TARTU ÜLIKOOL

Meta-analysis: current trends

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Introduction

Review papers often rely on naming works supporting some hypothesis

If the support is large then the hypothesis is probably true

What about conflicting evidence?

Introduction (2)

Suppose we can present the research hypothesis as a null hypothesis test (i.e. we test whether some effect is zero)

Supporting evidence is then the papers that have rejceted the null hypothesis

Introduction (3)

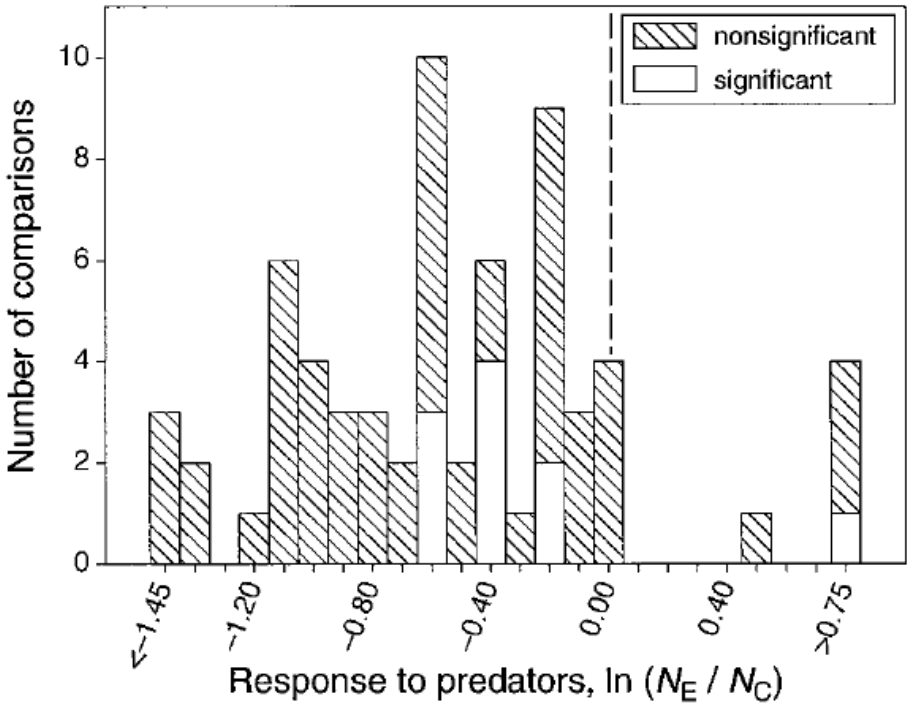
Rejection of the null hypothesis depends on

1. Effect size
2. Sample size
3. Chance

Even if effect size was the same for all studies, sample size varies

Introduction (4)

Just naming works supporting some hypothesis won't usually tell us anything (meaningful)



From: Osenberg et al. 1999

Resolving ecological questions through meta-analysis: goals, metrics, and models. *Ecology*

Introduction (5)

Unless all studies have enough power vote-counting is not useful at all

Even if the studies are comparable is **just** the presence of an effect even a question of interest?

