

RCTs for policy interventions?: a review of reviews and meta-regression

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Background

- Randomised controlled trials (RCTs)
 - Design of choice for clinical evaluations
 - More debate in the social sciences
- Lack of empirical evidence
- This is a 'heads up' presentation!
 - The full report will be available soon...

About this study

- Funded by the UK National Coordinating Centre for Research Methodology (NCCRM)
- Authors:
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- Collaboration between four centres in the UK
 1. EPPI-Centre, Social Science Research Unit, Institute of Education, University of London
 2. Centre for Reviews and Dissemination, University of York, York
 3. MRC Biostatistics Unit, Institute of Public Health, Cambridge
 4. Southampton Health Technology Assessments Centre, University of Southampton

Acknowledgements

- We are very grateful to our Advisory Group, Professors Doug Altman, Jos Kleijnen and Ann Oakley, and Angela Harden, for being generous with their time and providing valuable guidance throughout the study
- Thanks are also due to Steven Duffy for information support and Zarnie Khadjesari for screening and data extraction of reviews
- Lastly, we would like to thank the anonymous reviewers for their careful attention to the report

Objectives of this study

- To determine whether RCTs lead to the same effect size and variance as NRSs of similar policy interventions; and whether these findings can be explained by other factors associated with the interventions or their evaluation

‘Policy interventions’

- Difficult to define – even after reviewing existing literature extensively
- We used the following definition:
 - Policy interventions are those interventions which *establish or modify collective plans for action* so as to have *systematic impact on the public*. These policy interventions operate via institutions (e.g. hospitals, practitioner bodies, schools, public authorities, commercial bodies, patient organisations) and communities (e.g. geographical or social groups, networks, people with shared interests) and do not include personal policies of individuals.

Methods (1)

- Analyses of methodological studies, empirical reviews, and individual health and social services studies investigated the relationship between randomisation and effect size of policy interventions by:
 - Reviewing existing work
 - Carrying out a series of new empirical studies

Methods (2): reviews

- Two parts to this work:
 - Review of existing methodological studies
 - Systematic review of meta-analyses which looked for differences between RCTs and nRCTs

Methods (3): empirical studies

- The study employed three approaches:
 - Resampling studies
 - Investigating comparable ‘field’ studies
 - Meta-epidemiology

Methods (4): empirical studies

- **Resampling studies:** comparing controlled trials that are identical in all respects other than the use of randomisation
- Achieved by 'breaking' the randomisation in two RCTs to create smaller non-randomised trials and smaller randomised trials by re-sampling randomised and non-randomised comparisons from the data

Methods (5): empirical studies

- **Investigating comparable ‘field’ studies:** controlled trials drawn from systematic reviews that include both randomised and non-randomised studies. These include structured narrative reviews and sensitivity analyses within meta-analyses

Methods (6): empirical studies

- **Meta-epidemiology:** investigating associations between randomisation and effect size using a pool of more diverse randomised and non-randomised studies within broadly similar areas. These more diverse studies can be drawn from across reviews addressing different questions, or from broad sections of literature

Methods (7): model for investigating field trials and the meta-epidemiology

y_{ij} = estimated intervention effect for i th study in j th review

s_{ij} = its se

t_{ij} = 0 if RCT, 1 if non-RCT

Unknowns: $\sigma_{iR}^2, \sigma_{iN}^2, b_i$

$$y_{ij} = \delta_i + u_{ij} + b_i t_{ij} + e_{ij}$$

True intervention effect (overall treatment effect in each review)
Random effect
Bias term If NRCT
Random error

$u_{ij} \sim N(0, \sigma_{iR}^2)$
 $e_{ij} \sim N(0, S_{ij}^2)$

$u_{ij} \sim N(0, \sigma_{iN}^2)$

Model for the i th review

$$b_i \sim N(\beta, \Phi^2)$$

$$\sigma_{iR}^2, \sigma_{iN}^2 \text{ fixed}$$

Parameters of interest:

β expresses average bias of NRCTs (presupposes y s have common direction)

