

# Bias adjustment methods for meta-analyses of published observational studies

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# Meta-analysis of published observational studies

## PROBLEMS

- Varying quality
- Poor reporting / different presentations
- Different measures / outcomes
- Many sources of bias

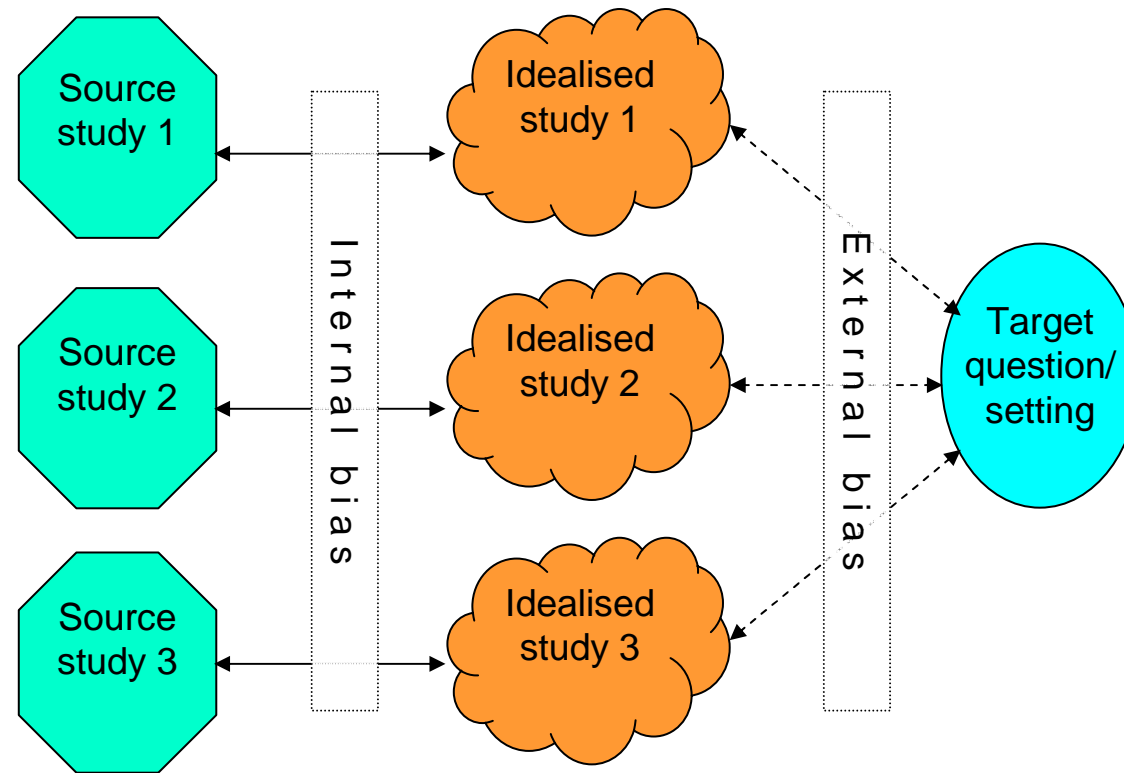
Can we combine apparently 'incompatible' studies:  
meta-analysis rather than systematic review?

**Example:** Six longitudinal observational studies of  
objectively measured physical activity and  
subsequent change in obesity in children

## Outline of approach

1. List **sources of bias** in each study
2. Transform results from each study onto a **common scale**
3. **Elicit opinions** about the size of each bias in each study, and their uncertainty
4. **Adjust results** in each study for the biases
5. Combine bias-adjusted results across studies in conventional **meta-analysis**

# Generic bias adjustment method



## Target setting

1. **Population:** UK children aged 4-11 years
2. **Exposure:** Objectively measured physical activity energy expenditure
3. **Outcome:** Subsequent change in % body fat
4. **Timescale:** 2-year period

## **Internal biases**

(rigour / quality)

Sample selection

Adjustment for confounders

Measurement of exposure

Attrition

Measurement of outcome

Other bias suspected

## **External biases**

(relevance)

Population

Exposure measure

Outcome measure

Timescale

Categories of bias are considered independent

## Choice of common scale for results

Relationship between baseline physical activity and change in obesity presented as:

(Adjusted) regression coefficient

(Adjusted) correlation coefficient

Often no SE or CI

Sample size (n) and P-value available

Calculations done on Fisher-transformed correlation scale (z):

$$z = \frac{1}{2} \ln \left( \frac{1+r}{1-r} \right)$$

$$SE(z) = 1/\sqrt{n-3}$$

Correlation scale (r) used for bias elicitation and presentation

Note: z is close to r in range -0.3 to +0.3

## Examples of bias checklist items

### Attrition bias (internal)

- Are the results unlikely to be affected by losses to follow-up?
- Are the results unlikely to be affected by exclusions from analysis (e.g. because of extreme values or missing values of confounders)?