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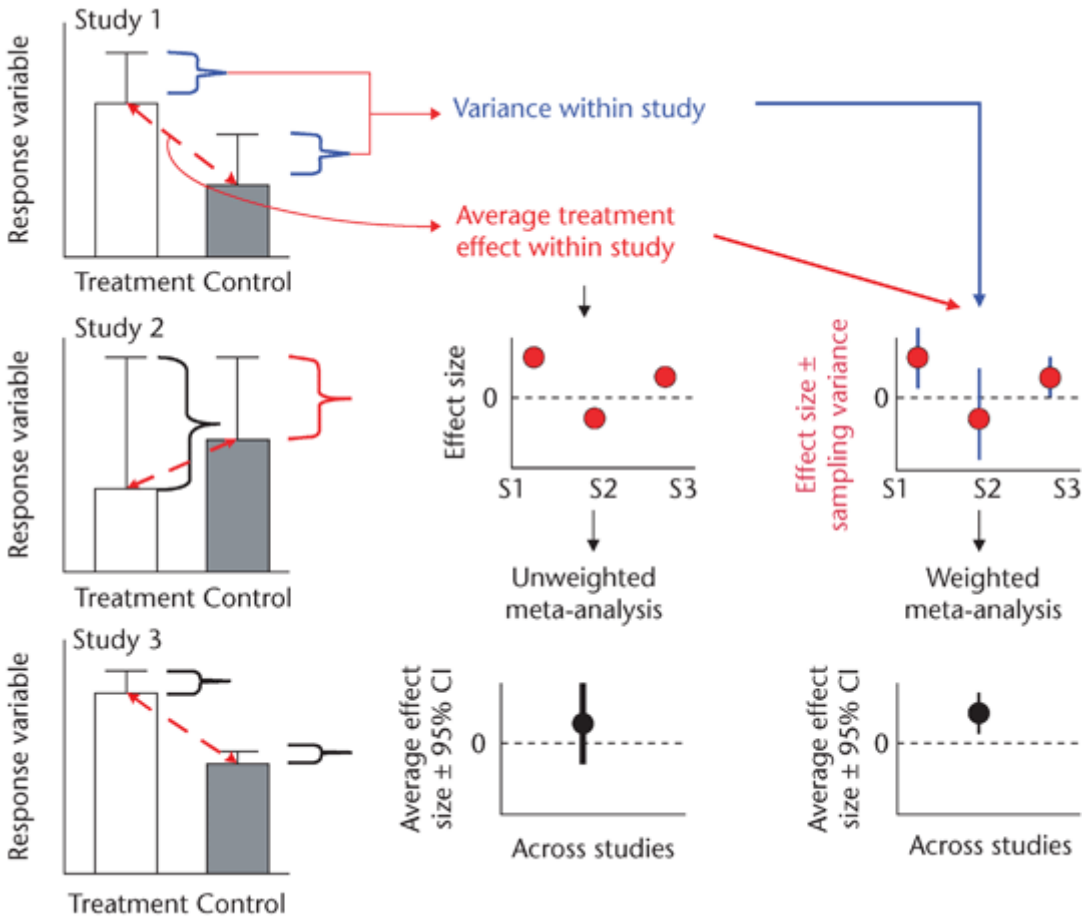
Overview

- General principles
- Current state of the art in meta-analysis
- Challenges
- Tools

Meta-analysis overview



From: Hillebrand 2008. Meta-analysis in Ecology. *Encyclopedia of Life Sciences*.

Study compatibility

Studies (however similar) are typically not fully compatible

- Study population
- Different covariates
- Experimental protocol
- Time

This means two things

1. We cannot just take parameter estimates
2. Even if we could, the parameter of interest (global mean etc) is not that meaningful

