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Meta-analysis: Basic concepts and analysis

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Outline

- Rationale
- Definitions
- Steps
- The forest plot
- Statistical methods
- Dealing with heterogeneity
- Conclusions


h. Daumier

Systematic reviews

- Systematic approach to minimize biases and random errors
- Always includes materials and methods section
- May include meta-analysis

Chalmers and Altman 1994

Meta-analysis

- A statistical analysis which combines the results of several independent studies considered by the analyst to be ‘combinable’

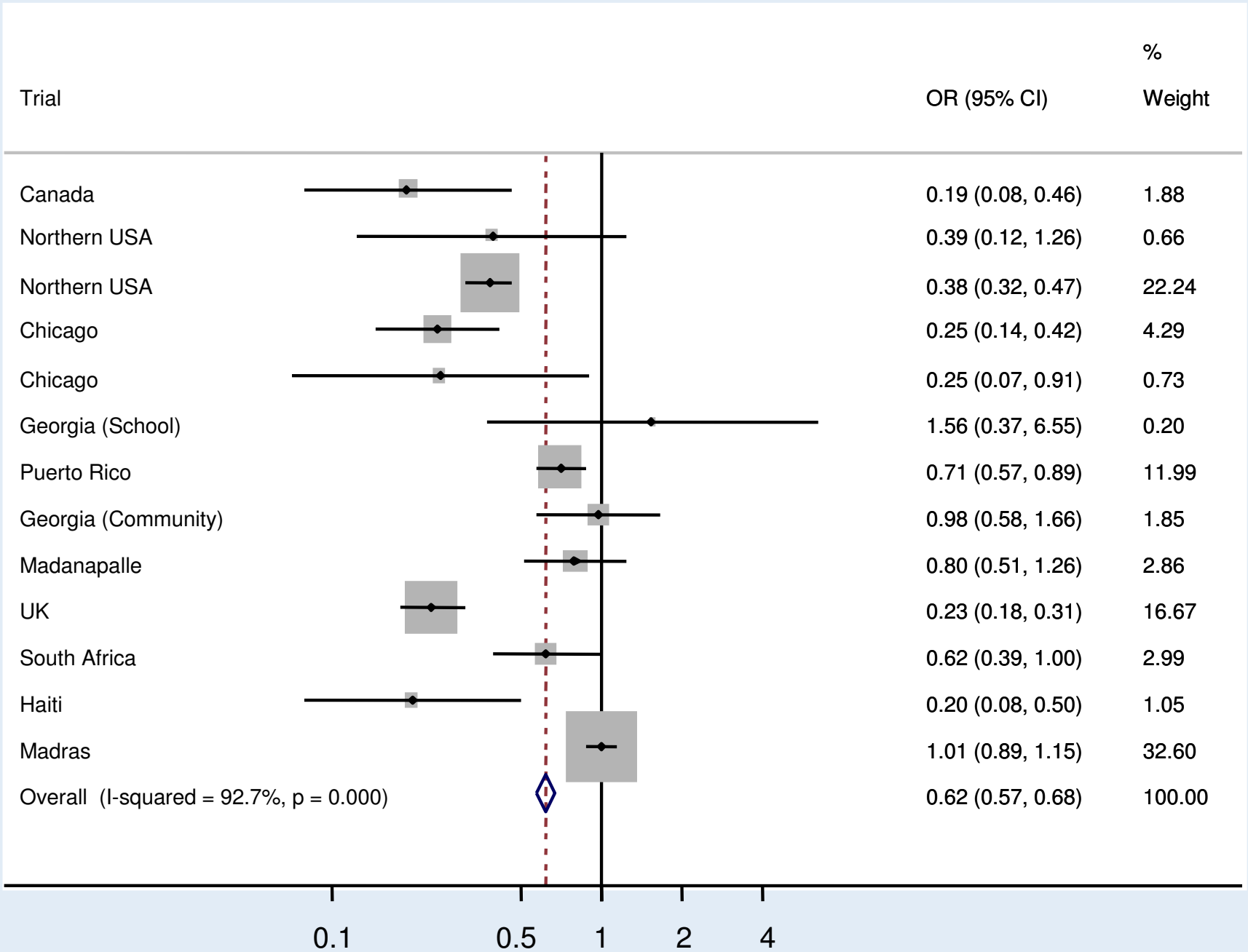
Huque 1988

Steps

- Formulate the question and define eligibility criteria
- Locate and select studies
- Critically appraise quality of studies
- Extract data
- Examine forest plots
- Consider meta-analysis
- Interpret results