### Timescale bias (external)

- Is follow-up time in idealised study identical to target follow-up time?

# Elicitation scales for biases

For each potential bias, assessor marks a 67% interval on the following scales (i.e. believes there is a two-thirds chance that the bias lies in this interval)

## Scale for additive biases

Bias favouring a negative relationship between variables

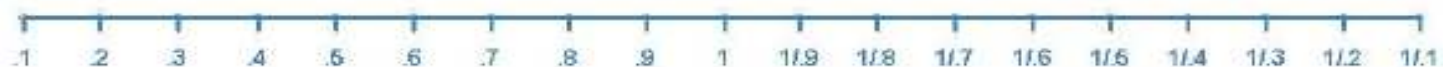
Bias favouring a positive relationship between variables



## Scale for proportional biases

Bias reduces magnitude of the relationship

Bias increases magnitude of the relationship



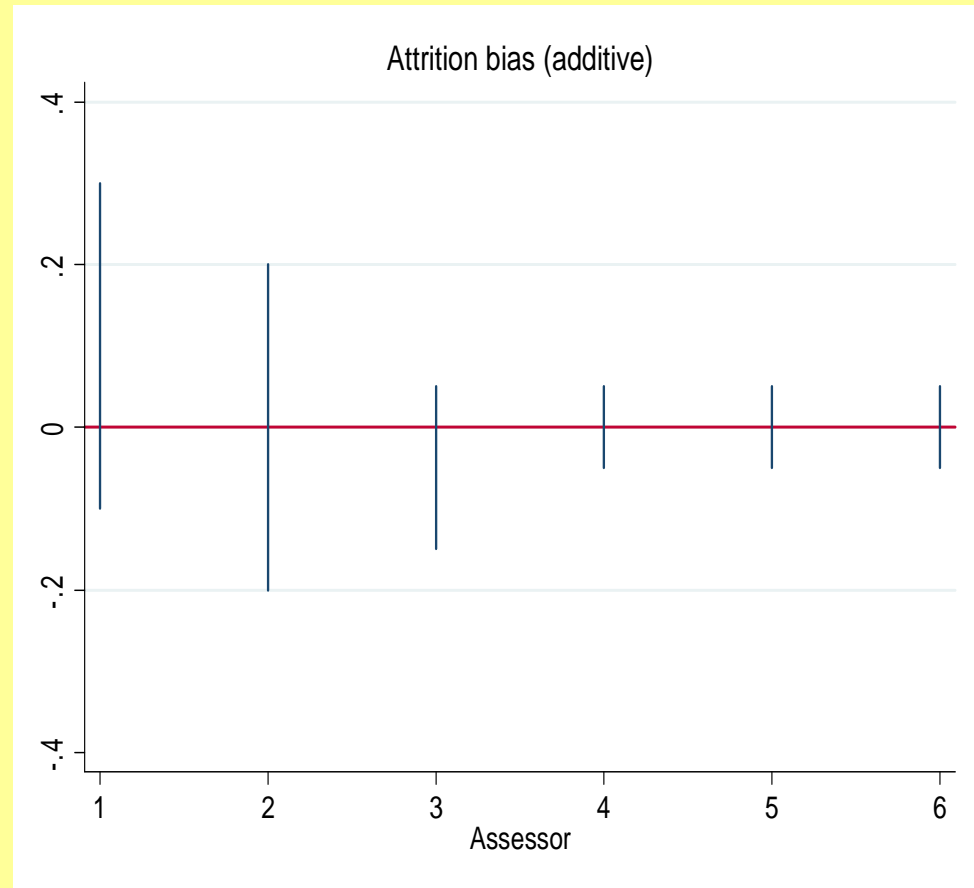
## Example of internal bias assessments

Made independently by 6 quantitatively trained assessors

Attrition bias in Figueroa-Colon *et al*, 2000:

- 39 out of 47 children had follow-up measurements
- Characteristics of exclusions not mentioned