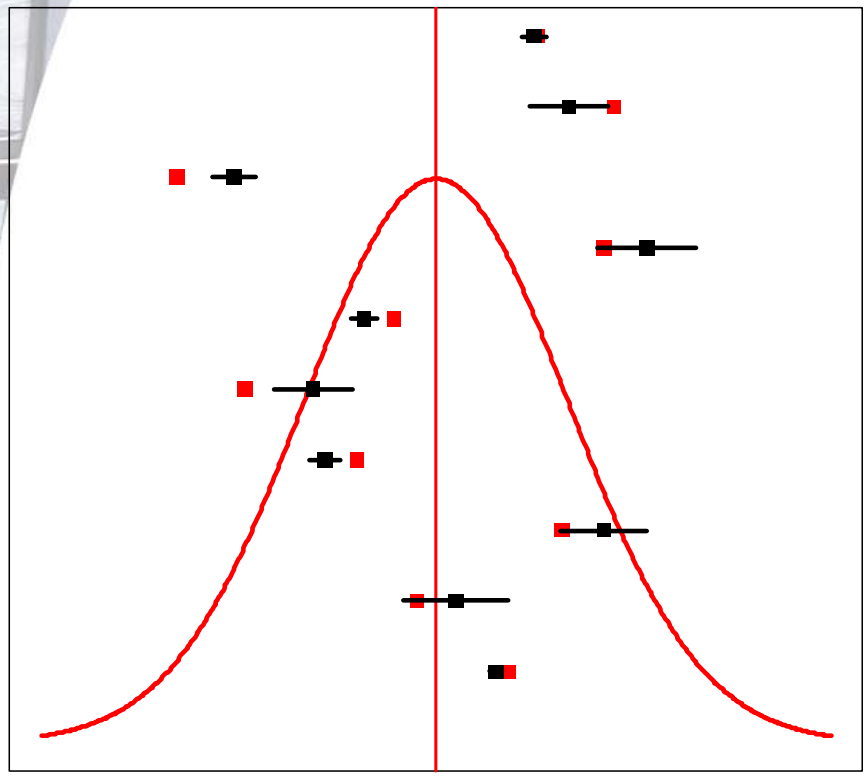
Standardized effect statistics

The choice depends on the problem but

- continuous-continuous -> correlation
- continuous-dichotomous -> standardized difference in the means
- dichotomous-c/d/other -> odds ratio

Usually these can be normalized with a transformation and standard errors for the normalized quantities can then be calculated

Random-Effects meta-analysis model



standardized effects

$$z_i = \mu + u_i + m_i$$

$$u_i \sim N(0, \sigma_u^2)$$

$$D(m_i) = \sigma_i^2$$

Meta-regression

Mixed-effects model where covariates are typically at study level

i.e. we try to explain some of the variance between the effects of different studies

$$z_i = \mu_i + u_i + m_i$$

$$\mu_i = \beta_0 + \sum \beta_i x_i$$

$$u_i \sim N(0, \sigma_u^2)$$

$$D(m_i) = \sigma_i^2$$

Notation as in: Nakagawa, Santos 2012. Methodological issues and advances in biological meta-analysis. *Evolutionary Ecology*

Several effects per study

We should not add study indicator to the fixed effects

So effects from the same study should share a random effect

$$z_i = \mu + u_j + e_i + m_i$$

$$u_j \sim N(0, \sigma_u^2)$$

$$c_i \sim N(0, \sigma_e^2)$$

$$D(m_i) = \sigma_i^2$$

Several species

We must add aditional components to account for the phylogeny

$$z_i = \mu + a_k + s_k + u_j + e_i + m_i$$

$$\mathbf{a} \sim N(\mathbf{0}, \sigma_a^2 \mathbf{A})$$

$$s_k \sim N(0, \sigma_s^2)$$

u_j, e_i, m_i as before

Link to comparative analysis

$$z_i = \mu + a_k + s_k + u_j + e_i + m_i$$

$$\mathbf{a} \sim N(\mathbf{0}, \sigma_a^2 \mathbf{A})$$

$$s_k \sim N(0, \sigma_s^2)$$

u_j, e_i, m_i as before

What if we look at this model from another persepctive – we model trait averages

How complicated is too complicated?

When we cannot estimate the random effects properly then we might take some shortcuts

E.g.

- Phylogenetic correlation at a family level
- Omit some random effects

Competing models

AIC, DIC are used

general considerations still true e.g.

actual separation between models is subjective

AIC is not appropriate when REML is used and fixed effects are not the same

Interpreting the model

Mean of the studied effect is the object of interest

However, we also want to explain the heterogenity (variance components)

Traditionally, Cochran's Q is used

$$Q = \sum \left(\frac{z_j - \hat{\mu}}{\sigma_j} \right)^2$$

However, it is quite useless in this context

Interpreting the model (2)

More useful is the direct use of variance components

$$I^2 = \frac{\sigma_u^2}{\sigma_u^2 + \sigma_m^2}$$

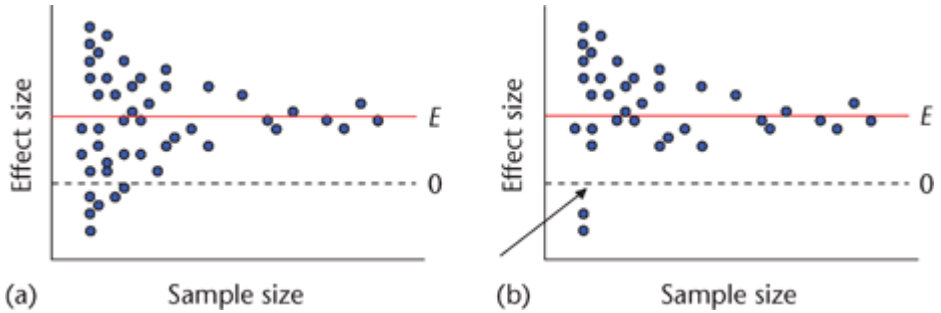
Which can be easily extended as

$$I_u^2 = \frac{\sigma_u^2}{\sigma_a^2 + \sigma_s^2 + \sigma_u^2 + \sigma_e^2 + \sigma_m^2}$$

What can go wrong?