Forest plots

- Boxes draw attention to the studies with the greatest weight
- Box area is proportional to the weight for the individual study
- The diamond (and broken vertical line) represents the overall summary estimate, with confidence interval given by its width
- Unbroken vertical line is at the null value (1)


Trial
OR (95% CI)
% Weight
Canada
0.19 (0.08, 0.46)
1.88
Northern USA
0.39 (0.12, 1.26)
0.66
Northern USA
0.38 (0.32, 0.47)
22.24
Chicago
0.25 (0.14, 0.42)
4.29
Chicago
0.25 (0.07, 0.91)
0.73
Georgia (School)
1.56 (0.37, 6.55)
0.20
Puerto Rico
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1.85
Madanapalle
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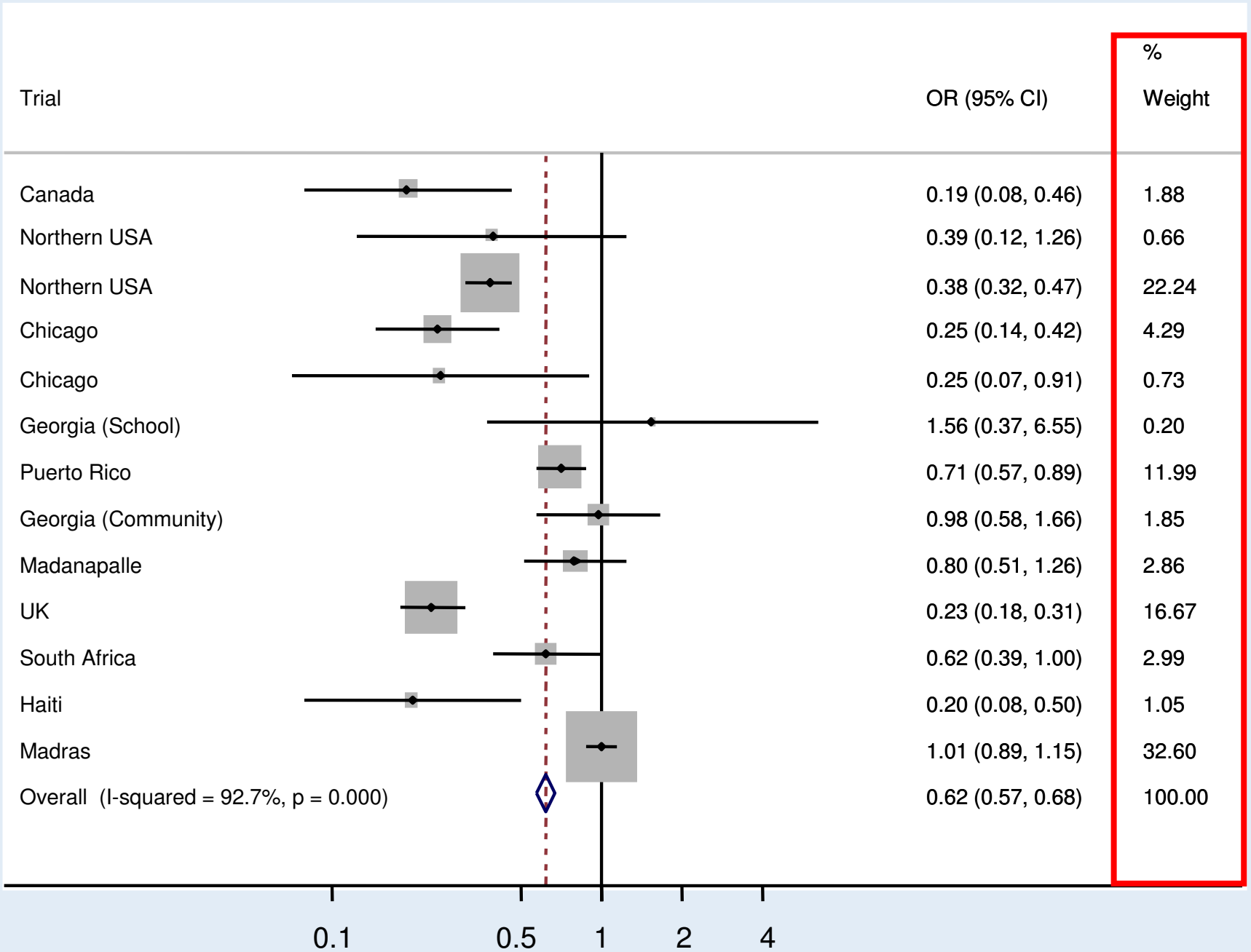
Haiti
0.20 (0.08, 0.50)
1.05
Madras
1.01 (0.89, 1.15)
32.60
Overall (I-squared = 92.7%, p = 0.000)
0.62 (0.57, 0.68)
100.00
0.1
0.5
1
2
4

