CESAB
CENTRE DE SYNTHÈSE ET D'ANALYSE
SUR LA BIODIVERSITÉ

Biodiversity knowledge synthesis: an introduction to meta-analyses and systematic reviews

How to calculate and combine effect-sizes?

October 2023

Beillouin Damien
Chercheur CIRAD- Hortsys

What is an effect-size?

A metric quantifying the **direction** and **magnitude** of an effect:

- Directly extracted from the publication, or calculated
- Common across all primary studies

? Difference with the p-value?

What is an effect-size?

A metric quantifying the **direction** and **magnitude** of an effect:

- Directly extracted from the publication, or calculated
- Common across all primary studies

? Difference with the p-value?

-It is possible to generate very significant p-values for effect sizes with little practical importance and vice versa

-With enough observations, even tiny differences in parameters become statistically significant

True or estimated effect-size?

An effect-size is commonly noted with the greek letter **theta** (θ):

- θ_k the 'true' effect-size of study k
- $\widehat{\theta_k}$ the observed effect-size of study k

The true and estimated effect-size differs because of the sampling error:

-$\theta_k = \widehat{\theta_k} + \varepsilon_k$

Aim of any study: to be as close as possible to the true effect size

True or estimated effect-size?

Unknown → $\theta_k = \widehat{\theta_k} + \varepsilon_k$ ← Unknown

$\widehat{\theta_k}$: Estimated through the mean value
(of a sampling distribution)

ε_k : Estimated through the standard error (SE).
(i.e. The standard deviation of the sampling distribution)
standard error of the **mean** : $SE = \frac{s}{\sqrt{n}}$; with n: sample size, s: standard dev.

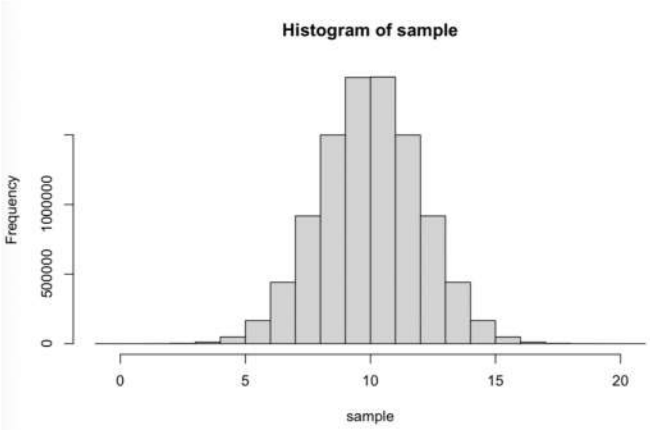
True or estimated effect-size?

$$\theta_k = \widehat{\theta_k} + \varepsilon_k$$

« The perfect world »

A random variable Mean Standard dev.

$$X \sim \mathcal{N}(\mu, \sigma^2)$$



$$X \sim \mathcal{N}(10, 2)$$

True or estimated effect-size?

$$\theta_k = \widehat{\theta_k} + \varepsilon_k$$

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A random variable Mean Standard dev.

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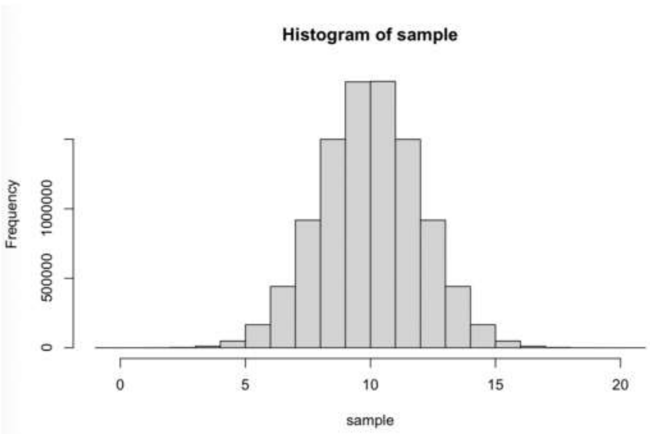
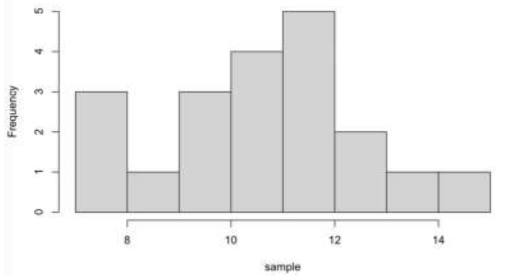


$$X \sim \mathcal{N}(10, 2)$$

Experiments

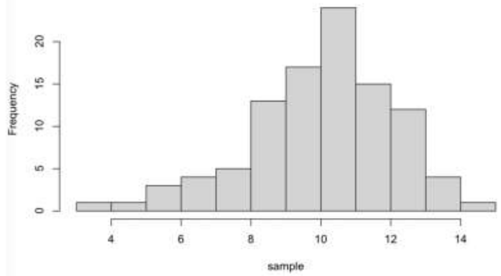
20 exp. units



Estimated Mean : 10.671

SE of the mean : 0.436

100 exp. units



Estimated Mean : 10.063

SE of the mean : 0.199

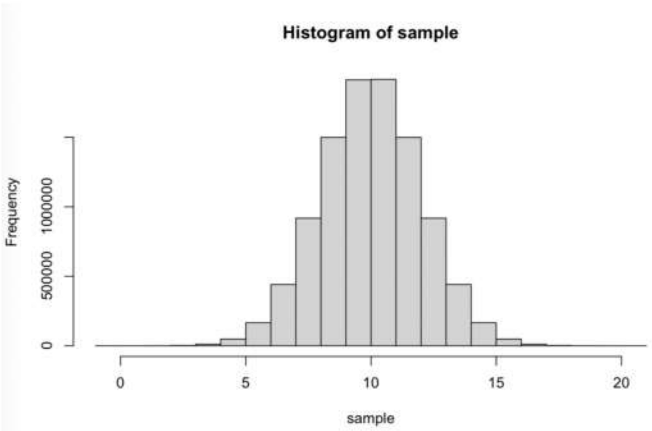
True or estimated effect-size?

$$\theta_k = \widehat{\theta_k} + \varepsilon_k$$

« The perfect world »

A random variable Mean Standard dev.

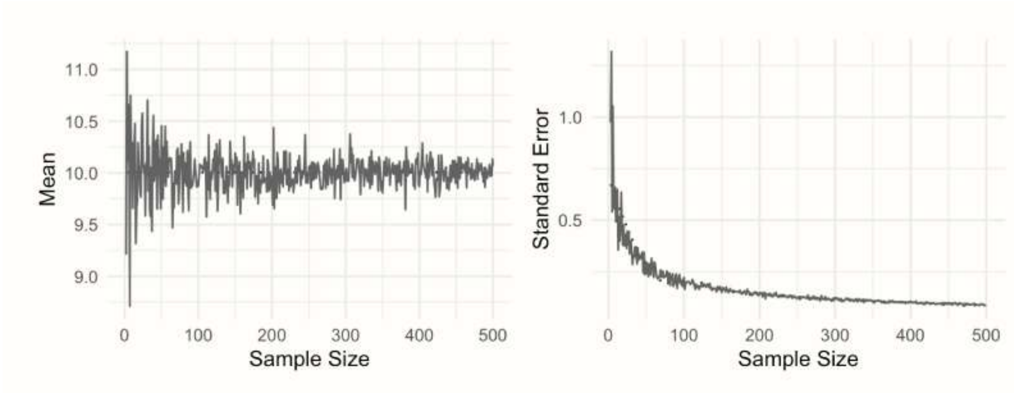
$$X \sim \mathcal{N}(\mu, \sigma^2)$$



$$X \sim \mathcal{N}(10, 2)$$

Experiments

The precision of the estimates increase with sample size



True or estimated effect-size?

$$\theta_k = \widehat{\theta_k} + \varepsilon_k$$

« The perfect world »

A random variable Mean Standard dev.

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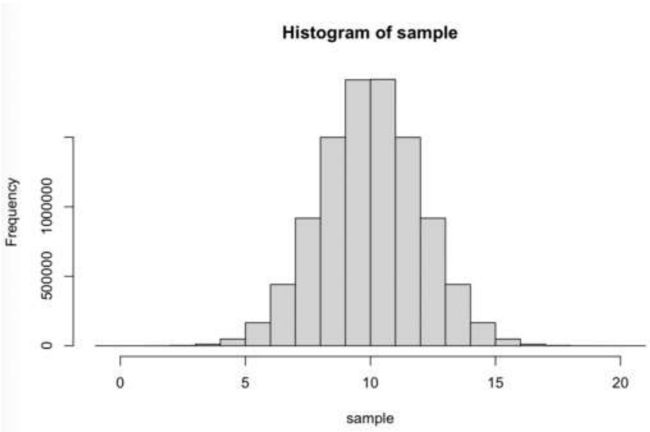

$$X \sim \mathcal{N}(10, 2)$$

Experiments

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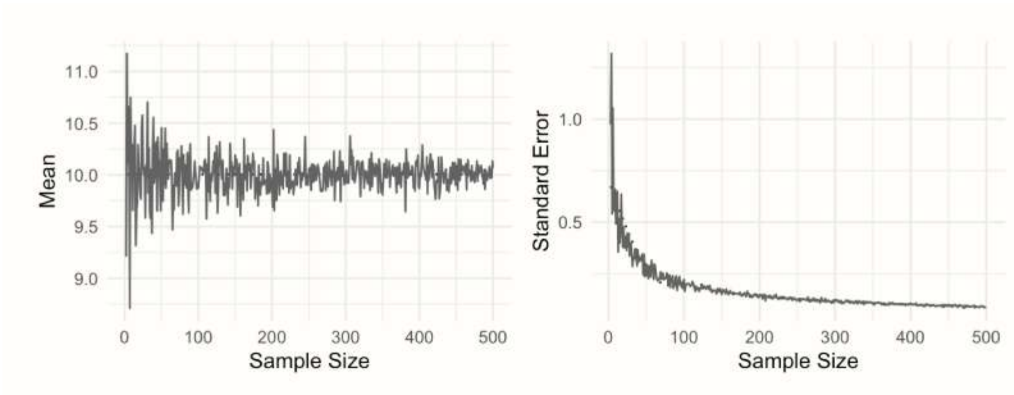

The different type of effect-sizes ($\widehat{\theta_k}$)

Single group effect:

- Mean
- sd
- CV

The different type of effect-sizes

Meta-Analysis > Work. 2006;26(4):335-41.

The use of the coefficient of variation in detecting sincerity of effort: a meta-analysis

Orit Shechtman [1], Stephen D Anton, William F Kanasky Jr, Michael E Robinson

Affiliations + expand

PMID: 16788253

Abstract

The coefficient of variation (CV) is used to determine sincerity of effort of strength measurements. However, there is a controversy in the literature concerning its validity and effectiveness. We used a meta-analytic approach and calculated the effect size between maximal and submaximal efforts for the CV of grip, elbow flexion and knee extension. We summarized findings concerning stability, sensitivity and specificity of the CV. We found large effect sizes (d > or = 0.8) for all comparisons indicating that submaximal efforts were more variable than maximal efforts. We also found large error rates and low stability of the CV. The error rates and stability values of the CV are unacceptable from both a clinical and a medico-legal standpoint. Therefore, the use of the CV for assessing sincerity of effort needs to be questioned.

The different type of effect-sizes

Single group effect:

- Proportion

The different type of effect-sizes

RESEARCH ARTICLE

Prevalence of human papillomavirus (HPV) in Brazil: A systematic review and meta-analysis

Verônica Colpani[1], Frederico Soares Falcetta[1☯], Augusto Bacelo Bidinotto[1☯], Natália Luiza Kops[1], Maicon Falavigna[1], Luciano Serpa Hammes[1], Adele Schwartz Benzaken[2,3], Ana Goretti Kalume Maranhão[4], Carla Magda Allan S. Domingues[4], Eliana Márcia Wendland[1,5]*

1 Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil, **2** Tropical Medicine Foundation Heitor Vieira Dourado, Manaus, Amazonas, Brazil, **3** Aids Health Care Foundation, Manaus, Amazonas, Brazil, **4** National Immunization Program, Ministry of Health, Bra Community Health, Federal University of Health Science c Brazil

☯ These authors contributed equally to this work.
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Rodrigues, 2018 (AM)	32	112	28.57	[20.43; 37.88]	0.8%	2.4%
Roteli–Martins, 2011	112	1509	7.42	[6.15; 8.86]	3.6%	2.6%
Santos–Filho, 2016 (AL)	51	515	9.90	[7.46; 12.81]	1.6%	2.5%
Silva, 2009 (RJ)	46	150	30.67	[23.41; 38.71]	1.1%	2.5%
Simões, 2017 (GO)	20	100	20.00	[12.67; 29.18]	0.6%	2.3%
Smith, 2002 (SP)	17	173	9.83	[5.83; 15.27]	0.5%	2.3%
Ströher, 2016 (RS)	1	51	1.96	[0.05; 10.45]	0.0%	0.8%
Tamegão–Lopes, 2014 (PA)	19	143	13.29	[8.19; 19.97]	0.6%	2.3%
Teixeira, 2016 (RS)	47	182	25.82	[19.63; 32.82]	1.2%	2.5%
Vieira, 2015 (PA)	26	265	9.81	[6.51; 14.04]	0.8%	2.4%
Fixed effect model		**19350**	**21.71**	**[21.09; 22.34]**	**100.0%**	**--**
Random effects model			**17.65**	**[14.80; 20.92]**	**--**	**100.0%**
Prediction interval				**[5.26; 45.29]**		

Heterogeneity: $I^2 = 96\%$, $\tau^2 = 0.4367$, $p < 0.01$

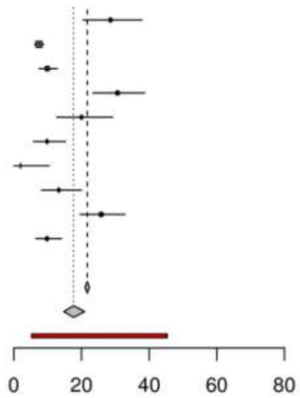

Fig 2. Overall prevalence of cervical infection by high-risk HPV genotypes. Forest plot of a metanalysis of studies reporting prevalence of infection of the cervix by HR-HPV genotypes in Brazil.