Φ expresses review-specific bias

If either is non-zero then NRCTs \neq RCTs

Methods (8): fitting the model

- Important to allow for different variances
 - Random effects meta-analysis in STATA for each outcome in each review separately for RCTs and nRCTs
 - Calculated the bias term as the difference between the two with standard error $se = \sqrt{se_1^2 + se_2^2}$
 - Finally we combined the bias terms from each review in a random effects meta-analysis

Hypothesised conclusions

- There is no systematic difference between RCTs and nRCTs
 - *nRCTs may be adequate*
- There are systematic differences; thus, either:
 - *nRCTs are adequate given appropriate adjustments; or*
 - *randomisation is required to control for unidentifiable differences*
- The variance of nRCTs is greater than that of RCTs – suggesting a non-systematic difference
 - *confidence intervals of nRCTs should be considered to be wider than stated and their statements regarding statistical significance should be treated with caution*

Results (1): review of previous methodological reviews

- These studies investigated whether randomisation influenced effect sizes
- Most also investigated the influence of other variables or modifiers of effect such as population, sample size, attrition, intervention, type of control group, publication status
- Studies located:
 - review of within-study comparisons of randomised and non-randomised participants
 - six single meta-analyses
 - one review of meta-analyses
- Topic areas included: juvenile delinquency, treatment of alcohol abuse, and other psychological, mental health or health care interventions

Results (2): review of previous methodological reviews

- Effect sizes from RCTs and nRCTs may differ in some circumstances
- These differences may well be associated with factors confounded with design
- Inter-relationships among variables make it difficult to determine the likely impact of any one factor

Results (3): review of previous meta-analyses

- Effect sizes were similar in five reviews
- Dissimilar in eight reviews
- Mixed in three
- Most reviews appeared to ignore variability associated with effect size
- Considerable variation in the studies pooled within reviews, in terms of population, intervention, outcome and other methodological details makes it difficult to separate the potential effect of random assignment from the potential effects of all the other variables