Fixed-effects Meta-analysis

- Characteristics of patients may vary between studies. Patients should only be compared to others in the same study
- Calculate a *weighted average* of treatment effects from each study.
- The weight is $w_i = 1/v_i$ where is v_i is the variance of the log odds ratio in study *I*
- Model assumes that the effect is the same (Fixed) in each study

$$\frac{\sum w_i \times \log \mathrm{OR}_i}{\sum w_i}$$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Heterogeneity between studies

- The fixed effect estimate is based on the assumption that the true effect does not differ between studies. We should check this assumption.
- To test the null hypothesis that the true treatment effect is the same in all studies we can calculate a *heterogeneity statistic*:

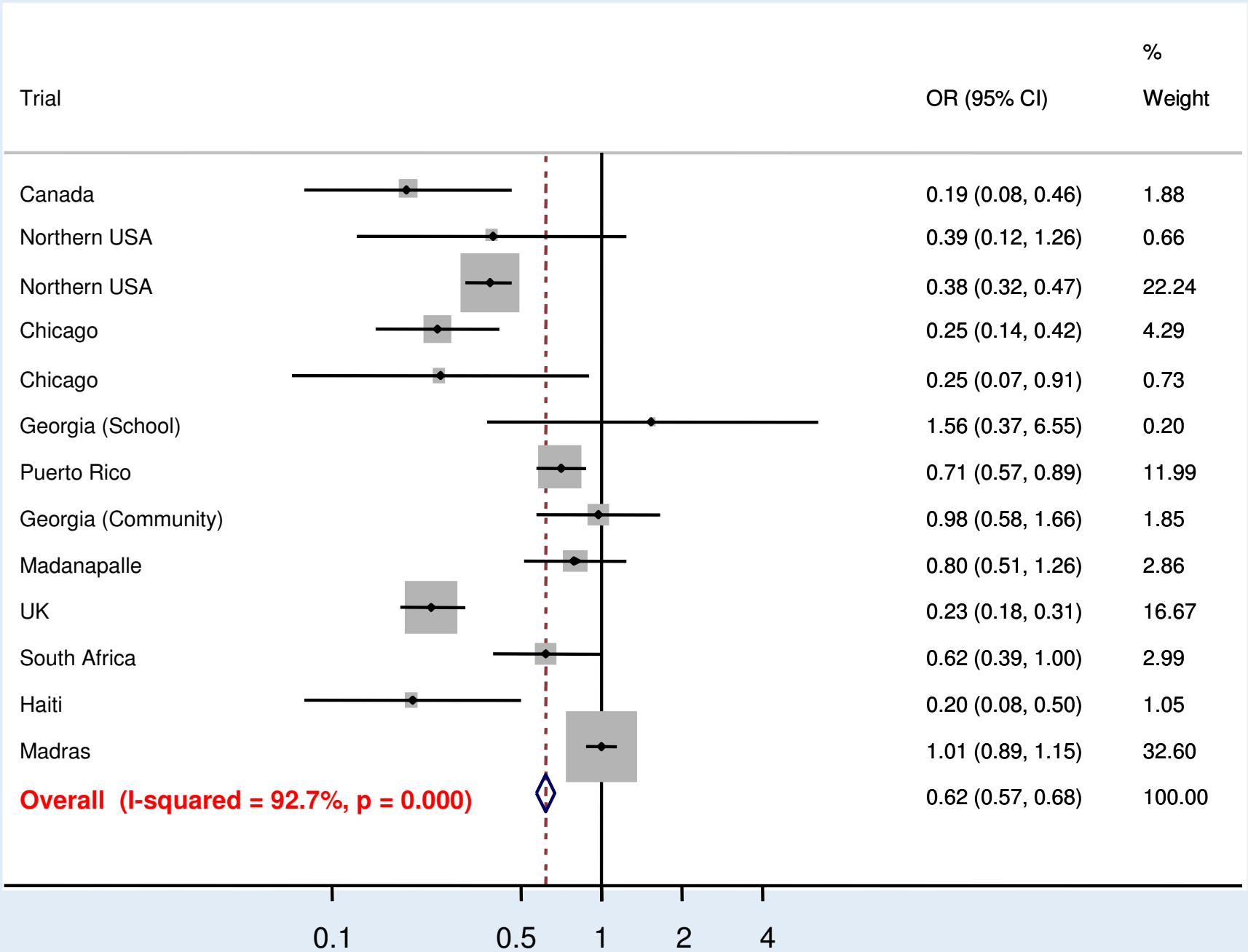
$$Q = \sum w_i (\log \mathrm{OR}_i - \log \mathrm{OR}_F)^2$$