The different type of effect-sizes

Proportions: *(k, n)*

$p = \frac{k}{n}$; with k: number of individuals in a subgroup and n: total sample size

$SE_p = \sqrt{\frac{p(1-p)}{n}}$;

To be retrieved:

(k, n)

BUT : $p \in [0,1]$ → logit transformation (i.e. log (odds ratio)) : $L \in (-\infty,\infty)$

$p_{logit} = log_e\left(\frac{p}{1-p}\right)$;

$SE_{logit} = \sqrt{\frac{1}{np} + \frac{1}{n(1-p)}}$;

Interpretation

Negative logit : p<0.5,
positive logits : p<0.5

For ex. used in epidemiological studies

The different type of effect-sizes

« Comparative » **effect**:

The different type of effect-sizes

Mean differences:

The different type of effect-sizes

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18 August 2020

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7 October 2020

LETTER

Cocoa agroforestry systems versus monocultures: a multi-dimensional meta-analysis

Wiebke Niether[1], Johanna Jacobi[2], Wilma J Blaser[3], Christian Andres[4] and Laura Armengot[5]

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[4] Department of Environmental Systems Science, ETH Zurich, 8092, Zurich, Switzerland
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Keywords: economic performance, system yield, pests and diseases, biodiversity, sustainability, *theobroma cacao*

Supplementary material for this article is available online

Abstract
Scientific knowledge, societal debates, and industry commitments around sustainable cocoa are increasing. Cocoa agroforestry systems are supposed to improve the sustainability of cocoa production. However, their combined agronomic, ecological, and socio-economic performance compared to monocultures is still largely unknown. Here we present a meta-analysis of 52 articles

The different type of effect-sizes

Mean differences:

$$MD_{between} = \overline{x_1} - \overline{x_2}; \text{with} x_1 \; and \; x_2 \; two \; independant \; groups$$

$$SE_{MD_{between}} = s_{pooled}\sqrt{\frac{1}{n_1} + \frac{1}{n_2}};$$

$$s_{pooled} = \sqrt{\frac{(n_1-1)s_1^2+(n_2-1)s_2^2}{(n_1-1)+(n_2-1)}}$$

To be retrieved:

$(\overline{x_1}, n_1, s_1^2, \overline{x_2}, n_2, s_2^2)$

e.g. Cocoa agroforestry systems versus monocultures (Neither et al., 2020)

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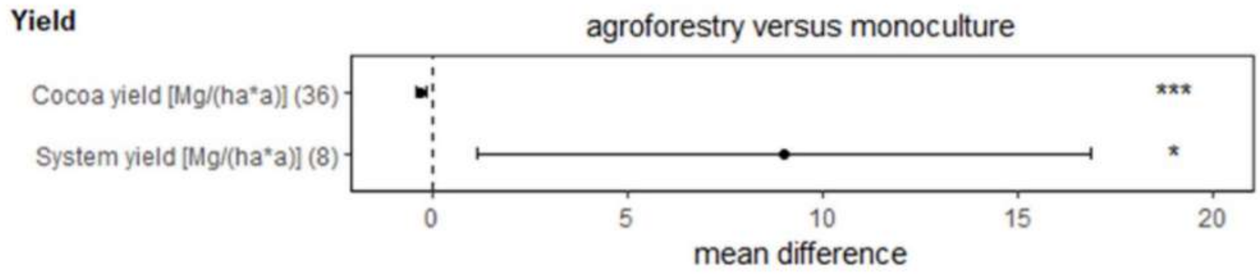

Figure 1. Mean difference of cocoa and total system yields in agroforestry systems compared with monocultures. The number of studies is shown in brackets; the horizontal bar shows the 95% confidence intervals; negative values indicate a higher mean value in monocultures; positive values indicate a higher mean value in cocoa agroforestry systems; levels of significance: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$, n.s.: not significant.

The different type of effect-sizes

Mean standardized differences = Cohen's *d*:

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Mean standardized differences = Cohen's *d*:

Oikos 126: 1078–1089, 2017
doi: 10.1111/oik.04118

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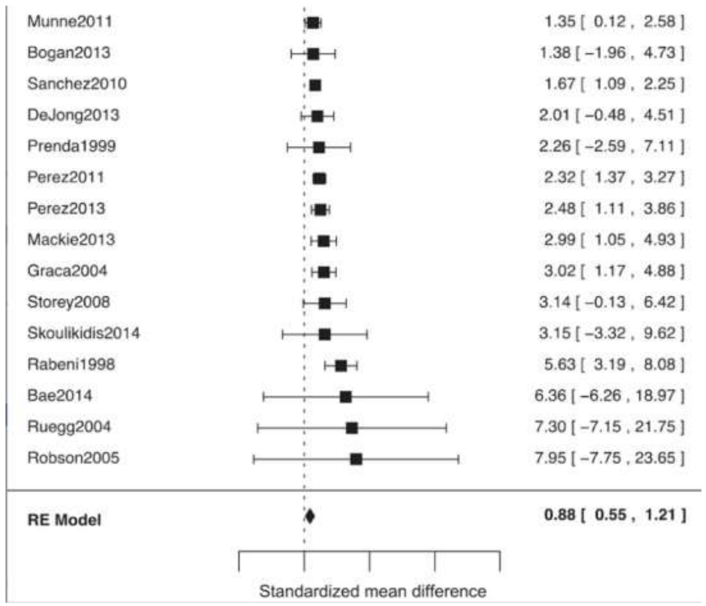
Biodiversity in perennial and intermittent rivers: a meta-analysis

Maria Soria, Catherine Leigh, Thibault Datry, Luis Mauricio Bini and Núria Bonada

M. Soria (http://orcid.org/0000-0001-9379-7626) (mariasoriaextremera@gmail.com) and N. Bonada (http://orcid.org/0000-0002-2983-3335), Dept de Biologia Evolutiva, Ecologia i Ciències Ambientals, Facultat de Biologia, Inst. de Recerca de la Biodiversitat (IRBio), Univ. de Barcelona, ES-08028 Barcelona, Catalonia, Spain. – C. Leigh (http://orcid.org/0000-0003-4186-1678) and T. Datry (http://orcid.org/0000-0003-1390-6736), Irstea, UR MALY, Centre de Lyon-Villeurbanne, Villeurbanne Cedex, France. CL also at: Australian Rivers Inst. and Griffith School of Environment, Griffith Univ., Nathan, QLD, Australia. – L. M. Bini (http://orcid.org/0000-0003-3398-9399), Inst. de Ciências Biológicas, Depto de Ecologia, Univ. Federal de Goiás, Goiânia/GO, Brazil.

Comprehensive knowledge of the effects of disturbances on biodiversity is crucial for conservation and management, not least because ecosystems with low biodiversity may be the most vulnerable. In rivers, the role of disturbance in shaping aquatic biodiversity has mainly focused on floods. Perennial rivers (PRs) often flood, whereas intermittent rivers (IRs) flood, stop flowing and dry. Despite the recent and significant increase in research on IRs, controversy remains about whether they are more or less biodiverse than PRs. Our aim was to determine (Q1) if PRs and IRs differ in biodiversity and (Q2) if the direction and magnitude of the differences (effect sizes) are related to environmental (climate, season,



The different type of effect-sizes

Mean standardized differences = Cohen's *d*:

$$SMD_{between} = \frac{\overline{x_1} - \overline{x_2}}{s_{pooled}} ; \text{with} x_1 \; and \; x_2 \; two \; independant \; groups$$

$$SE_{SMD_{between}} = \sqrt{\frac{n_1 + n_2}{n_1 n_2} + \frac{SMD^2_{between}}{2(n_1 + n_2)}} ;$$

To be retrieved:

$(\overline{x_1}, n_1, s_1^2, \overline{x_2}, n_2, s_2^2)$

BUT bias when the sample size of a study is small, especially when n≤ 20 (L. V. Hedges 1981).

Interpretation

SMD= 2 -> a difference of 2 standard deviations

Hedges'$g*$ =$SMD_{between}$ X $(1 - \frac{3}{4n-9})$

The different type of effect-sizes

Ratio:

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Contents lists available at SciVerse ScienceDirect

Agriculture, Ecosystems and Environment

journal homepage: www.elsevier.com/locate/agee

Review

A global meta-analysis of the biodiversity and ecosystem service benefits of coffee and cacao agroforestry

Matthias De Beenhouwer[a], Raf Aerts[b], Olivier Honnay[a,*]

[a] Plant Conservation and Population Biology, University of Leuven, Kasteelpark Arenberg 31-2435, BE-3001 Leuven, Belgium
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ARTICLE INFO

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Received 11 January 2013
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Keywords:
Agroecosystems

ABSTRACT

In tropical regions, the extent of agricultural land is rapidly increasing at the expense of natural forest with associated losses of biodiversity and ecosystem services. Agroforestry has long been proposed as a more sustainable agricultural system, conserving biodiversity and ecosystem services, while providing significant local livelihood. In this context, cacao and coffee agroforestry is often regarded as more compatible with conservation of ecosystem integrity than cacao and coffee plantations. Using meta-analytical techniques and mixed models on data from 74 studies conducted across Africa, Latin America and Asia, a global quantitative synthesis was performed to assess the impact on biodiversity and on

The different type of effect-sizes

Ratio:

$R_{xy} = \frac{\overline{x_1}}{\overline{x_2}}$; with x_1 *and* x_2 *two independant groups*

$\log(R) = \log(\overline{x_1}) - \log(\overline{x_2})$

$$SE_R = s_{pooled}\sqrt{\frac{1}{n_1(\overline{x_1})^2} + \frac{1}{n_2(\overline{x_2})^2}}$$

To be retrieved:

$(\overline{x_1}, n_1, s_1^2, \overline{x_2}, n_2, s_2^2)$

The different type of effect-sizes

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Review

A global meta-analysis of the biodiversity and ecosystem service benefits of coffee and cacao agroforestry

CrossMark

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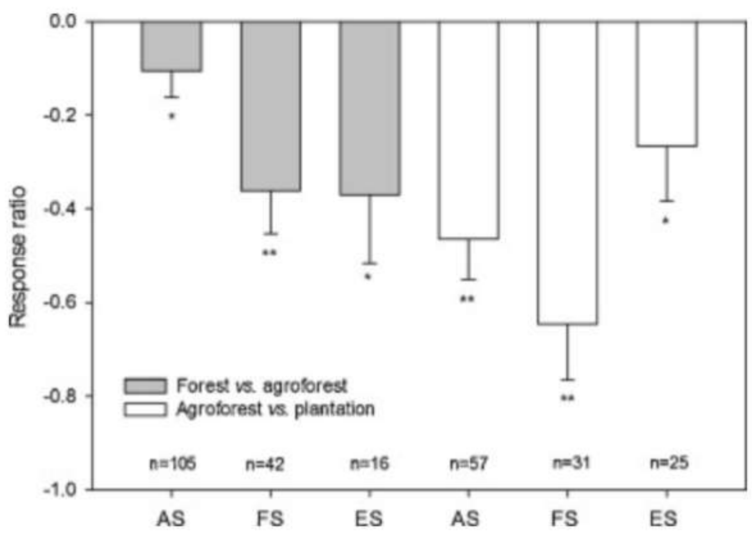


The different type of effect-sizes

Risk Ratio:

The different type of effect-sizes

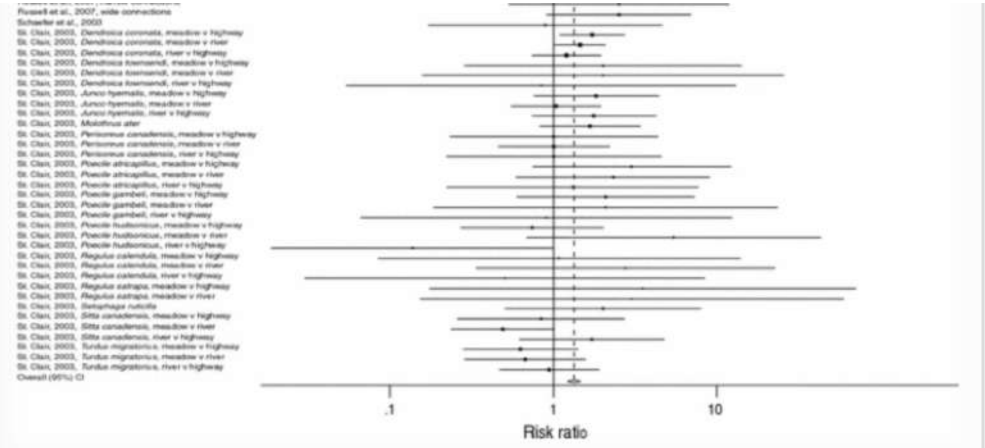
A meta-analysis on the impact of different matrix structures on species movement rates

**Amy E. Eycott · Gavin B. Stewart ·
Lisette M. Buyung-Ali · Diana E. Bowler ·
Kevin Watts · Andrew S. Pullin**

Received: 1 March 2011 / Accepted: 9 July 2012

Abstract Many biodiversity conservation strategies aim to increase species movement by changing the landscape between suitable areas of habitat. We applied systematic review and meta-analytical methods to robustly assess evidence on the impact of matrix structure on movement rates, with the hypothesis that

on animals, including rela
birds and butterflies but al
We were able to detect that
greater through matrix of a
species' habitat despite the
of matrix types, species ar



Risk ratios for experiments comparing emigration rates through different matrix types, sorted by experimental design: studies above the *horizontal dashed line* measured emigration by

The different type of effect-sizes

Risk Ratio:

	Event	No Event	
Treatment	a	b	n_{treat}
Control	c	d	n_{control}
	n_E	$n_{\neg E}$	

To be retrieved:

(a, b, c, d)

$$p_{E-treat} = \frac{a}{a+b};\; p_{E-control} = \frac{c}{c+d}; \log(RR) = \log(\frac{p_{E-treat}}{p_{E-control}})$$

$$SE_{\log(RR)} = \sqrt{\frac{1}{a} + \frac{1}{c} - \frac{1}{a+c} - \frac{1}{c+d}}$$

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« Association » **effect**:

- Correlation

The different type of effect-sizes

PNAS RESEARCH ARTICLE | AGRICULTURAL SCIENCES OPEN ACCESS

Check for updates

Complex agricultural landscapes host more biodiversity than simple ones: A global meta-analysis

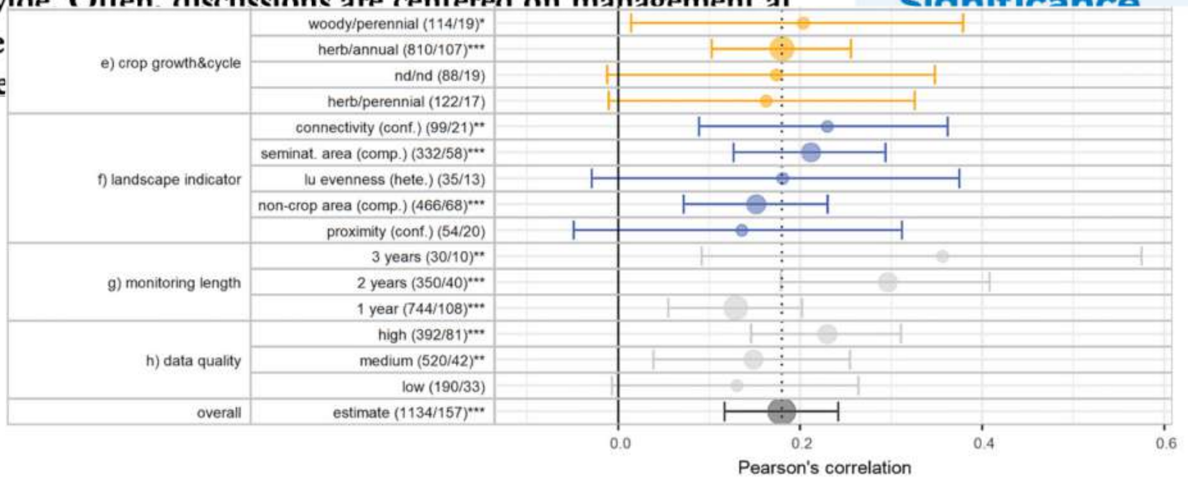
Natalia Estrada-Carmona[a,1], Andrea C. Sánchez[a], Roseline Remans[a], and Sarah K. Jones[a]

Edited by Arun Agrawal, University of Michigan-Ann Arbor, Ann Arbor, MI; received February 24, 2022; accepted July 5, 2022

Managing agricultural landscapes to support biodiversity conservation requires pro-
found structural changes worldwide. Often, discussions are centered on management at
the field level. However, a wide
and targeting agricultural policie

Significance

world's



The different type of effect-sizes

Correlations:

$r_{xy} = \frac{\sigma_{xy}^2}{\sigma_x \sigma_y} = \frac{COV(x,y)}{\sigma_x \sigma_y}$; with x and y two variables

$SE_{r_{xy}} = \frac{1-r_{xy}^2}{\sqrt{n-2}}$;

To be retrieved:

(r, n)

BUT : the range of proportions is restricted between 0 and 1 : problematic -> Fisher's z

$z = 0.5 log_e \left(\frac{1+r}{1-r}\right)$;

$SE_z = \frac{1}{\sqrt{n-3}}$;

e.g. Correlation of native and exotic species richness (Peng et al., 2019)

How to pool effect-sizes?

Vote counting :

Should be avoided whenever possible.

-Do not account for different weights given to each study

-Do not inform and the magnitude of the effect

How to pool effect-sizes?

Fixed-effect model:

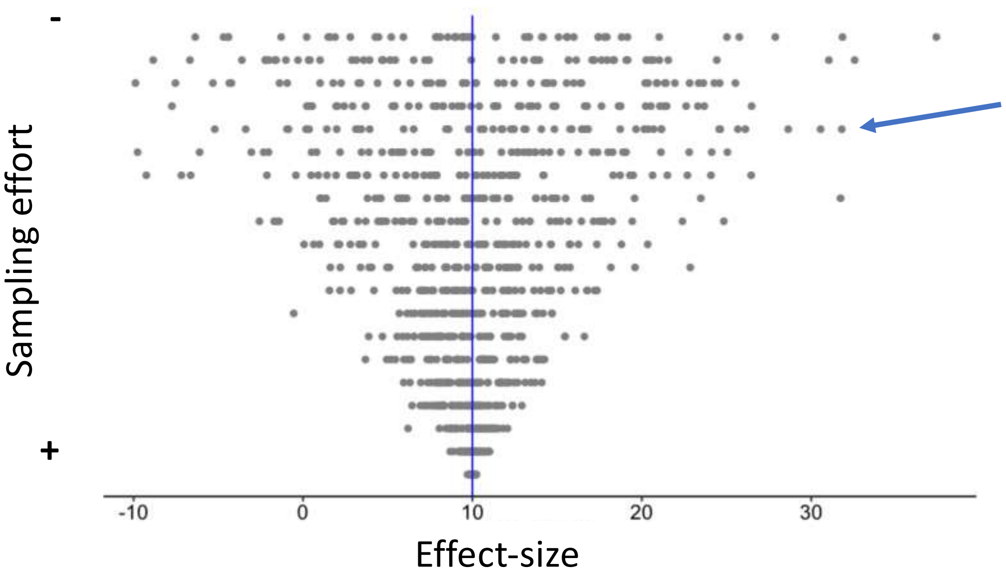
all effect sizes stem from a single population

-> all studies share the **same** true effect size

$$\widehat{\theta_k} = \theta + \varepsilon_k; \ \ \varepsilon_{k \sim} \mathrm{N}(0, s_k^2)$$

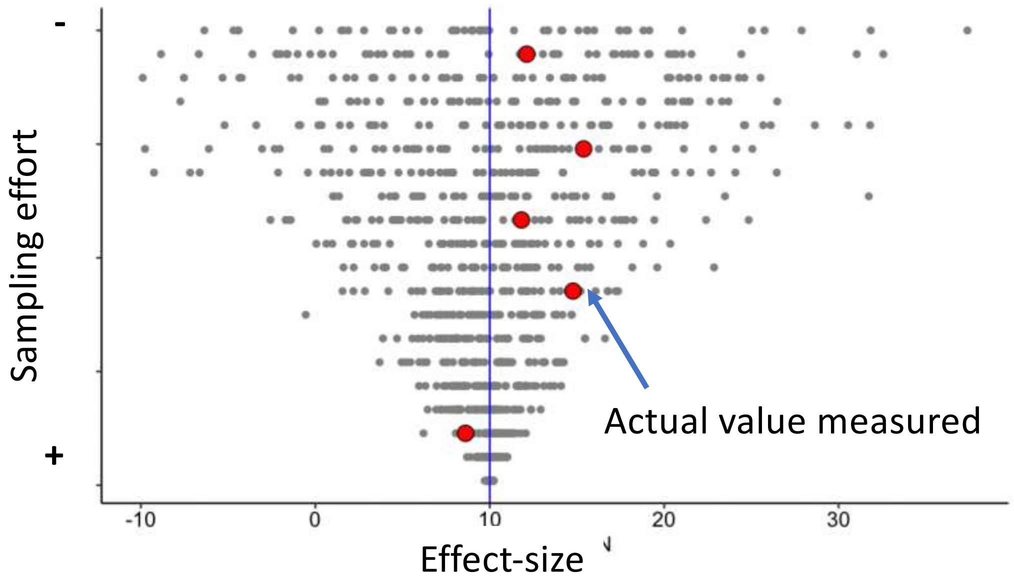
The true effect size for study k is not only true for k specifically, but for **all** studies in our meta-analysis

How to pool effect-sizes?



Probability to find a certain value
for an ecffect size for different sampling effort

How to pool effect-sizes?



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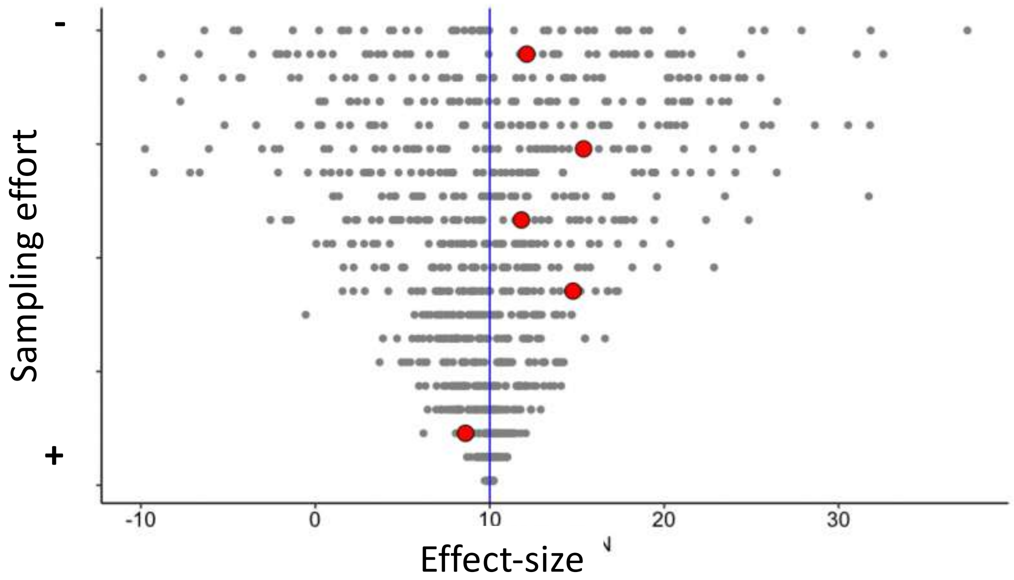
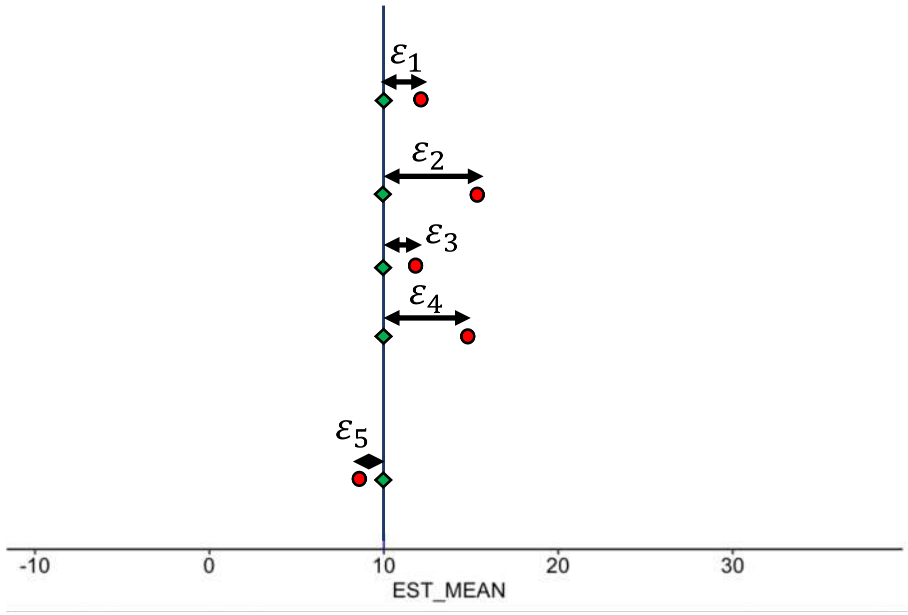


Fixed-effect model:



How to pool effect-sizes?