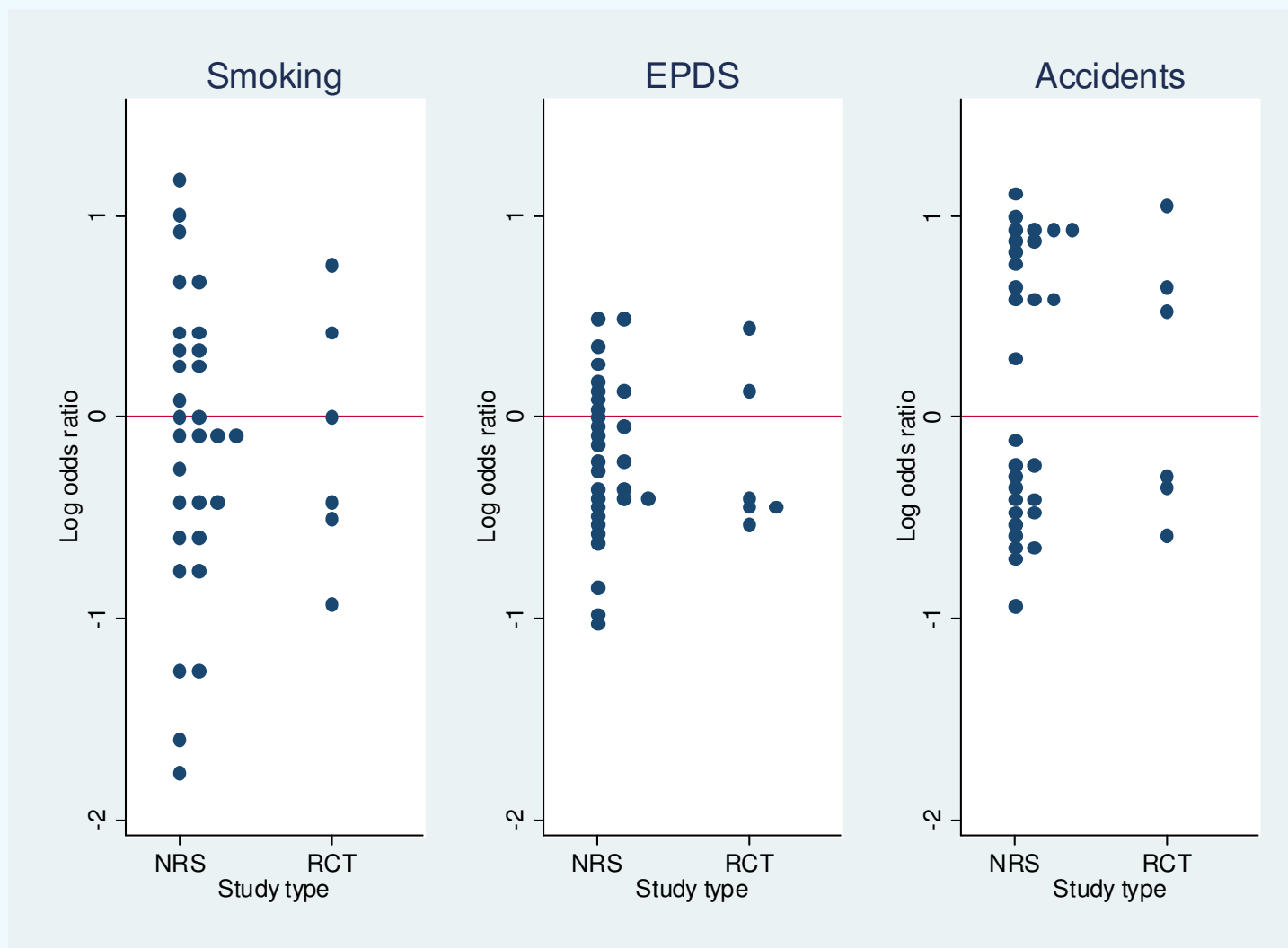
Results (4): re-sampling studies

- Two cluster randomised trials were used (many thanks to the investigators who gave us anonymised access to their data!)
- Trial 1
 - 731 participants
 - we created 6 RCTs and 30 nRCTs
- Trial 2
 - 160 participants
 - 4 RCTs and 12 nRCTs

Results (5): re-sampling studies

- We carried out three analyses, comparing the variances of the RCTs and nRCTs:
 - in unadjusted form
 - matching areas on baseline characteristics
 - adjusting for baseline differences using logistic regression

Results (6): re-sampling studies (example)



Results (7): re-sampling studies

- nRCTs *can* give the same answers as RCTs
- This was a tightly controlled examination where the only factor which was different between the RCTs and nRCTs was randomisation

