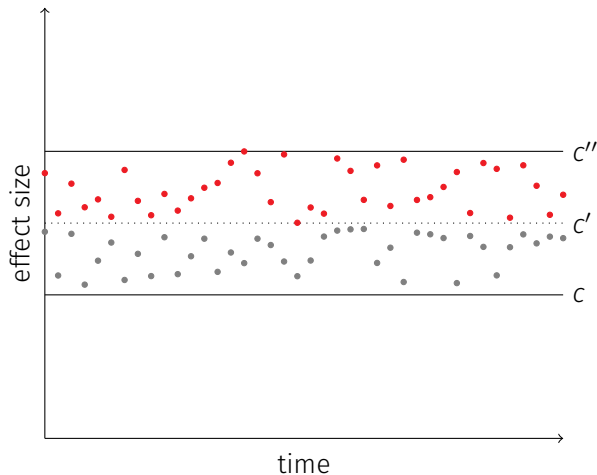
# The calliper test

$$c' = z_{(1-\alpha)}; \quad c'' = c + e; \quad c = c' - e; \quad k' \in [c, c'']; \quad k'' \in [c', c''].$$



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$$K'' \sim \text{Bin}(k', p = 0.5)$$

# The calliper test

	$k$	$\mu_1$	$k'$	$k''$	$q_{(1-\alpha/2)}$	bias detected?
full sample (no bias, A)	200	0	4	3	4	no
	200	0.3	15	6	11	no

Critical value: 97.5%-quantile of  $\text{Bin}(k', 0.5)$ -distribution

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	$k$	$\mu_1$	$k'$	$k''$	$q_{(1-\alpha/2)}$	bias detected?
full sample (no bias, A)	200	0	4	3	4	no
	200	0.3	15	6	11	no
significant studies (B)	13	0	3	3	3	no
	38	0.3	6	6	5	yes

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	200	0.3	15	6	11	no
significant studies (B)	13	0	3	3	3	no
	38	0.3	6	6	5	yes
significant studies and 10% of non-significant studies (C)	32	0	3	3	3	no
	55	0.3	7	6	6	no

Critical value: 97.5%-quantile of  $\text{Bin}(k', 0.5)$ -distribution

## Correcting Publication Bias

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- publication probability:

$$\text{ppr}(S_n, \pi) = \pi + (1 - \pi)\delta(S_n)$$

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- expected publication probability:

$$\mathbb{E}[\text{ppr}(S_n, \pi)] = \pi \Pr(\text{ppr} = \pi) + \Pr(\text{ppr} = 1)$$

# Publication probabilities and truncated distributions

- publication probability:

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- expected publication probability:

$$\mathbb{E}[\text{ppr}(S_n, \pi)] = \pi \Pr(\text{ppr} = \pi) + \Pr(\text{ppr} = 1)$$

- truncated probability density function of  $S_n$ :

$$f_{S_n}^*(s_n) = \frac{\text{ppr}(s_n, \pi)}{\mathbb{E}[\text{ppr}(S_n, \pi)]} f_{S_n}(s_n)$$

Let

$$\mu_{\text{sig}} = E[\bar{X}_{n_j} \mid S_{n_j} > q_{(1-\alpha)}]; \quad \mu_{\text{ns}} = E[\bar{X}_{n_j} \mid S_{n_j} \leq q_{(1-\alpha)}]$$

Let

$$\begin{aligned}\mu_{\text{sig}} &= E[\bar{X}_{n_j} \mid S_{n_j} > q_{(1-\alpha)}]; & \mu_{\text{ns}} &= E[\bar{X}_{n_j} \mid S_{n_j} \leq q_{(1-\alpha)}] \\ \sigma_{\text{sig}}^2 &= \text{Var}[\bar{X}_{n_j} \mid S_{n_j} > q_{(1-\alpha)}]; & \sigma_{\text{ns}}^2 &= \text{Var}[\bar{X}_{n_j} \mid S_{n_j} \leq q_{(1-\alpha)}].\end{aligned}$$