Fixed-effect model:

Weights w_k

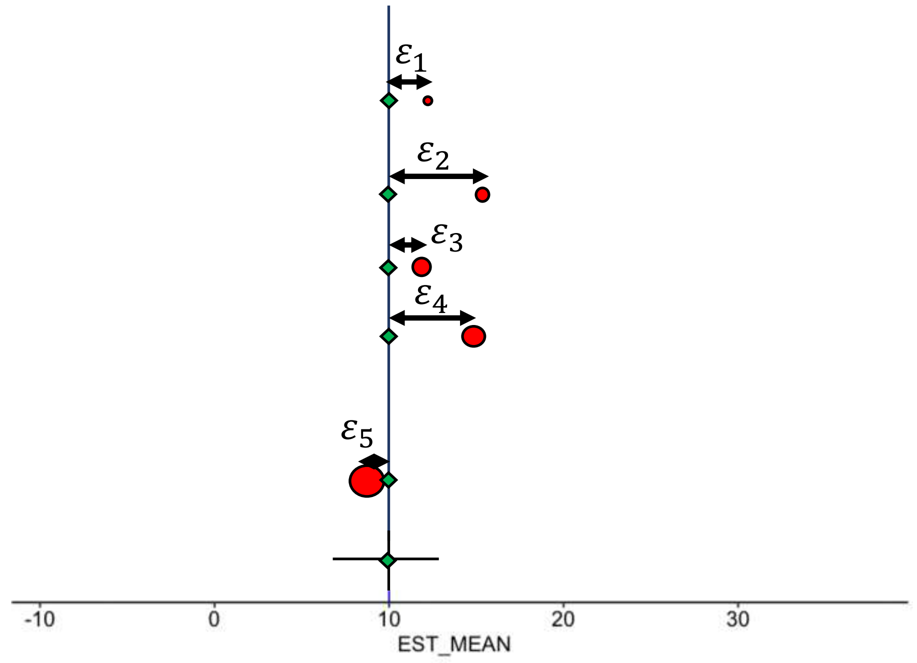
The usual statistical method for combining results of multiple studies is to weight studies by the amount of information they contribute

$$w_k = \frac{1}{s_k^2}$$

$$Pour\ rappel: \quad \widehat{\theta_k} = \theta + \varepsilon_k; \quad \varepsilon_{k\sim} \mathrm{N}(0, s_k^2)$$

How to pool effect-sizes?

Fixed-effect model:



How to pool effect-sizes?

Fixed-effect model:

BUT does not account for:

The outcome of interest could have been measured in many ways.
The type of treatment may not have been exactly the same.
The intensity and duration of treatment could differ.
The target population of the studies may not have been exactly the same for each study.
The control groups used may have been different.

→ between-study **heterogeneity**

How to pool effect-sizes?

Fixed-effect model:

all effect sizes stem from a single population
-> all studies share the **same** true effect size

$$\widehat{\theta_k} = \theta + \varepsilon_k$$

Random-effect model:

There is a distribution of true effect-sizes

$$\widehat{\theta_k} = \theta_k + \varepsilon_k$$

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Random-effect model:

There is a distribution of true effect-sizes

$$\widehat{\theta_k} = \theta_k + \varepsilon_k$$

$$\theta_k = \mu + \zeta_k$$

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Fixed-effect model:

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-> all studies share the **same** true effect size

$$\widehat{\theta_k} = \theta + \varepsilon_k$$

Random-effect model:

There is a distribution of true effect-sizes

$$\widehat{\theta_k} = \theta_k + \varepsilon_k$$

$$\theta_k = \mu + \zeta_k$$

$$\widehat{\theta_k} = \mu + \zeta_k + \varepsilon_k$$

How to pool effect-sizes?

Random-effect model:

$$\widehat{\theta_k} = \mu + \zeta_k + \varepsilon_k$$

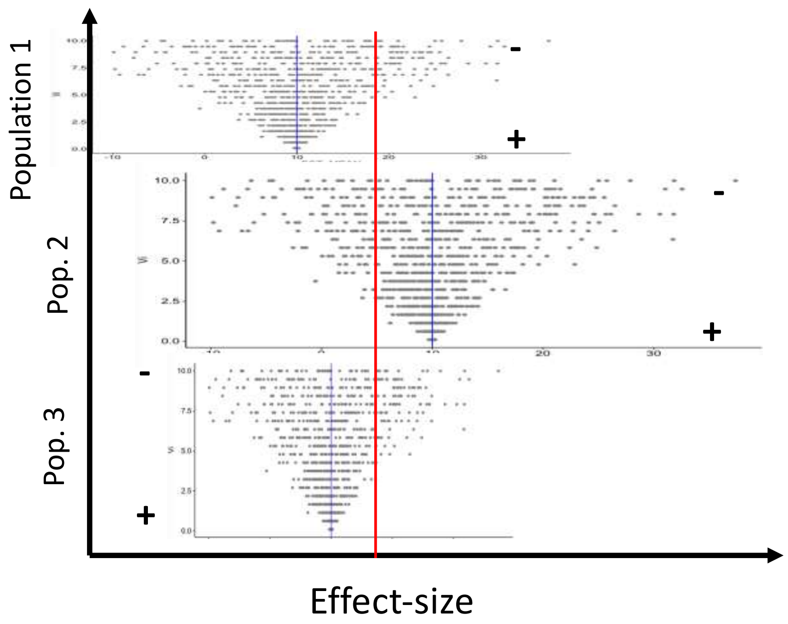
μ is the overall mean (or meta-analytic mean)

$\zeta_k \sim \mathcal{N}(0, \mathcal{T}^2)$ $\mathcal{T}^2$ is the between study variance

$\varepsilon_k \sim \mathcal{N}(0, v_k)$ v_k is the within study variance

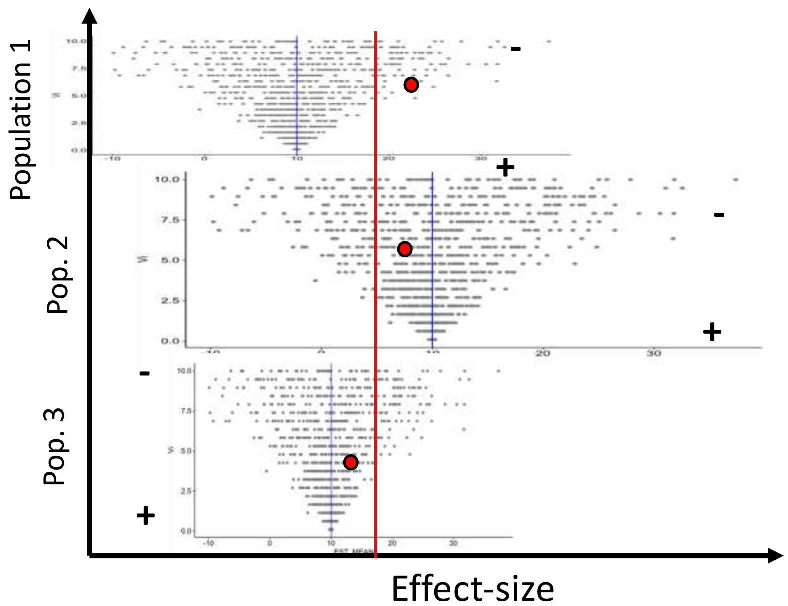
How to pool effect-sizes?

Mixed-effect model:



How to pool effect-sizes?

Mixed-effect model:



How to pool effect-sizes?

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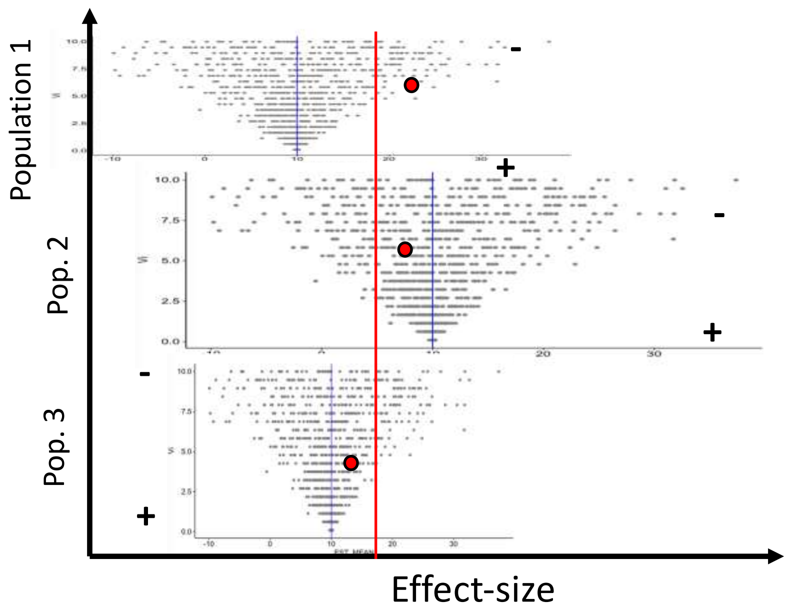
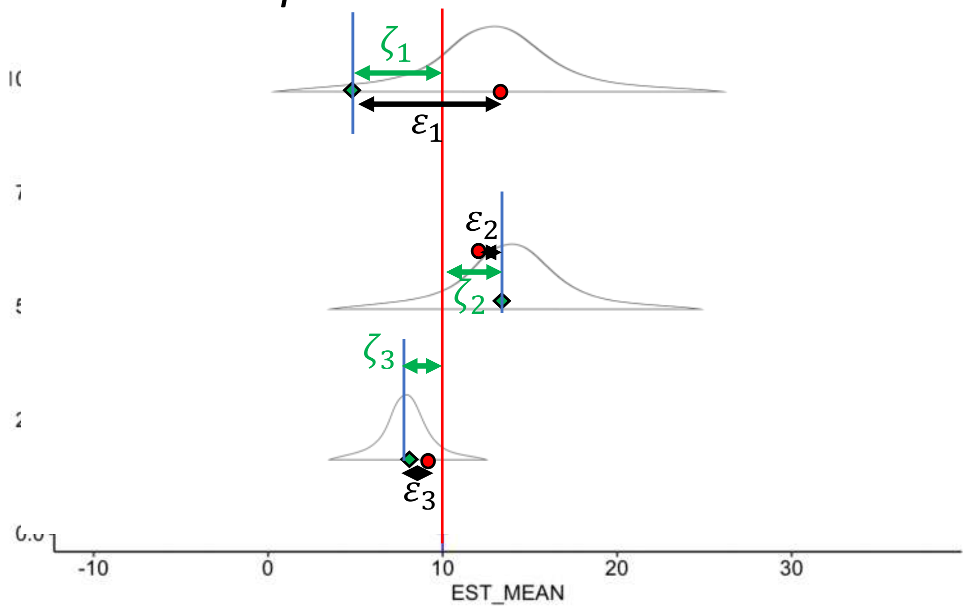


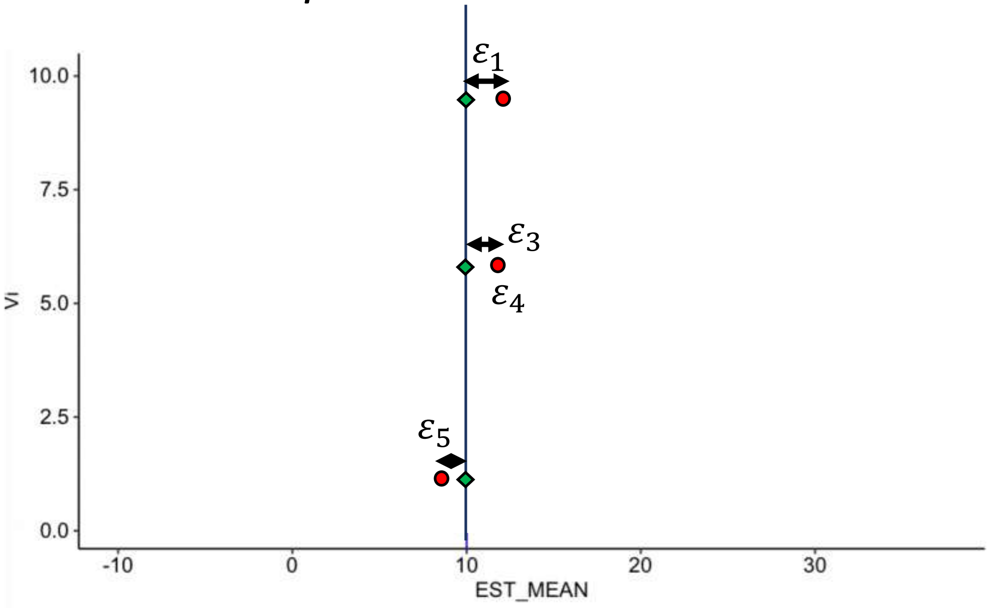
« The experimental world »



How to pool effect-sizes?