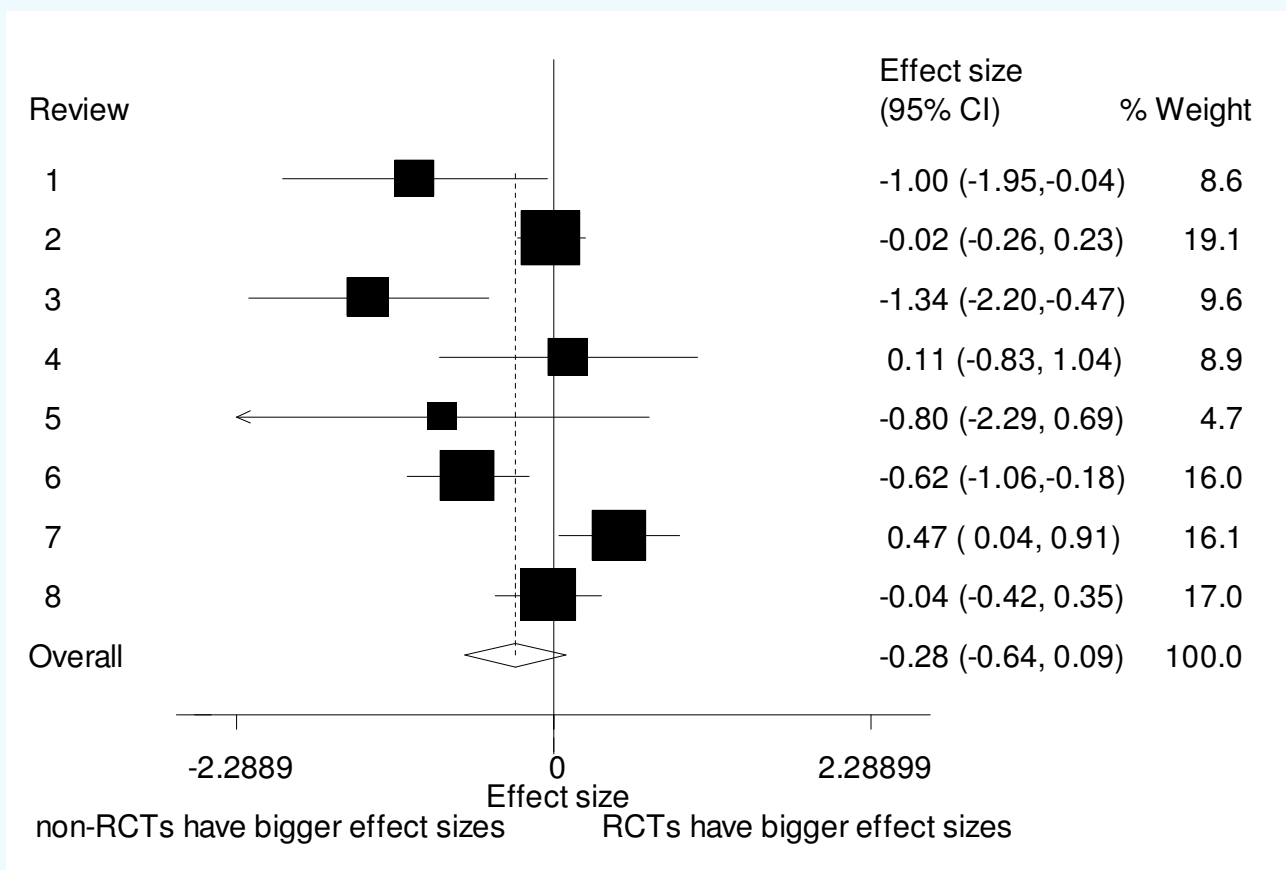
Results (8): comparable 'field' studies and meta-epidemiology

- Two datasets:
 - Nearly 196 RCTs and nRCTs taken from nine health promotion systematic reviews conducted by the EPPI-Centre
 - 126 RCTs and nRCTs taken from a series of reviews conducted by Colorado State University in the area of youth and disability
 - Many thanks to Brian Cobb and his team for giving us access to these studies

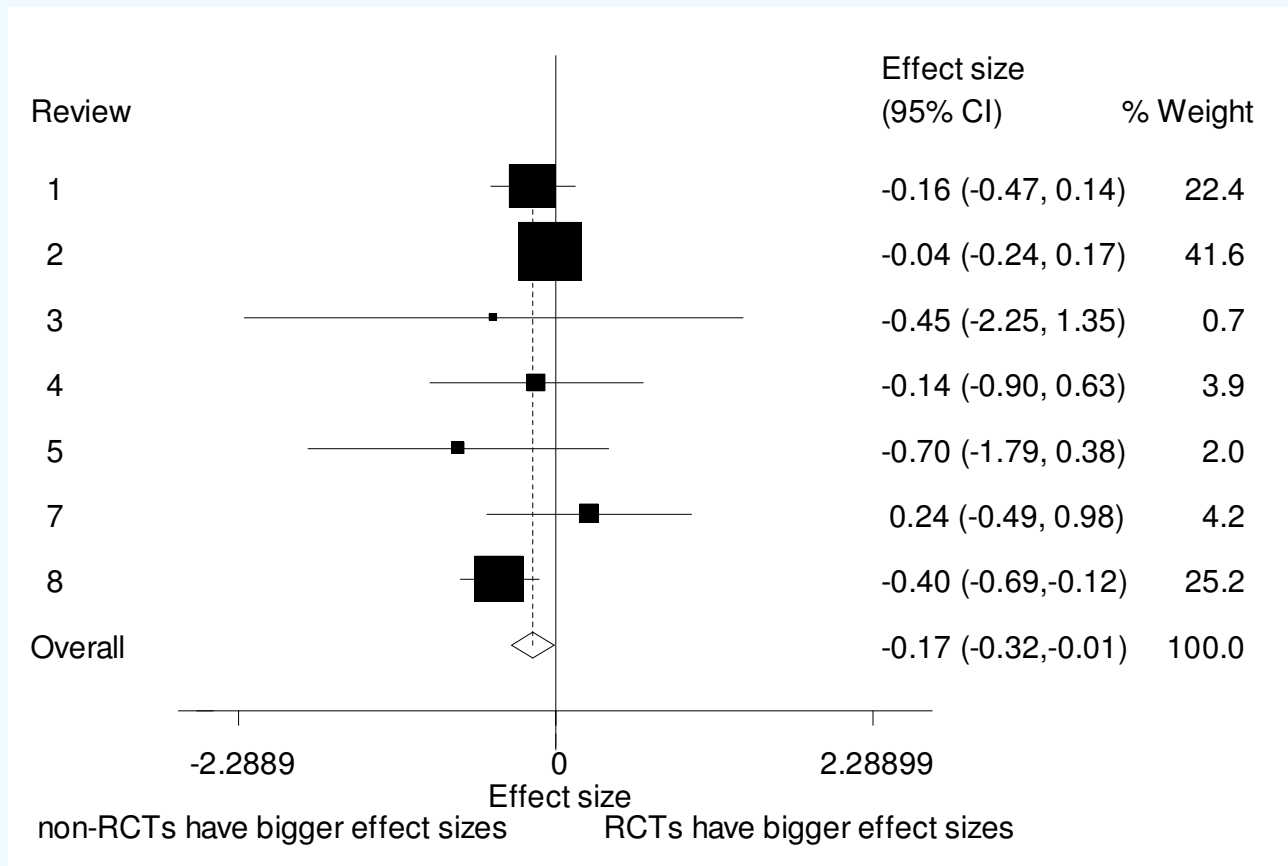
Results (9): comparable 'field' studies and meta-epidemiology