# Reweight by publication probability

Let

$$\begin{aligned}\mu_{\text{sig}} &= E[\bar{X}_{n_j} \mid S_{n_j} > q_{(1-\alpha)}]; & \mu_{\text{ns}} &= E[\bar{X}_{n_j} \mid S_{n_j} \leq q_{(1-\alpha)}] \\ \sigma_{\text{sig}}^2 &= \text{Var}[\bar{X}_{n_j} \mid S_{n_j} > q_{(1-\alpha)}]; & \sigma_{\text{ns}}^2 &= \text{Var}[\bar{X}_{n_j} \mid S_{n_j} \leq q_{(1-\alpha)}].\end{aligned}$$

Then

$$\bar{X}_{n_j} \mid S_n \sim \begin{cases} \mathcal{N}\left(\mu_{\text{sig}} \text{ppr}_j, \sigma_{\text{sig}}^2 \frac{\text{ppr}_j^2}{n_j}\right), & \text{if } S_n > q_{(1-\alpha)}; \\ \mathcal{N}\left(\mu_{\text{ns}} \text{ppr}_j, \sigma_{\text{ns}}^2 \frac{\text{ppr}_j^2}{n_j}\right), & \text{if } S_n \leq q_{(1-\alpha)}. \end{cases}$$



The biased weight  $w_j^* = w_j \text{ppr}_j$  yields biased estimator

$$\bar{X}_N = \frac{\sum_{j=1}^k \bar{X}_{n_j} w_j^*}{\sum_{j=1}^k w_j^*} \sim \mathcal{N}(\mu^*, \sigma^*)$$

## Reweight by publication probability

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with

$$\mu^* = \frac{\sum_{j=1}^s w_j^* \mu_{\text{sig}} + \sum_{j=s+1}^k w_j^* \mu_{\text{ns}}}{\sum_{j=1}^k w_j^*}$$

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with

$$\mu^* = \frac{\sum_{j=1}^s w_j^* \mu_{\text{sig}} + \sum_{j=s+1}^k w_j^* \mu_{\text{ns}}}{\sum_{j=1}^k w_j^*}$$
$$\sigma^* = \frac{\sum_{j=1}^s (w_j^*)^2 \sigma_{\text{sig}} / n_j + \sum_{j=s+1}^k (w_j^*)^2 \sigma_{\text{ns}} / n_j}{(\sum_{j=1}^k w_j^*)^2}$$

## Reweight by publication probability

Reweight each biased weight  $w_j^*$  by inverse of the publication probability to get unbiased estimator:

$$\bar{\chi}_N^* = \frac{\sum_{j=1}^k \bar{\chi}_{n_j} w_j^* / \text{ppr}_j}{\sum_{j=1}^k w_j^* / \text{ppr}_j} \sim \mathcal{N}(\mu, \sigma^2 / N)$$

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Inspired by Hansen and Hurwitz (1943).

## Reweight by publication probability

	$k$	$\mu_1$	$\bar{X}_N$	$\bar{X}_N^*$
full sample (no bias, A)	200	0	-0.02	-0.07
	200	0.3	0.27	0.15

## Reweight by publication probability

	$k$	$\mu_1$	$\bar{x}_N$	$\bar{x}_N^*$
full sample (no bias, A)	200	0	-0.02	-0.07
	200	0.3	0.27	0.15
significant studies (B)	13	0	0.69	0.69
	38	0.3	0.61	0.61

# Reweight by publication probability

	$k$	$\mu_1$	$\bar{x}_N$	$\bar{x}_N^*$
full sample (no bias, A)	200	0	-0.02	-0.07
	200	0.3	0.27	0.15
significant studies (B)	13	0	0.69	0.69
	38	0.3	0.61	0.61
significant studies and 10% of non-significant studies (C)	32	0	0.15	-0.17
	55	0.3	0.51	0.27



# Maximise truncated likelihood

Truncated likelihood of  $\mu$  given by

$$\mathcal{L}^*(\mu \mid v_{n_1}, \dots, v_{n_k}) = \frac{\mathcal{L}(\mu \mid v_{n_1}, \dots, v_{n_k})}{\mathbb{E}[\text{ppr}(V_{n_j}, \pi) \mid \mu]} \prod_{j=1}^k \text{ppr}(v_{n_j}, \pi).$$

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Can be maximised by grid search.