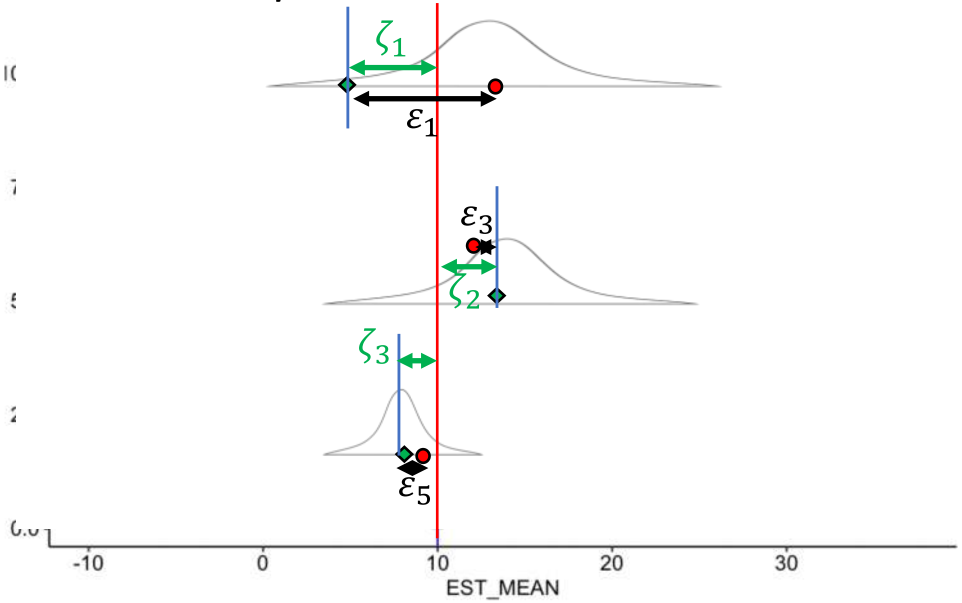
Fixed-effect model:

« The experimental world »

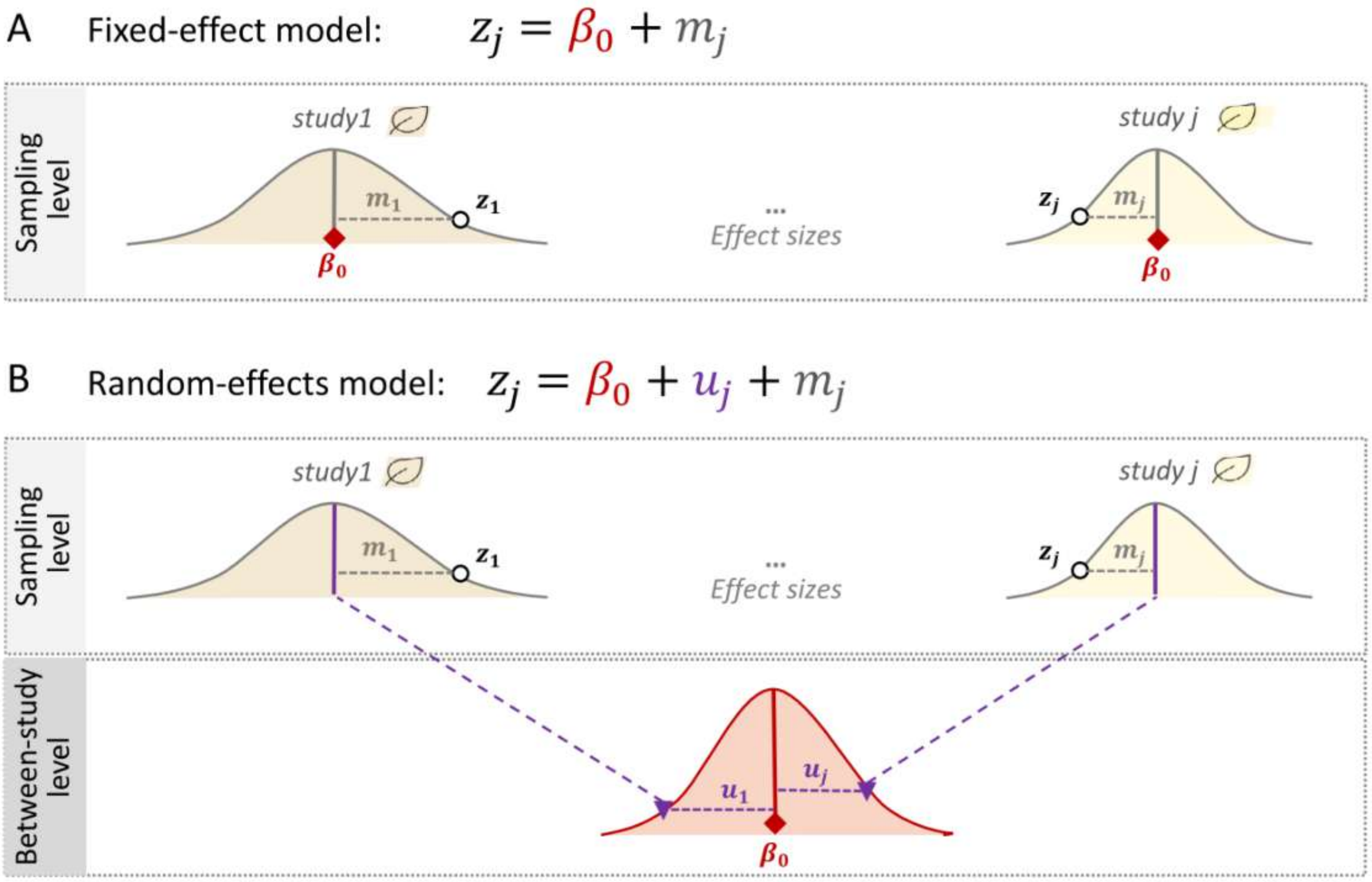


Mixed-effect model:

« The experimental world »



How to pool effect-sizes?



How to pool effect-sizes?

Mixed-effect model:

Weights w_k

The usual statistical method for combining results of multiple studies is to weight studies by the amount of information they contribute

$$w_k = \frac{1}{v_k^2 + \mathcal{T}^2}$$

Pour rappel : $\widehat{\theta_k} = \mu + \zeta_k + \varepsilon_k , \zeta_k \sim \mathcal{N}(0, \mathcal{T}^2); \varepsilon_k \sim \mathcal{N}(0, v_k)$

How to estimate $\mathcal{T}^2$?

Invited Review

Research Synthesis Methods

Received 26 June 2014, Revised 20 May 2015, Accepted 24 June 2015 Published online in Wiley Online Library

(wileyonlinelibrary.com) DOI: 10.1002/jrsm.1164

Methods to estimate the between-study variance and its uncertainty in meta-analysis

Areti Angeliki Veroniki,[a*] Dan Jackson,[b] Wolfgang Viechtbauer,[c] Ralf Bender,[d] Jack Bowden,[e] Guido Knapp,[f] Oliver Kuss,[g] Julian PT Higgins,[h,i] Dean Langan[i] and Georgia Salanti[j]

Meta-analyses are typically used to estimate the overall/m
inference about between-study variability, which is typically
parameter, is usually an additional aim. The DerSimonian ai

Group

Cochrane Methods

Articles

Recommendations for quantifying the uncertainty in the summary intervention effect and estimating the between-study heterogeneity variance in random-effects meta-analysis

Areti Angeliki Veroniki, Dan Jackson, Wolfgang Viechtbauer, Ralf Bender, Guido Knapp, Oliver Kuss, Dean Langan

ronto,

has also been suggested that the quantile-approximation[12], t, and Knapp and Hartung[17,19] (HKSJ for heterogeneity > 0) methods have coverage closer to the nominal level than the Wt method.[12] An advantage of the HKSJ method is that it is insensitive to the magnitude and estimator of heterogeneity, as well the number of studies included in a meta-analysis.[8]

A prediction interval of the possible intervention effect in an individual setting can also be calculated, to facilitate the interpretation of the meta-analysis result.[20-22]

Inference for the between-study heterogeneity variance

The heterogeneity variance can be estimated using various approaches, including the method proposed by DerSimonian and

Received: 9 November 2017 | Revised: 23 May 2018 | Accepted: 13 August 2018

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RESEARCH ARTICLE

WILEY Research Synthesis Methods

Methods to calculate uncertainty in the estimated overall effect size from a random-effects meta-analysis

Areti Angeliki Veroniki[1,2] | Dan Jackson[3] | Ralf Bender[4] | Oliver Kuss[5,6] | Dean Langan[7] | Julian P.T. Higgins[8] | Guido Knapp[9] | Georgia Salanti[10]

[1] Li Ka Shing Knowledge Institute, St.

How to estimate $\mathcal{T}^2$?

Mixed-effect model:

Methods to estimates $\mathcal{T}^2$

DerSimonian-Laird (DL) *(default estimator in Revman, C*omprehensive Meta-Analysis, meta package)

Restricted Maximum Likelihood (REML) *(default estimator in metafor package)*

Paule-Mandel (PM)

…

How to estimate $\mathcal{T}^2$?

Mixed-effect model:

Methods to better consider the distribution estimates $\mathcal{T}^2$

(a correction applicable after each of the previous mentionned estimators of $\mathcal{T}^2$*)*

- Knapp-Hartung Adjustments

How to pool effect-sizes?

Three levels meta-analysis :

Statistical independence of the effect sizes is one of the core assumptions when we pool effect sizes in a meta-analysis

BUT:

-One author could report several effect-sizes (multiples experiments, control, …)
-An overall structure of the data (Climate effect, country effect, ….)

→ Nested Three levels met-analyses

How to pool effect-sizes?

Random-effect model (2 levels):

There is a distribution of true effect-sizes

$$\widehat{\theta_k} = \theta_k + \varepsilon_k$$

$$\theta_k = \mu + \zeta_k$$

$$\widehat{\theta_k} = \mu + \zeta_k + \varepsilon_k$$

Random-effect model (3 levels):

There is a distribution of true effect-sizes

$$\widehat{\theta_{jk}} = \theta_{jk} + \varepsilon_{jk}$$

$$\theta_{jk} = \kappa_j + \zeta_{(2)jk}$$

$$\kappa_j = \mu + \zeta_{(3)j}$$

$$\widehat{\theta_k} = \mu + \zeta_{(2)jk} + \zeta_{(3)j} + \varepsilon_{jk}$$

How to pool effect-sizes?