- Considerable variation
- RCTs produced smaller effect sizes than nRCTs in EPPI-Centre systematic reviews
- Larger effect sizes than nRCTs in the studies reviewed by Colorado State University
- Confounders explored further in the EPPI-Centre reviews

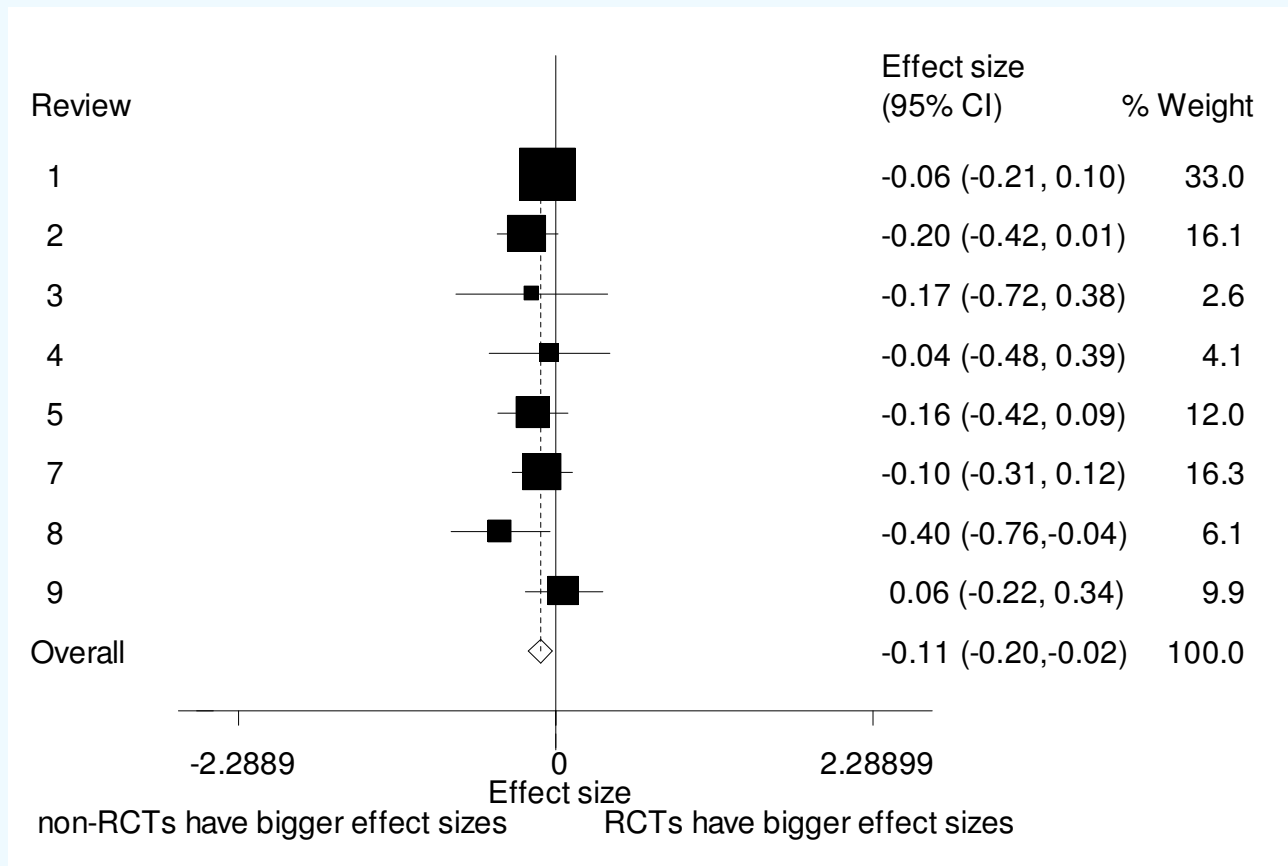
Results (10): knowledge (EPPI-Centre reviews)