- To calculate a *P*-value, this is compared with the χ^2 distribution on (*k*-1) degrees of freedom (*k* is no. of studies).
- The greater the average distance between the individual study OR and the summary OR, the more evidence against the null hypothesis that the true treatment effect is the same in all studies.

Quantifying heterogeneity

- Higgins and Thompson (*BMJ* 2003; **327**: 557-560) proposed that the amount of heterogeneity should be measured using the I^2 statistic:
  $I^2 = (Q - df) / Q \times 100\%$

- This can be interpreted as the proportion of the total variation in study estimates that is due to heterogeneity.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32.60
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0.62 (0.57, 0.68)
100.00
0.1
0.5
1
2
4

What should we do if there is heterogeneity between studies?

a) Report estimates from individual studies

b) Model the heterogeneity between studies

   i. *Allow* for it in the statistical model – random-effects meta-analysis

   ii. Seek to *explain* it

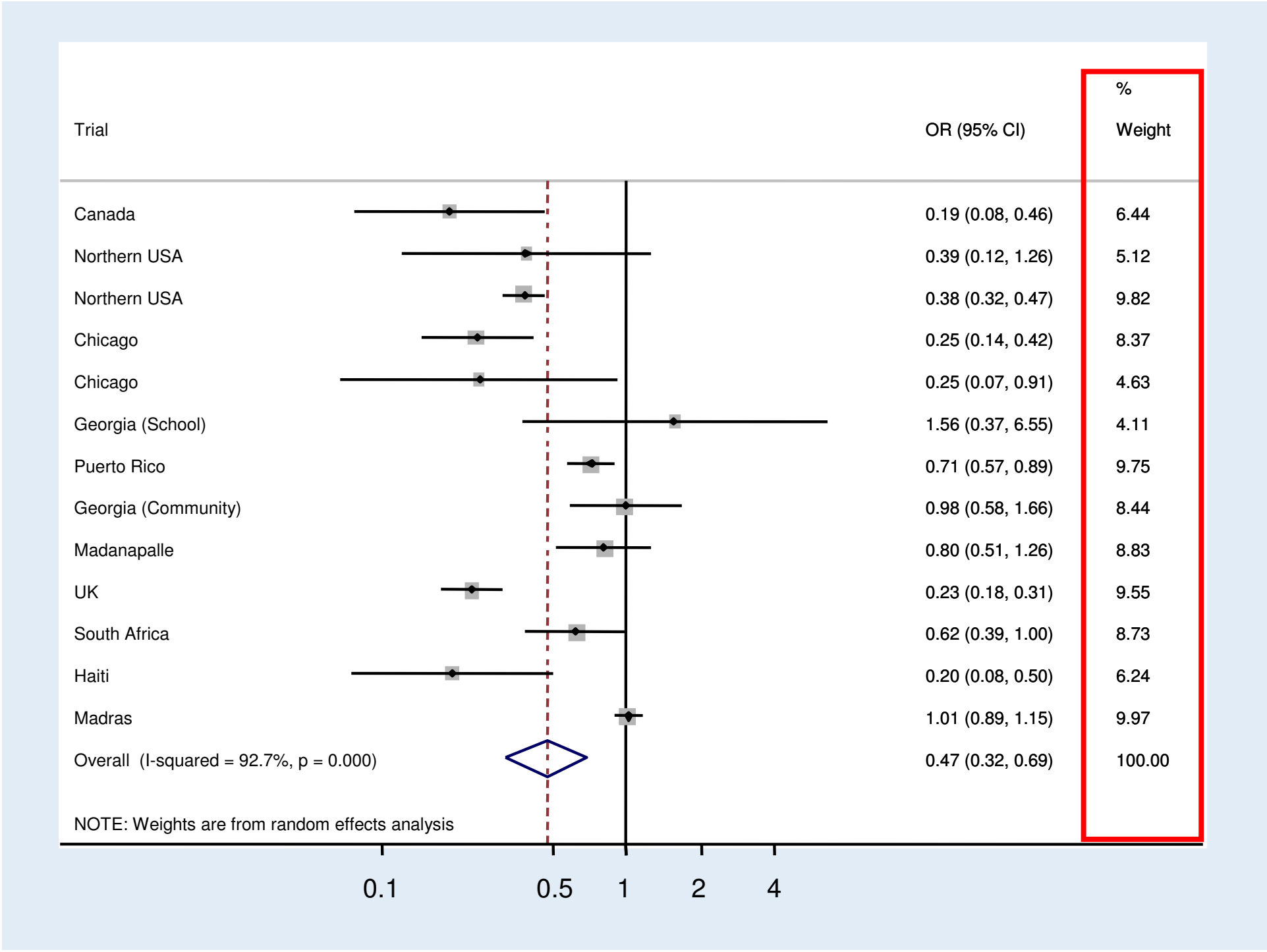
Random-effects meta-analysis (1)

- We suppose the *true* treatment effect in each study is randomly, normally distributed between studies, with variance τ^2 ("tau-squared")
- Estimate the between-study variance τ^2, and use this to modify the weights used to calculate the summary estimate
- The usual estimate of τ^2 is called the DerSimonian and Laird estimate, or "method of moments" estimate

Random-effects meta-analysis (2)

Random-effects estimate: $\log \mathrm{OR}_R = \dfrac{\sum w_i^* \log \mathrm{OR}_i}{\sum w_i^*}$