Random-effect model (three levels):

$$\widehat{\theta_k} = \mu + \zeta_{(2)jk} + \zeta_{(3)j} + \varepsilon_{jk}$$

μ is the overall mean (or meta-analytic mean)

$\zeta_{(2)kj} \sim \mathcal{N}(0, \mathcal{T}^2_{(2)})$ $\mathcal{T}^2_{(2)}$ is the within cluster variability

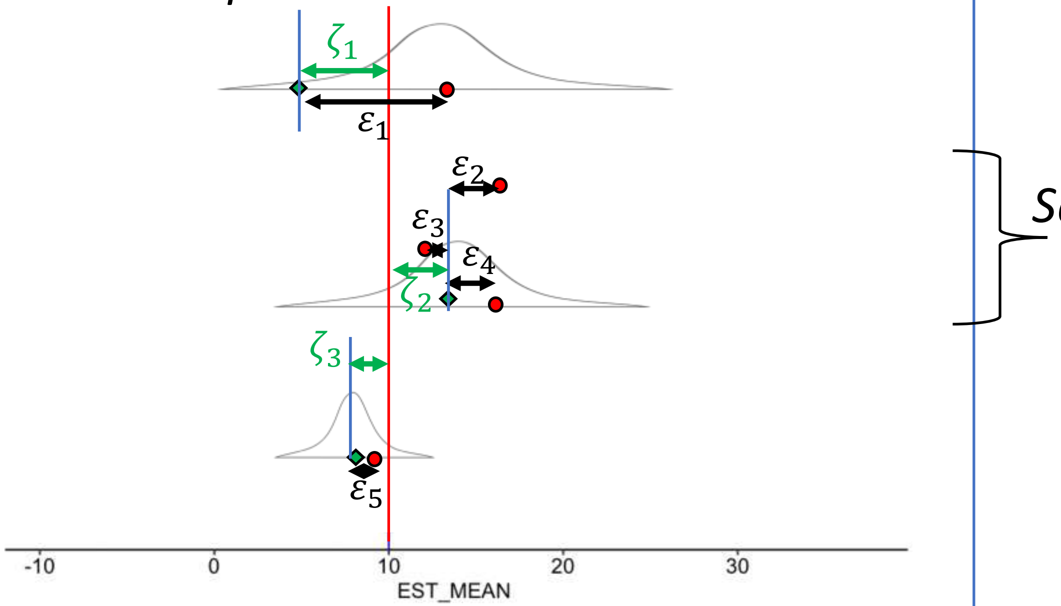
$\zeta_{(3)j} \sim \mathcal{N}(0, \mathcal{T}^2_{(3)})$ $\mathcal{T}^2_{(3)}$ is the between cluster variability

$\varepsilon_{kj} \sim \mathcal{N}\left(0, v_{jk}\right)$ v_{jk} is the within study in cluster variance

How to pool effect-sizes?

Mixed-effect model:

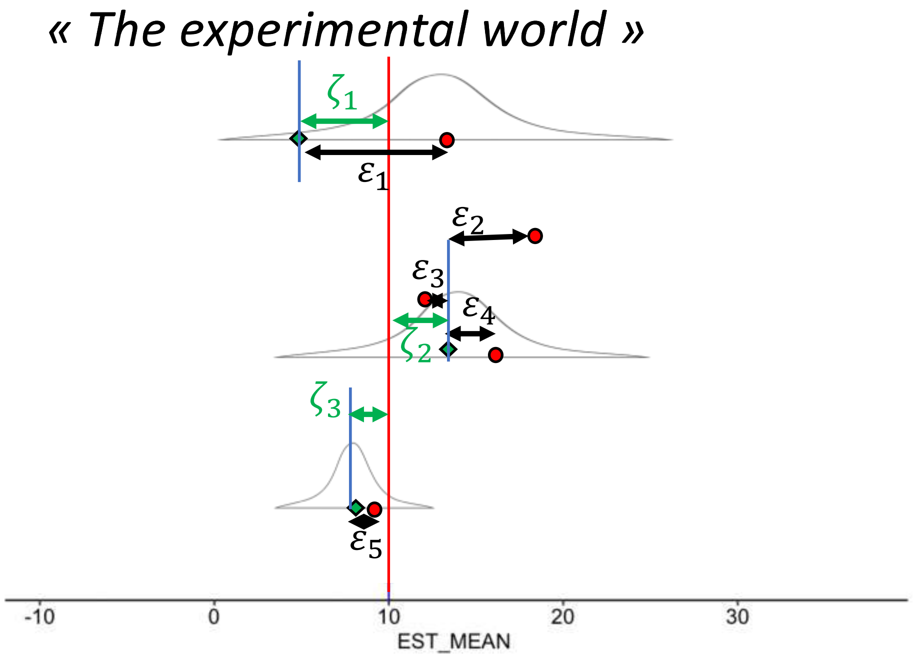
« The experimental world »



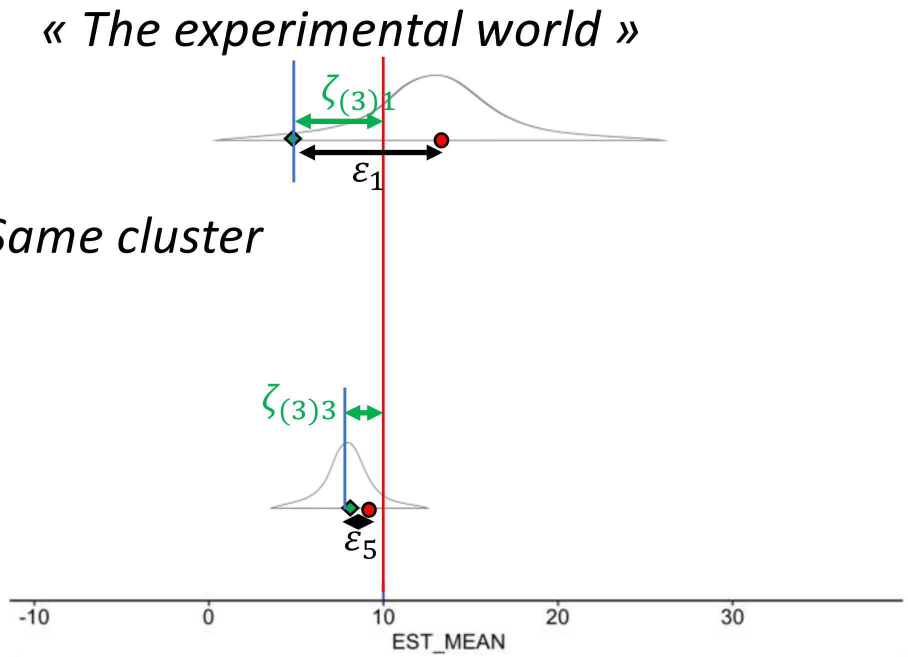
Same cluster

How to pool effect-sizes?

Mixed-effect model:



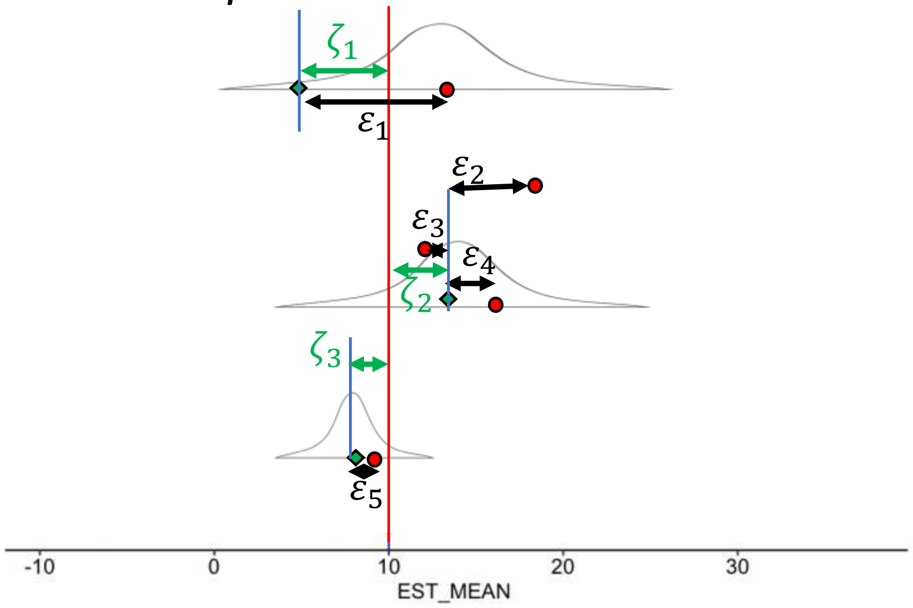
Same cluster



How to pool effect-sizes?

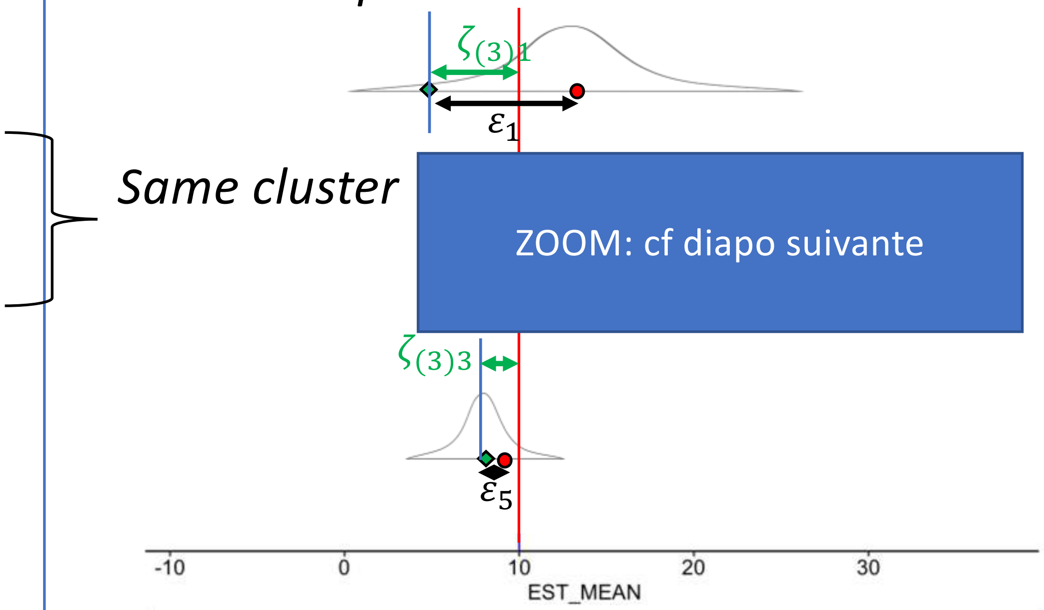
Mixed-effect model:

« The experimental world »

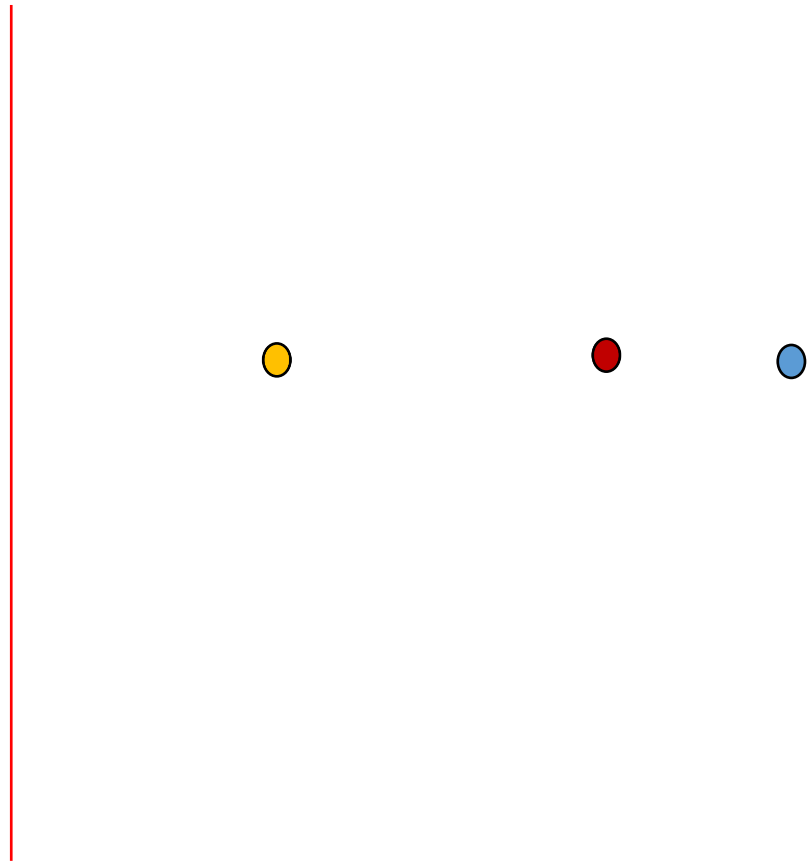


« The experimental world »