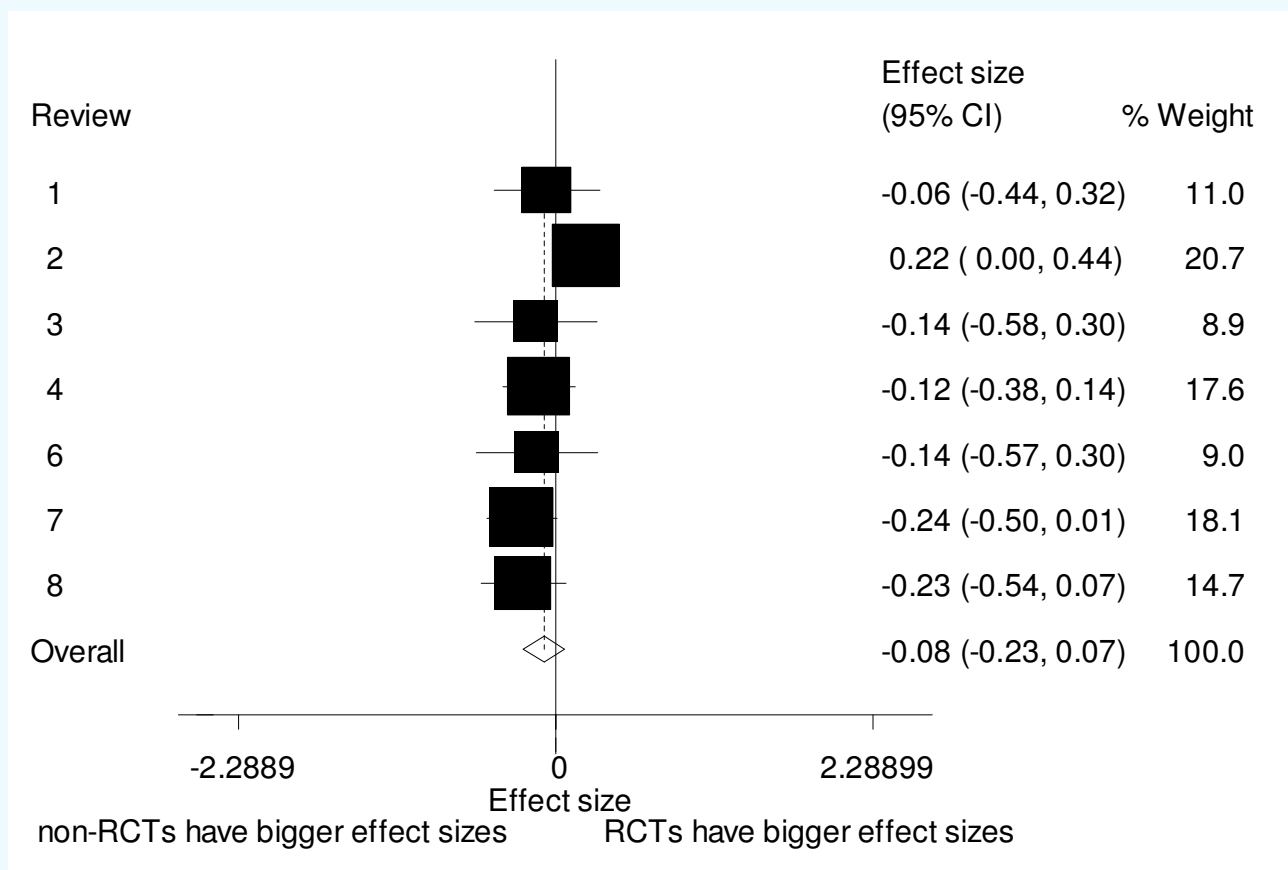
Results (11): attitudes (EPPI-Centre reviews)