Considered an additive bias



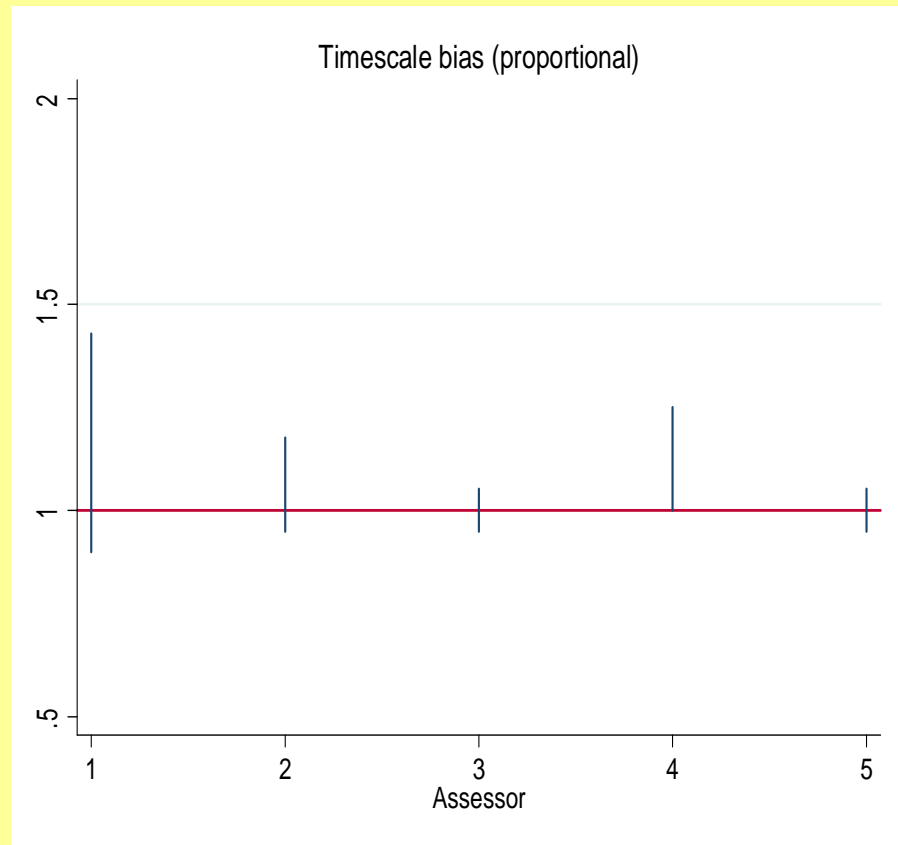
## Example of external bias assessments

Made independently by 5  
subject matter specialists

Timescale bias in Figueroa-  
Colon *et al*, 2000:

- Mean follow-up time:  
1.6 (SD 0.4) years
- Target follow-up time:  
2 years

Considered a proportional  
bias



## Combining additive biases for each study

67% interval for bias  $\equiv$  mean  $\pm$  1 SD

Combining across biases for each assessor:

Total bias = sum of each mean bias

Variance (total bias) = sum of variances of each bias

Pooling across assessors:

Median total bias

Median variance (total bias)

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“typical  
assessor”

Application to study results:

Adjusted estimate = study estimate – total bias

Variance (adjusted estimate) =

Variance (study estimate) + Variance (total bias)