where $w_i^* = \dfrac{1}{v_i + \tau^2}$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Northern USA
0.39 (0.12, 1.26)
5.12
Northern USA
0.38 (0.32, 0.47)
9.82
Chicago
0.25 (0.14, 0.42)
8.37
Chicago
0.25 (0.07, 0.91)
4.63
Georgia (School)
1.56 (0.37, 6.55)
4.11
Puerto Rico
0.71 (0.57, 0.89)
9.75
Georgia (Community)
0.98 (0.58, 1.66)
8.44
Madanapalle
0.80 (0.51, 1.26)
8.83
UK
0.23 (0.18, 0.31)
9.55
South Africa
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Haiti
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6.24
Madras
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9.97
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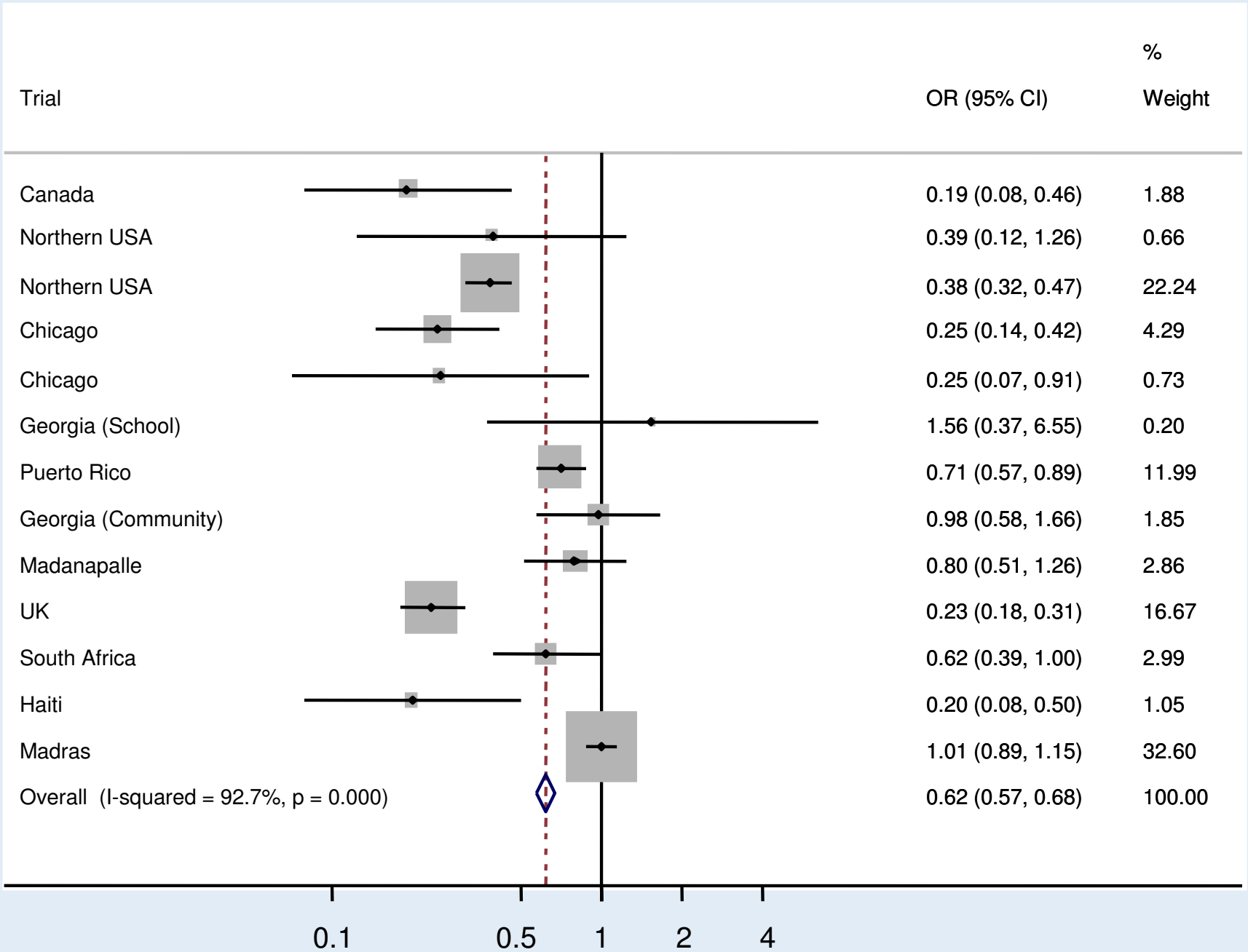
0.47 (0.32, 0.69)
100.00
NOTE: Weights are from random effects analysis
0.1
0.5
1
2
4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Summary

- **Meta-analysis:** calculate a *summary* effect estimate which is a weighted average of the estimated treatment effects from individual studies
- **Fixed-effect meta-analysis:**
  - *assume* treatment effect is the same in each study
  - weights $w_i = \frac{1}{v_i}$
  - (minimise the variability of the summary log odds ratio)
- **Random-effects meta-analysis:**
  - treatment effect varies between studies
  - weights $w_i^* = \frac{1}{v_i + \tau^2}$


THE FAR SIDE
By GARY LARSON
DAMNED if you do
DAMNED if you don't
"C'mon, c'mon — it's either one or the other."