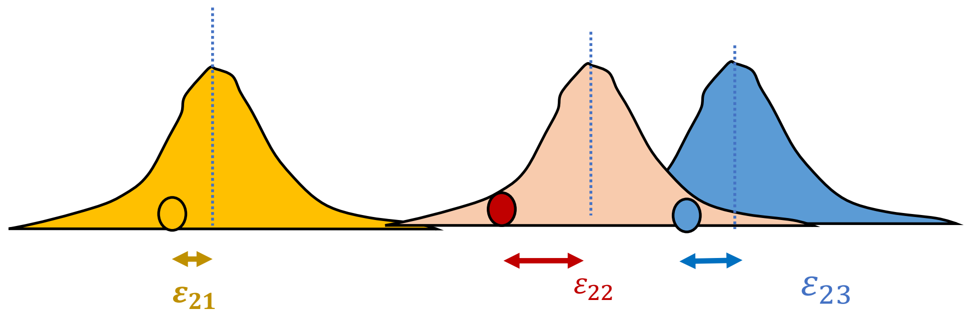
Same cluster



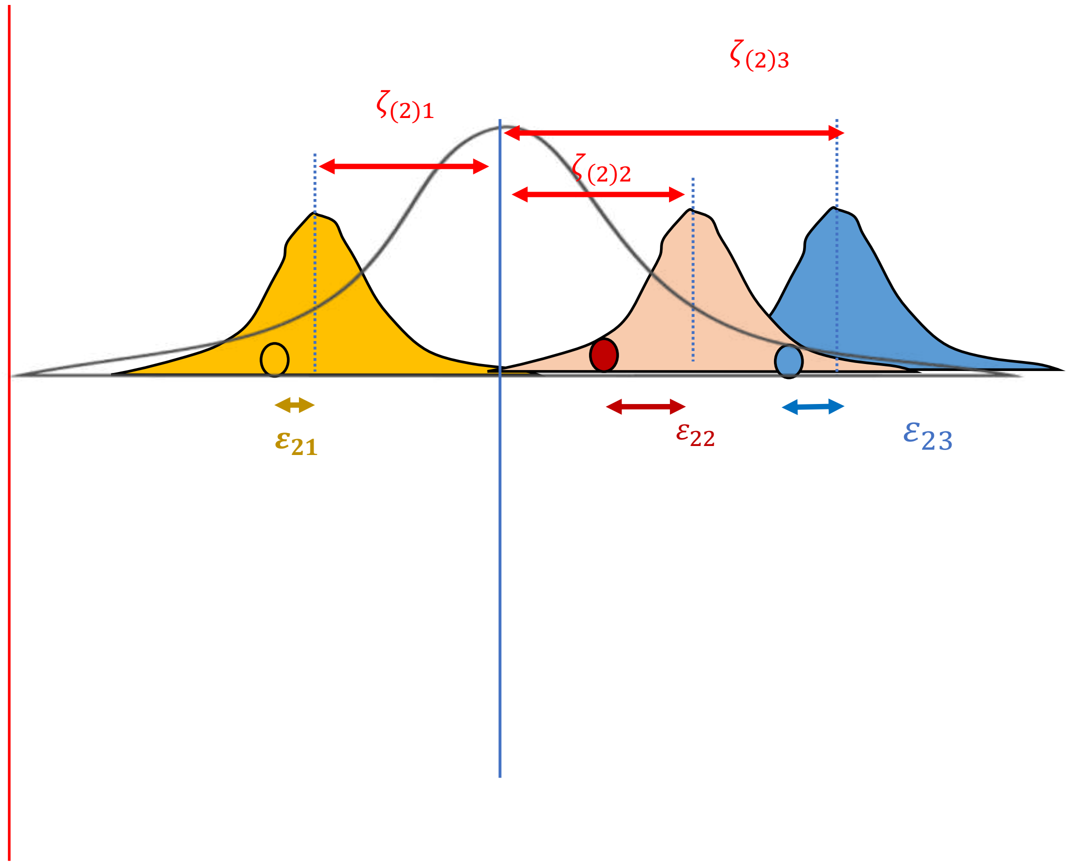
How to pool effect-sizes?



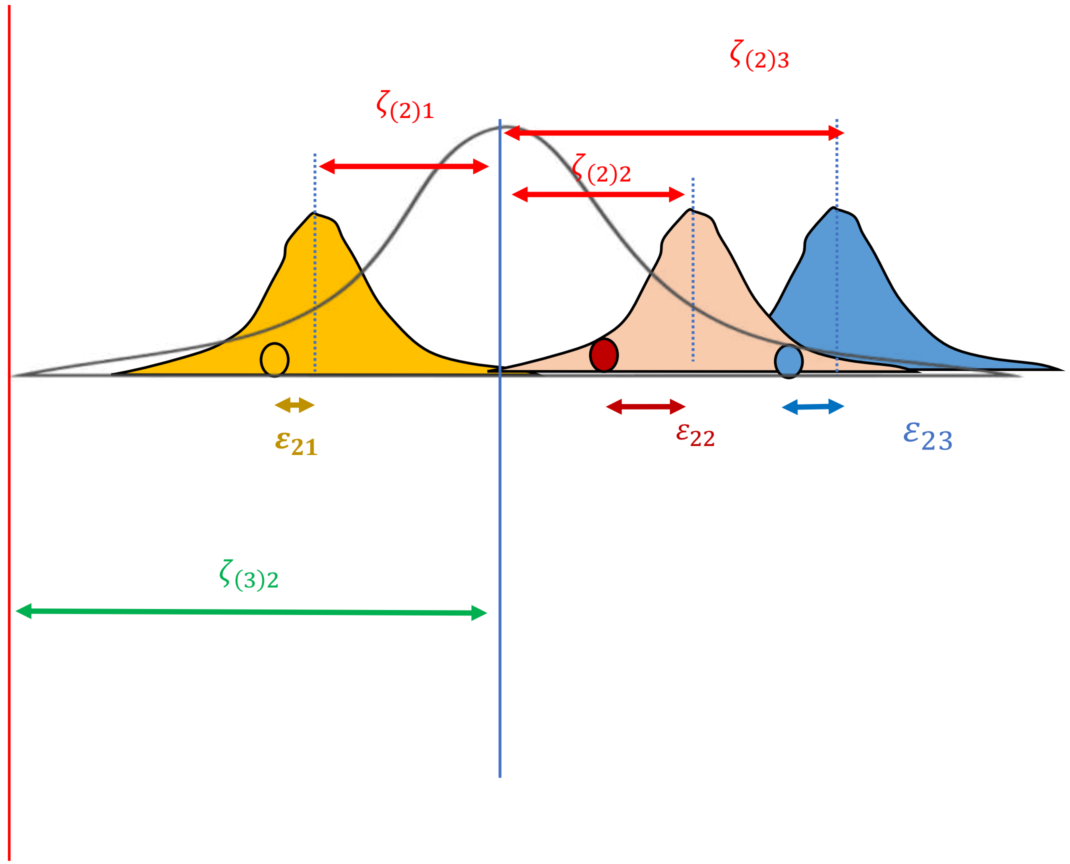
How to pool effect-sizes?



How to pool effect-sizes?



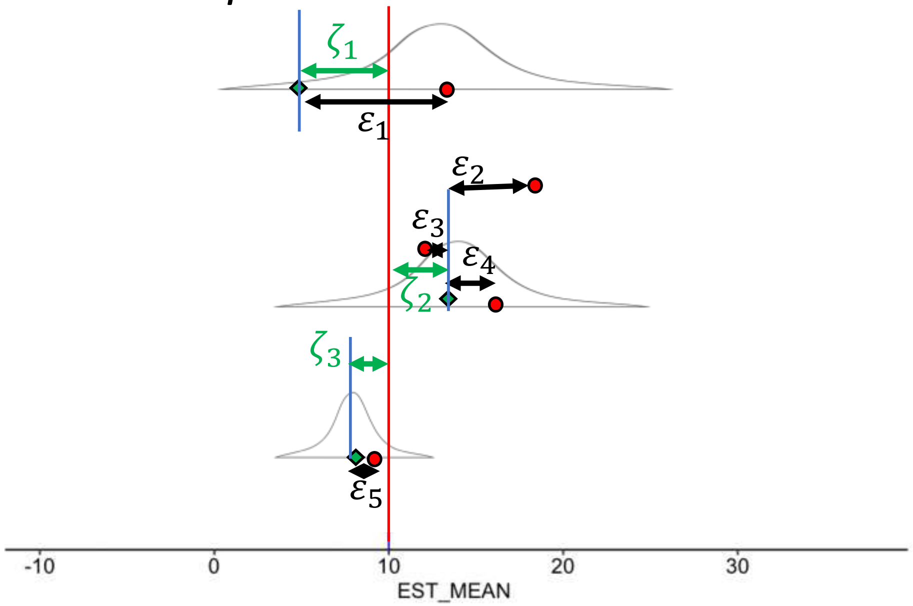
How to pool effect-sizes?



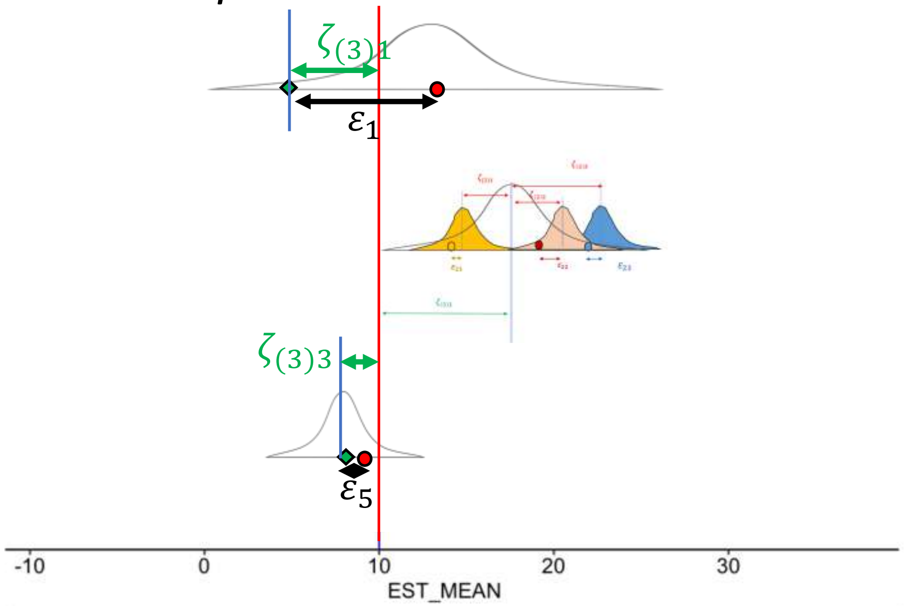
How to pool effect-sizes?

Mixed-effect model:

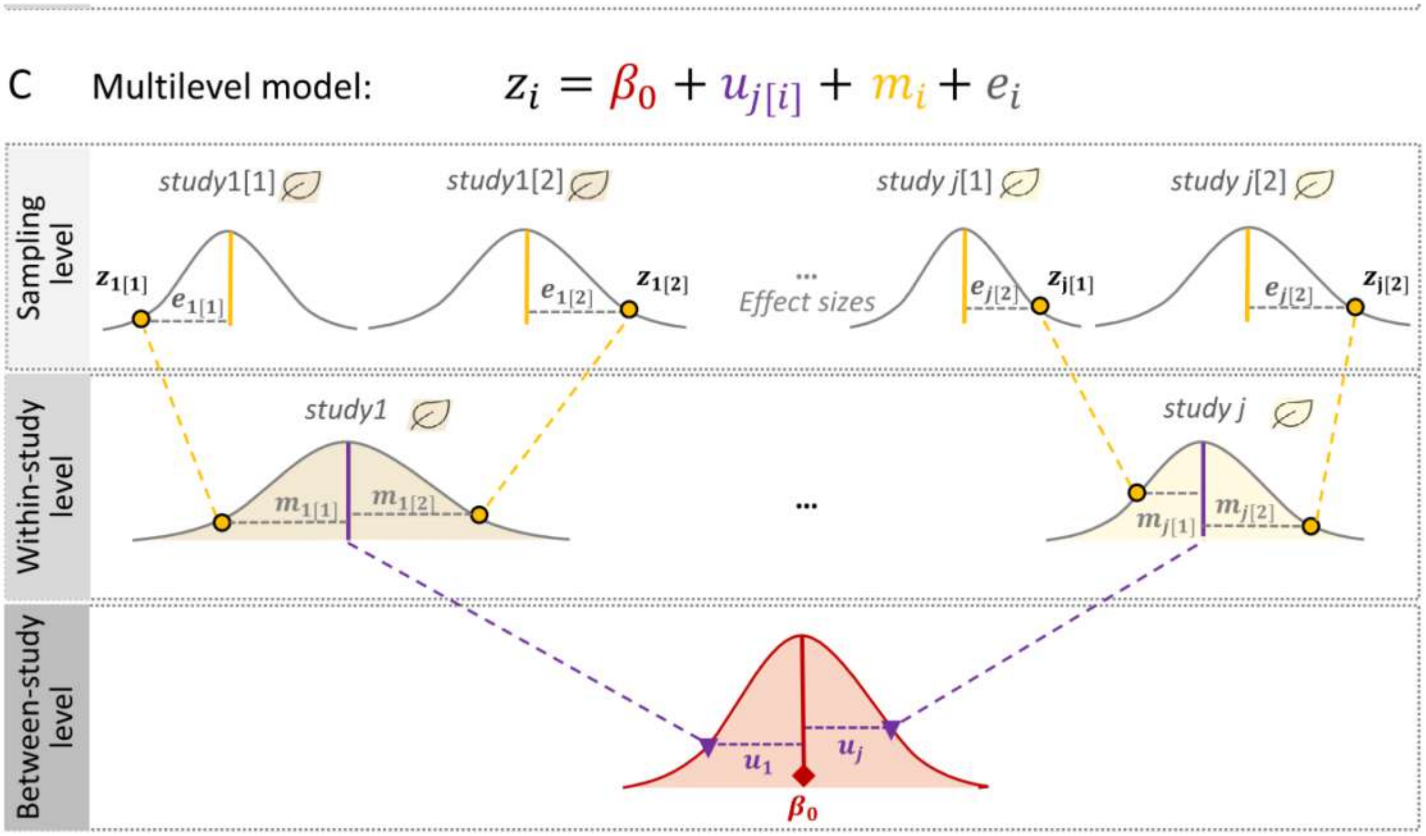
« The experimental world »



« The experimental world »



How to pool effect-sizes?