Results (12): behaviour (EPPI-Centre reviews)



Results (13): health state (EPPI-Centre reviews)



Results (14): investigation of confounding factors

- Potential confounding factors were explored in the EPPI-Centre reviews
- RCTs have smaller effect sizes; though:
 - their sample sizes tend to be smaller with participants allocated individually (both attributes associated to some extent with effect size) and
 - their theoretical frameworks more readily apparent
- Other attributes commonly associated with quality were not associated with randomisation or effect size: attrition rates, time to follow-up or quality of reporting

Results (15): multivariate meta-regression

	unadjusted	adjusted
Knowledge	-0.275 (-0.641, 0.091)	-0.269 (-0.465, -0.073)
Attitudes	-0.166 (-0.319, -0.012)	-0.165 (-0.369, 0.040)
Behaviour	-0.111 (-0.199, -0.023)	-0.192 (-0.330, -0.053)
Health state	-0.084 (-0.234, 0.066)	0.052 (-0.149, 0.254)

Conclusions

- The re-sampling studies provide no evidence that the absence of randomisation directly influences effect sizes in a systematic way
- Many of the examples reviewed and the new analyses reveal that randomisation *is* associated with changes in effect sizes of policy interventions in field trials
- Despite extensive analysis, we have identified no consistent explanations for these differences

The full report

- The full report should be available later this year as an HTA monograph
- Please email me if you'd like to be notified when it's published



Understandings of healthy eating

healthy eating concepts

'Good' and 'bad' foods

Health consequences

Item

Effect (CI)

Weight

Size

Fruit and vegetable intake - physical activity component (without Resnicow)

Gortmaker et al (1999)

0.36(0.10, 0.62)

6.8

356

Hooper et al (1996)

0.44(0.12, 0.75)

4.7

97

Parcel et al (1999)

-0.11(-0.29, 0.08)

13.9

352

Perry et al (1993b)

0.02(-0.11, 0.14)

28.0

1136

0.06(-0.03, 0.16)

Fruit and vegetable intake - no physical activity component (without Resnicow)

Anderson et al

0.46(0.00, 0.92)

2.2

120

Aud GW et al (1993b)

0.48(0.03, 0.94)

2.2

115

Aud GW et al (1999)

0.53(-0.12, 1.18)

1.1

647

Baranowski T et al (2000)

0.12(-0.05, 0.30)

14.9

1172

Cullen (1997)

0.26(-0.03, 0.55)

5.3

210

Epstein et al (2001)

1.00(0.17, 1.86)

0.7

25

Henry et al (2001)

0.16(-0.45, 0.77)

1.3

42

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Chosen foods

Influences on foods eaten

Provided foods

Food in the school

Food in the home

Food preferences

Perceptions of health benefits

Knowledge behaviour gap

Roles and responsibilities

Non-influencing factors

Factors further constraining and already limited choice

School dinners as a social occasion

Promotion and provision of healthy foods contradiction

Parental influence and food rules

Breaking rules and asserting independence