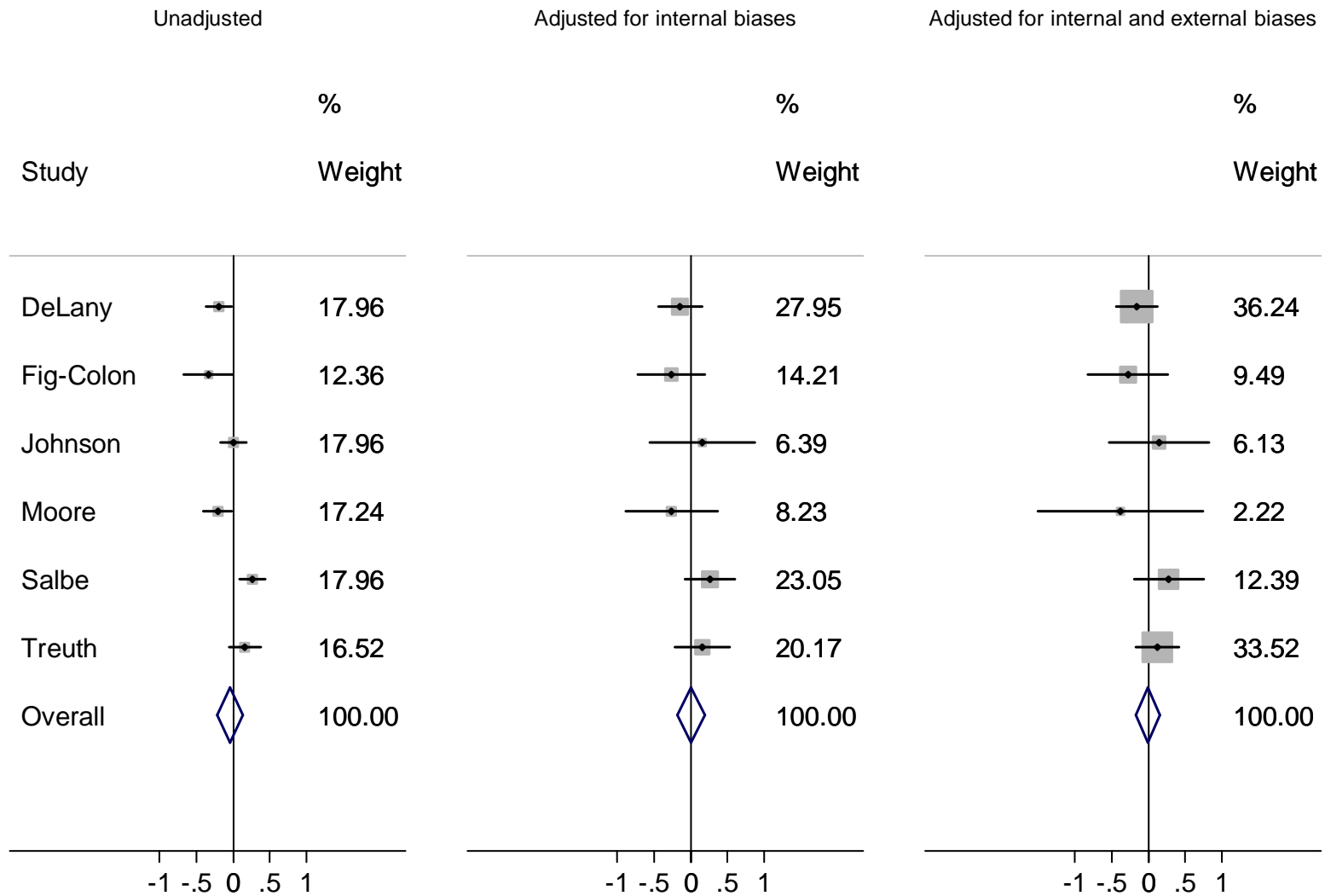
Proportional biases can also be handled

## Unadjusted and bias-adjusted results for Figueroa-Colon *et al*, 2000

Correlation of baseline physical activity energy expenditure  
and change in % body fat

	<u>Correlation (95% CI)</u>	<u>Corresponds to:</u>
Unadjusted	-0.34 (-0.67 to -0.01)	Published study
Adjusted for internal biases	-0.27 (-0.73 to +0.19)	Idealised version of study
Adjusted for internal and external biases	-0.28 (-0.82 to +0.27)	Target setting

# Random-effects meta-analysis of 6 studies



Results presented using Fisher transformed correlation scale

# Unadjusted and bias-adjusted meta-analysis

Correlation of baseline physical activity energy expenditure and change in % body fat

	<u>Correlation (95% CI)</u>	<u>Heterogeneity (I<sup>2</sup>)</u>
Unadjusted	-0.04 (-0.22 to +0.14)	78%
Adjusted for internal biases	0.00 (-0.18 to +0.19)	15%
Adjusted for internal and external biases	-0.01 (-0.18 to +0.16)	0%

## Comments

Adaptation of Turner *et al*, JRSS(A) 2009 to the context of observational studies

### Assumptions:

Bias categories are independent

Biases considered additive or proportional

Assessors are informed and sensible

Sensitivity analysis: e.g. results for each assessor

Publication bias is not addressed

# Conclusions

Process has become possible by **breaking down task** into small components (each source of bias in each study discussed and assessed)

Results from apparently incompatible observational studies have been **combined** to address a specific policy question

In our example, **inconsistency** between studies was reduced to zero after adjusting for biases

The system for bias assessment and adjustment can be applied by others, and adapted to **different contexts**

**Reference:** Turner *et al*, JRSS(A) 2009; 172: 21-47.

# Approach for handling biases