# Maximise truncated likelihood

	$k$	$\mu_1$	$\bar{x}_N$	$\hat{\mu}$	$\hat{\pi}$
full sample (no bias, A)	200	0	-0.02	-0.02	0.66
	200	0.3	0.27	0.27	1

# Maximise truncated likelihood

	$k$	$\mu_1$	$\bar{x}_N$	$\hat{\mu}$	$\hat{\pi}$
full sample (no bias, A)	200	0	-0.02	-0.02	0.66
	200	0.3	0.27	0.27	1
significant studies (B)	13	0	0.69	0.31	0
	38	0.3	0.61	0.31	0

# Maximise truncated likelihood

	$k$	$\mu_1$	$\bar{x}_N$	$\hat{\mu}$	$\hat{\pi}$
full sample (no bias, A)	200	0	-0.02	-0.02	0.66
	200	0.3	0.27	0.27	1
significant studies (B)	13	0	0.69	0.31	0
	38	0.3	0.61	0.31	0
significant studies and 10% of non-significant studies (C)	32	0	0.15	-0.07	0.05
	55	0.3	0.51	0.33	0.16

## Conclusion

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Reliable empirical data about origin of publication bias is key.

Pre-registration can both reduce publication bias and improve correction accuracy.

# Next Steps






- Systematically evaluate performance of methods
- Extend assessment to additional methods
- Create ensemble models

# Coming Full Circle



Fighting publication bias is like hunting the Woozle—all too often it forces you to go in circles

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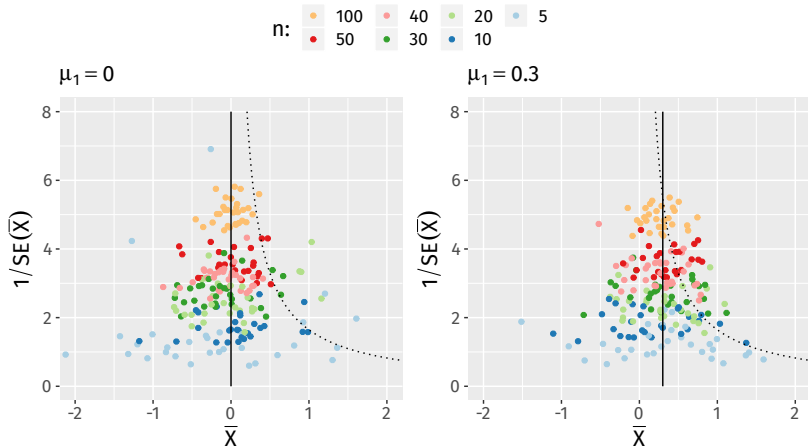


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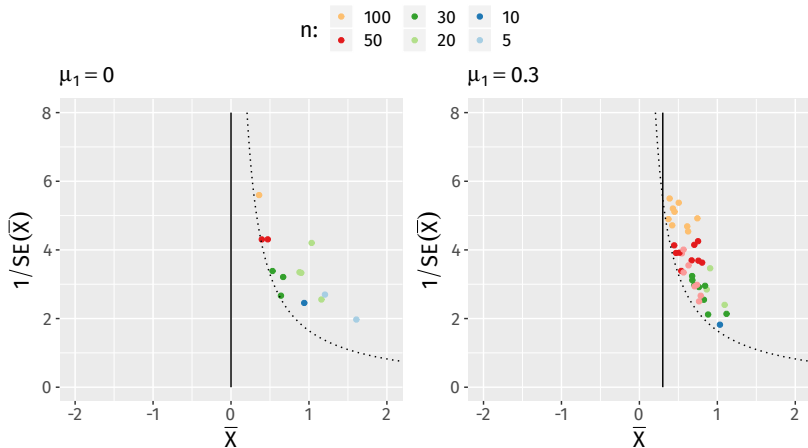
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# Quantify correlation between effect size and standard error



No correlation

# Quantify correlation between effect size and standard error



Negative correlation

## Rank correlation between effect size and standard error

Non-parametric test proposed by Begg and Mazumdar (1994):



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$$Z_j = \frac{\bar{X}_{n_j} - \bar{X}_N}{\sqrt{V_j}} \sim \mathcal{N}(0, 1);$$