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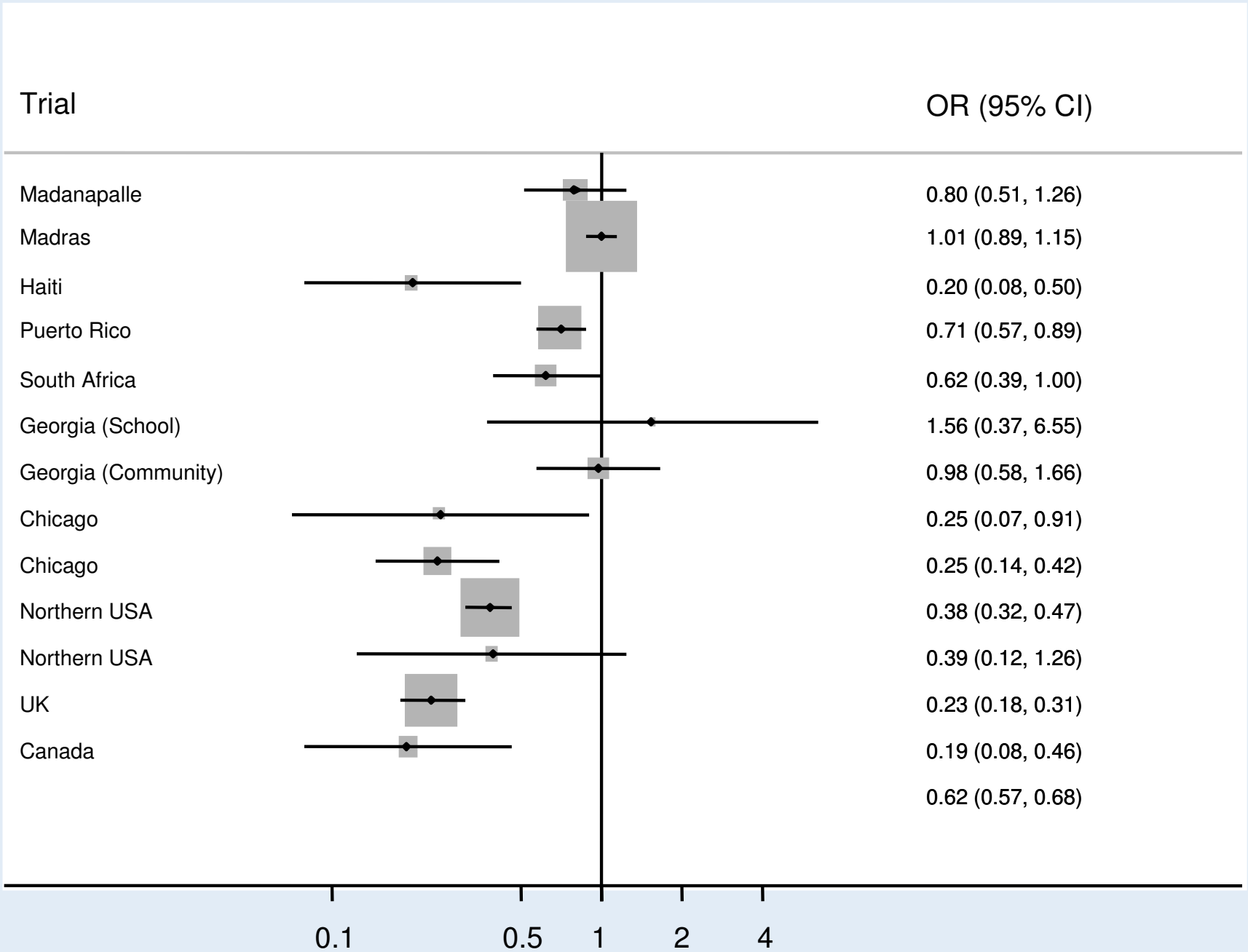
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