Biased sample of studies

not significant = not published



From: Hillebrand 2008. Meta-analysis in Ecology. *Encyclopedia of Life Sciences*.

What can go wrong? (2)

We must still look at the predicted random effects to assess our model

We should not misinterpret the results

i.e mean might be different from zero but actual effect size varies considerably across studies

Detecting publication bias

A basic test is rank correlation between effect size and sampling variance (Begg's test)

Or we could normalize the effects and regress them against sampling variance (Egger's test)

Again problems with heterogenity

Detecting publication bias (2)

Possible imporvement could be

$$\frac{e_i + m_i}{\sigma_i} = b_0 + b_1 \frac{1}{\sigma_i}$$

where we test the statistical signifance of the slope

Assessing bias relevancy

Essentially sensitivity analysis

Failsafe calculation – how many studies with no effect to overthrow our conclusion

Trim and fill method – let's restore the symmetric funnel and re-estimate

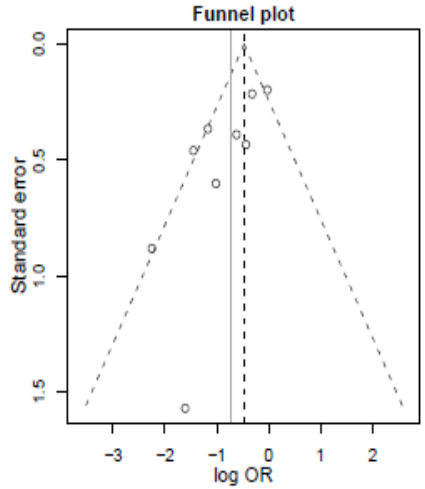
Assessing bias relevancy (2)

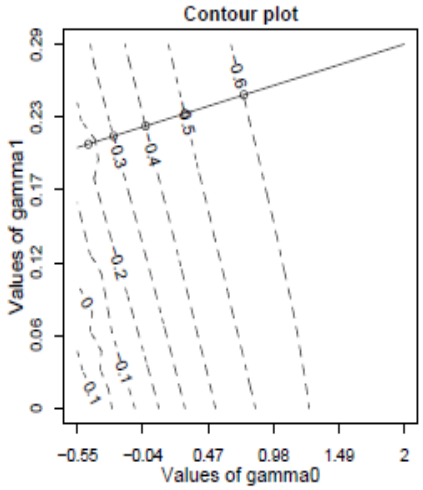
Selection model -- more elaboarate approach

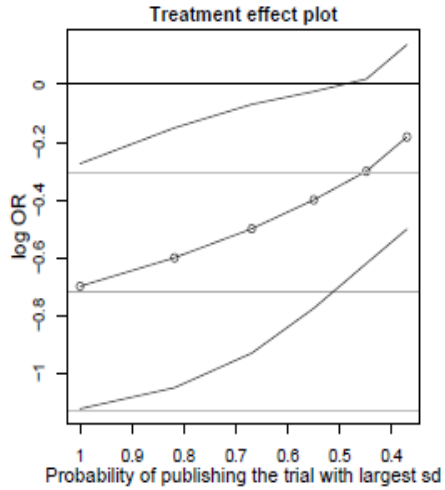
We model the correlation between $u_i + m_i$ and δ_i. The latter influence the probability of publication $\mathbb{P}\{Z > 0\}$.