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$$Z_j = \frac{\bar{X}_{n_j} - \bar{X}_N}{\sqrt{v_j}} \sim \mathcal{N}(0, 1); \quad v_j = 1/w_j - 1/\sum_{i=1}^k w_i.$$

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$$Z_k = \frac{\sum_{i=1}^{k-1} \sum_{j=i+1}^k \text{sgn}(Z_i - Z_j) \text{sgn}(v_i - v_j)}{\sqrt{(2k+5)k(k-1)/18}} \sim \mathcal{N}(0, 1).$$

## Rank correlation between effect size and standard error

	$k$	$\mu_1$	$\bar{x}_N$	$ \tau/\sigma_\tau $	bias detected?
full sample (no bias, A)	200	0	-0.02	1.33	no
	200	0.3	0.27	0.51	no

Critical value: 1.96 (97.5%-quantile of  $\mathcal{N}(0, 1)$ -distribution)

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	$k$	$\mu_1$	$\bar{x}_N$	$ \tau/\sigma_\tau $	bias detected?
full sample (no bias, A)	200	0	-0.02	1.33	no
	200	0.3	0.27	0.51	no
significant studies (B)	13	0	0.69	2.81	yes
	38	0.3	0.61	5.70	yes

Critical value: 1.96 (97.5%-quantile of  $\mathcal{N}(0, 1)$ -distribution)

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	$k$	$\mu_1$	$\bar{x}_N$	$ \tau/\sigma_\tau $	bias detected?
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	200	0.3	0.27	0.51	no
significant studies (B)	13	0	0.69	2.81	yes
	38	0.3	0.61	5.70	yes
significant studies and 10% of non-significant studies (C)	32	0	0.15	0.36	no
	55	0.3	0.51	1.60	no

Critical value: 1.96 (97.5%-quantile of  $\mathcal{N}(0, 1)$ -distribution)

## Regress effect size against standard error

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$$T_k = \frac{\hat{\beta}_0 - \beta_0}{s_{\hat{\beta}_0}} = \frac{\hat{\beta}_0}{s_{\hat{\beta}_0}} \sim t(\nu = k - 2)$$

## Rank correlation between effect size and standard error

	$k$	$\mu_1$	$\bar{x}_N$	$ t $	$q_{(1-\alpha/2)}$	bias detected?
full sample (no bias, A)	200	0	-0.02	1.30	1.97	no
	200	0.3	0.27	0.95	1.97	no

Critical value: 97.5%-quantile of  $t(\nu)$ -distribution

## Rank correlation between effect size and standard error

	$k$	$\mu_1$	$\bar{x}_N$	$ t $	$q_{(1-\alpha/2)}$	bias detected?
full sample (no bias, A)	200	0	-0.02	1.30	1.97	no
	200	0.3	0.27	0.95	1.97	no
significant studies (B)	13	0	0.69	3.77	2.20	yes
	38	0.3	0.61	8.54	2.03	yes

Critical value: 97.5%-quantile of  $t(\nu)$ -distribution

# Rank correlation between effect size and standard error

	$k$	$\mu_1$	$\bar{x}_N$	$ t $	$q_{(1-\alpha/2)}$	bias detected?
full sample (no bias, A)	200	0	-0.02	1.30	1.97	no
	200	0.3	0.27	0.95	1.97	no
significant studies (B)	13	0	0.69	3.77	2.20	yes
	38	0.3	0.61	8.54	2.03	yes
significant studies and 10% of non-significant studies (C)	32	0	0.15	1.02	2.04	no
	55	0.3	0.51	4.05	2.01	yes

Critical value: 97.5%-quantile of  $t(\nu)$ -distribution

# Maximise truncated likelihood

Grid search:

1. Define a set of candidate values  $\{\mu_1, \dots, \mu_m\}$  and  $\{\pi_1, \dots, \pi_n\}$  for  $\mu$  and  $\pi$ , respectively.

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2. For each combination of  $\mu$  and  $\pi$ , calculate the likelihood.
3. Choose the candidate value for  $\mu$  and  $\pi$  that yields the highest likelihood.

# Publication bias—the bane of scientific publishing



Publication bias in a nutshell (Image: Hilda Bastian)

## Trim-and-fill: Closing gaps in funnel plots