How to pool effect-sizes?

Sub-group analyses

We assume that the different effect-sizes fall into different **subgroups** and that each subgroup has its own true overall effect

Possible to analyse subgroups in fixed- and random-effect models

How to pool effect-sizes?

Sub-group analyses

Why don't we run a separate meta-anaysis for each group?

Estimates of the various variances (i.e. $\mathcal{T}^2$, ..) will also differ from subgroup to subgroup, but could be very imprecise (when n is low)

Rather : We consider a **common** estimate of the between-study heterogeneity for each subgroups (better estimated).

How to pool effect-sizes?

Sub-group analyses

Assess if there is a **true** difference between the groups

Perform a statistical hypothesis test (compare the variance between vs. Within the groups)
In meta-analyses-> Cochran's Q test (available by default).

Interpretation : at least one subgroup is part of a different population of studies (or not)

How to pool effect-sizes?

Meta-regressions:

Subgroup analyses are a special form of **meta-regression**

Use the value of some variable x to predict the value of another variable y, and applied to **entire studies**

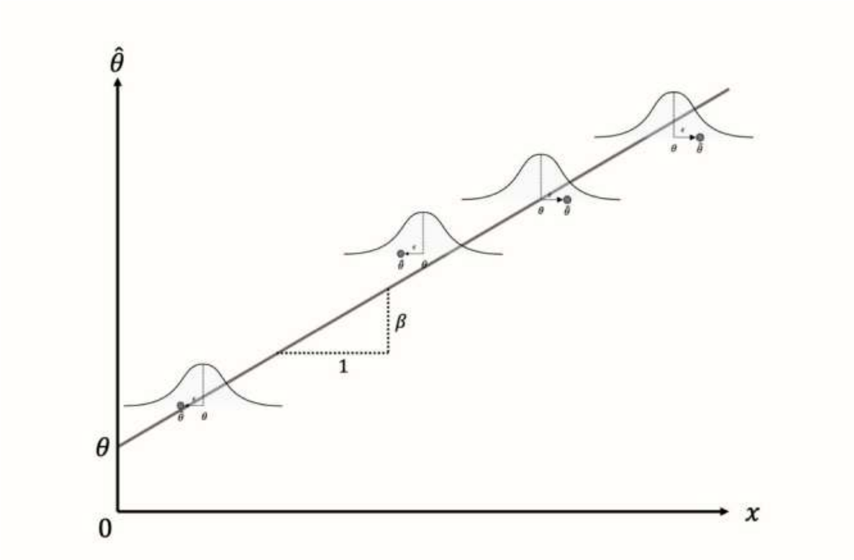
How to pool effect-sizes?

Meta-regressions (mixed effect models):

$$\widehat{\theta_k} = \mu + \beta x_k + \zeta_k + \varepsilon_k$$

β the regression coefficient

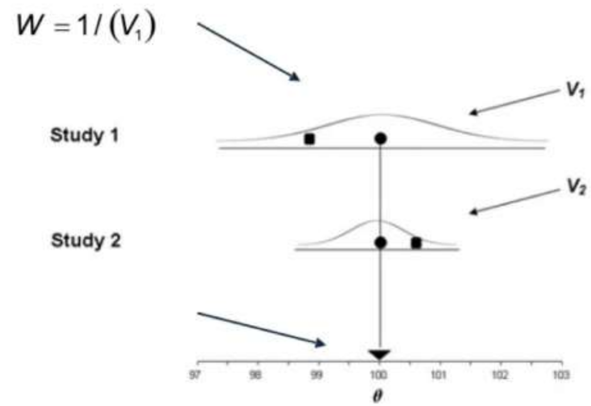
Estimated through weighted least squares (WLS)



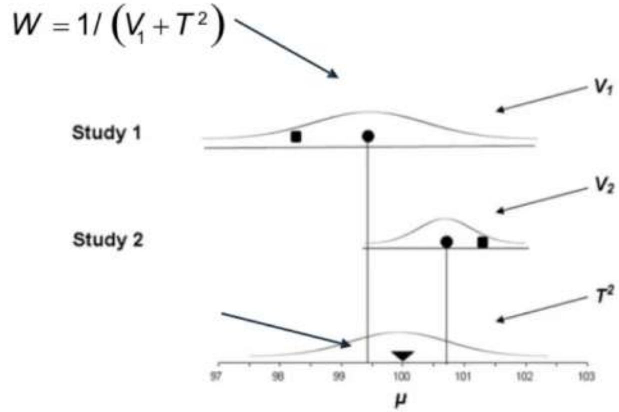
Analysis of heterogeneity

Remember, heterogenity impact weights (of random effect meta-analyses)

Weights when $T^2 = 0$

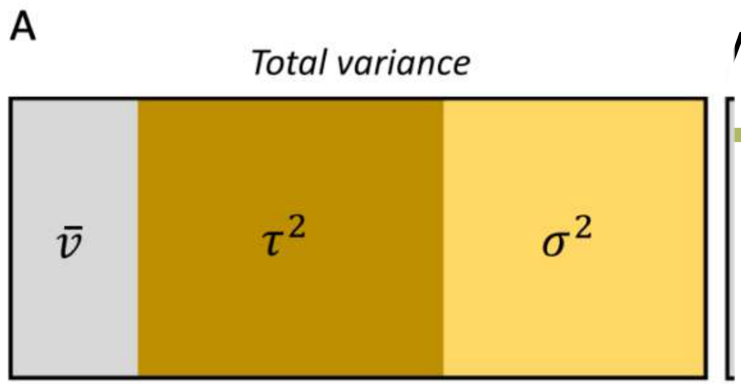


Weights when $T^2 > 0$



Analysis of heterogeneity

The I^2 statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance



Quantifying heterogeneity: I^2

$$I^2_{total} = \frac{\tau^2 + \sigma^2}{\tau^2 + \sigma^2 + \bar{v}}$$

$$I^2_{study} = \frac{\tau^2}{\tau^2 + \sigma^2 + \bar{v}}$$

$$I^2_{effect} = \frac{\sigma^2}{\tau^2 + \sigma^2 + \bar{v}}$$

The different type of effect-sizes

RESEARCH ARTICLE

Prevalence of human papillomavirus (HPV) in Brazil: A systematic review and meta-analysis

Verônica Colpani[1], Frederico Soares Falcetta[1☯], Augusto Bacelo Bidinotto[1☯], Natália Luiza Kops[1], Maicon Falavigna[1], Luciano Serpa Hammes[1], Adele Schwartz Benzaken[2,3], Ana Goretti Kalume Maranhão[4], Carla Magda Allan S. Domingues[4], Eliana Márcia Wendland[1,5]*

1 Hospital Moinhos de Vento, Porto Alegre, Rio Grande do Sul, Brazil, **2** Tropical Medicine Foundation Heitor Vieira Dourado, Manaus, Amazonas, Brazil, **3** Aids Health Care Foundation. Manaus. Amazonas. Brazil. **4** National Immunization Program, Ministry of Health, Bra Community Health, Federal University of Health Science c Brazil

☯ These authors contributed equally to this work.
* elianawend@gmail.com

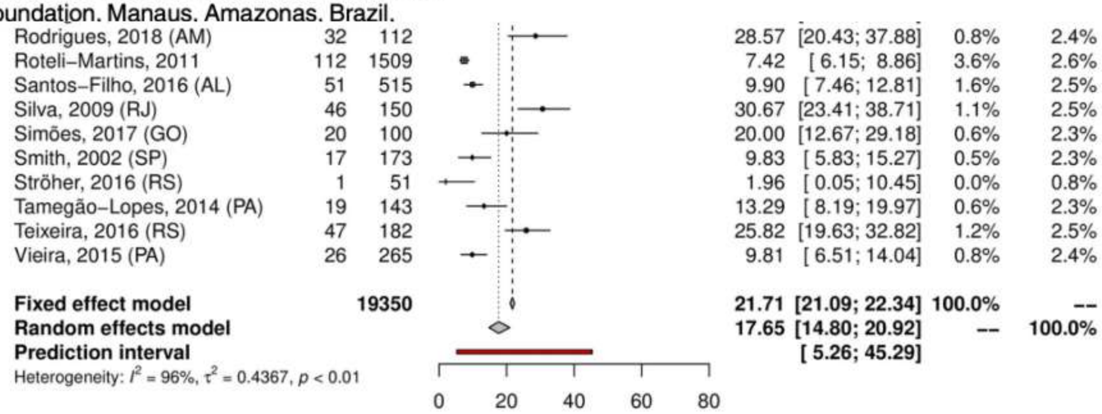


Fig 2. Overall prevalence of cervical infection by high-risk HPV genotypes. Forest plot of a metanalysis of studies reporting prevalence of infection of the cervix by HR-HPV genotypes in Brazil.

Mise en pratique

- library(metafor)

```
> head(dat.bcg)
  trial               author year tpos  tneg cpos  cneg ablat     alloc
1     1              Aronson 1948    4   119   11   128    44    random
2     2     Ferguson & Simes 1949    6   300   29   274    55    random
3     3      Rosenthal et al 1960    3   228   11   209    42    random
4     4    Hart & Sutherland 1977   62 13536  248 12619    52    random
5     5 Frimodt-Moller et al 1973   33  5036   47  5761    13 alternate
6     6      Stein & Aronson 1953  180  1361  372  1079    44 alternate
>
```

Results from 13 clinical trials examining the effectivess of the bacillus Calmette-Guerin (BCG) vaccine for preventing tuberculosis

Mise en pratique

- On calcule l'effect size. Ici le log du relative risque entre vaccins et non vaccins

dat <- escalc(measure="RR", ai=tpos, bi=tneg, ci=cpos, di=cneg, data=dat.bcg)

```
n1i <- ai + bi
n2i <- ci + di
ni <- n1i + n2i
p1i.u <- ai.u/n1i.u
p2i.u <- ci.u/n2i.u
p1i <- ai/n1i
p2i <- ci/n2i
if (measure == "RR") {
  if (addyi) {
    yi <- log(p1i) - log(p2i)
  }
```

Mise en pratique

- La nouvelle table de résultats

author	year	tpos	tneg	cpos	cneg	ablat	alloc	yi	vi
Aronson	1948	4	119	11	128	44	random	-0.8893	0.3256
Ferguson & Simes	1949	6	300	29	274	55	random	-1.5854	0.1946
Rosenthal et al	1960	3	228	11	209	42	random	-1.3481	0.4154
Hart & Sutherland	1977	62	13536	248	12619	52	random	-1.4416	0.0200
Frimodt-Moller et al	1973	33	5036	47	5761	13	alternate	-0.2175	0.0512
Stein & Aronson	1953	180	1361	372	1079	44	alternate	-0.7861	0.0069
Vandiviere et al	1973	8	2537	10	619	19	random	-1.6209	0.2230
TPT Madras	1980	505	87886	499	87892	13	random	0.0120	0.0040
Coetzee & Berjak	1968	29	7470	45	7232	27	random	-0.4694	0.0564
Rosenthal et al	1961	17	1699	65	1600	42	systematic	-1.3713	0.0730
Comstock et al	1974	186	50448	141	27197	18	systematic	-0.3394	0.0124
Comstock & Webster	1969	5	2493	3	2338	33	systematic	0.4459	0.5325
Comstock et al	1976	27	16886	29	17825	33	systematic	-0.0173	0.0714

Mise en pratique

- An equal-effects model can be fitted to these data using the rma.uni() function with:

```
rma(yi, vi, method="EE", data=dat)
rma(yi, vi, data=dat)
```

Mise en pratique

- Les résultats

```
Random-Effects Model (k = 13; tau^2 estimator: REML)

tau^2 (estimated amount of total heterogeneity): 0.3132 (SE = 0.1664)
tau (square root of estimated tau^2 value):      0.5597
I^2 (total heterogeneity / total variability):   92.22%
H^2 (total variability / sampling variability):  12.86

Test for Heterogeneity:
Q(df = 12) = 152.2330, p-val < .0001

Model Results:

estimate       se     zval     pval    ci.lb    ci.ub
 -0.7145   0.1798  -3.9744   <.0001  -1.0669  -0.3622      ***

---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Mise en pratique

- Les résultats

```
Random-Effects Model (k = 13; tau^2 estimator: REML)

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---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```