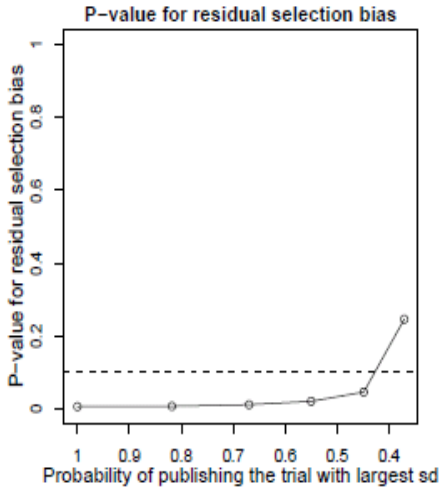
$$Z = a + \frac{b}{\sigma_i} + \delta_i, \; b > 0$$

Assessing bias relevancy (3)









From:
Carpenter et al. 2009.
Copas: an R package for fitting the Copas selection model.
The R journal

Tools

Models described are just linear mixed models

Not often easy to fit them with general software (e.g. package lme4 in R)

Often dedicated software is used (Metawin)

Tools (2)

Things are moving on fast and commercial things just can't keep up

Metafor in R is a dedicated state-of-the-art package

Package MCMCglmm (in R) can do all that is needed

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A former botanist

A mathematician

Meta-analysis is catalyst for interdisciplinary work

Thank you

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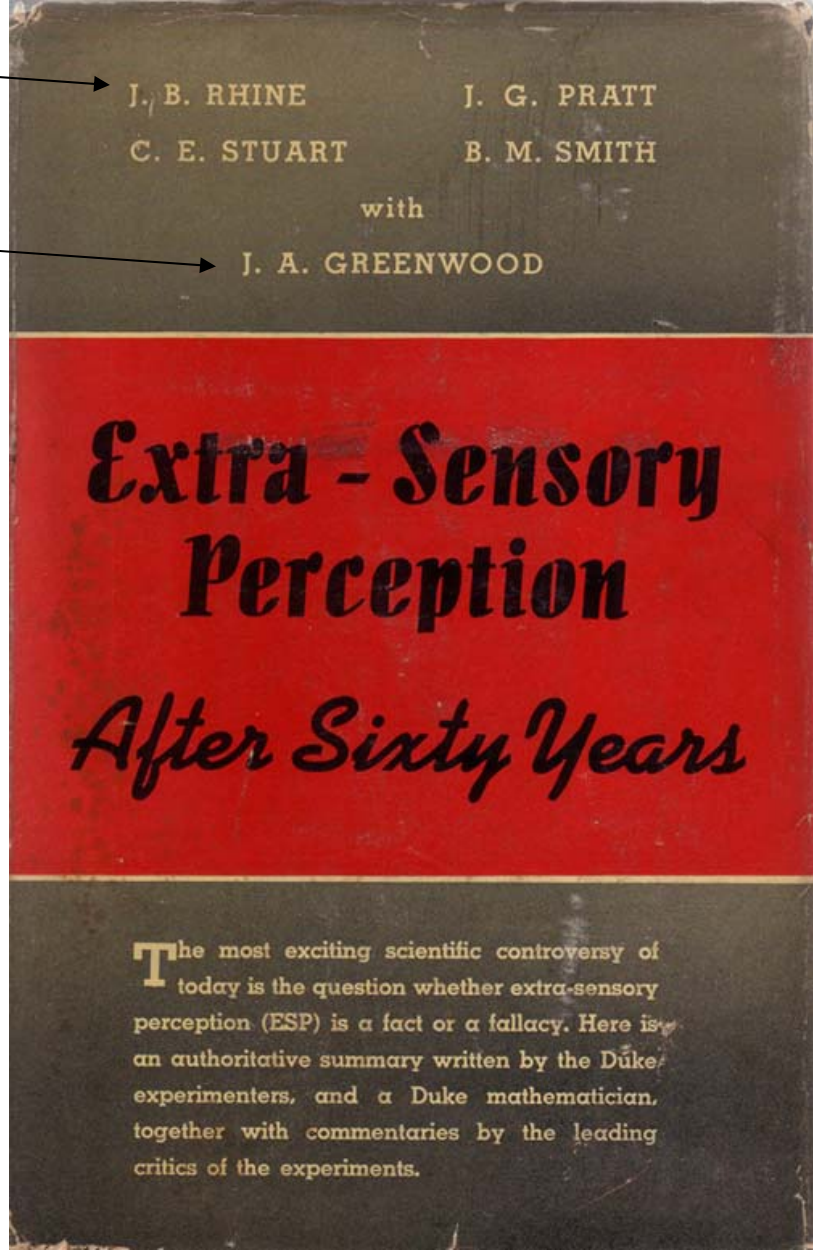
Questions



First meta-analysis in science (1940)