EVAL 6970: Meta-Analysis
Meta-Regression and Complex Data Structures

Dr. Chris L. S. Coryn

Kristin A. Hobson

Fall 2013

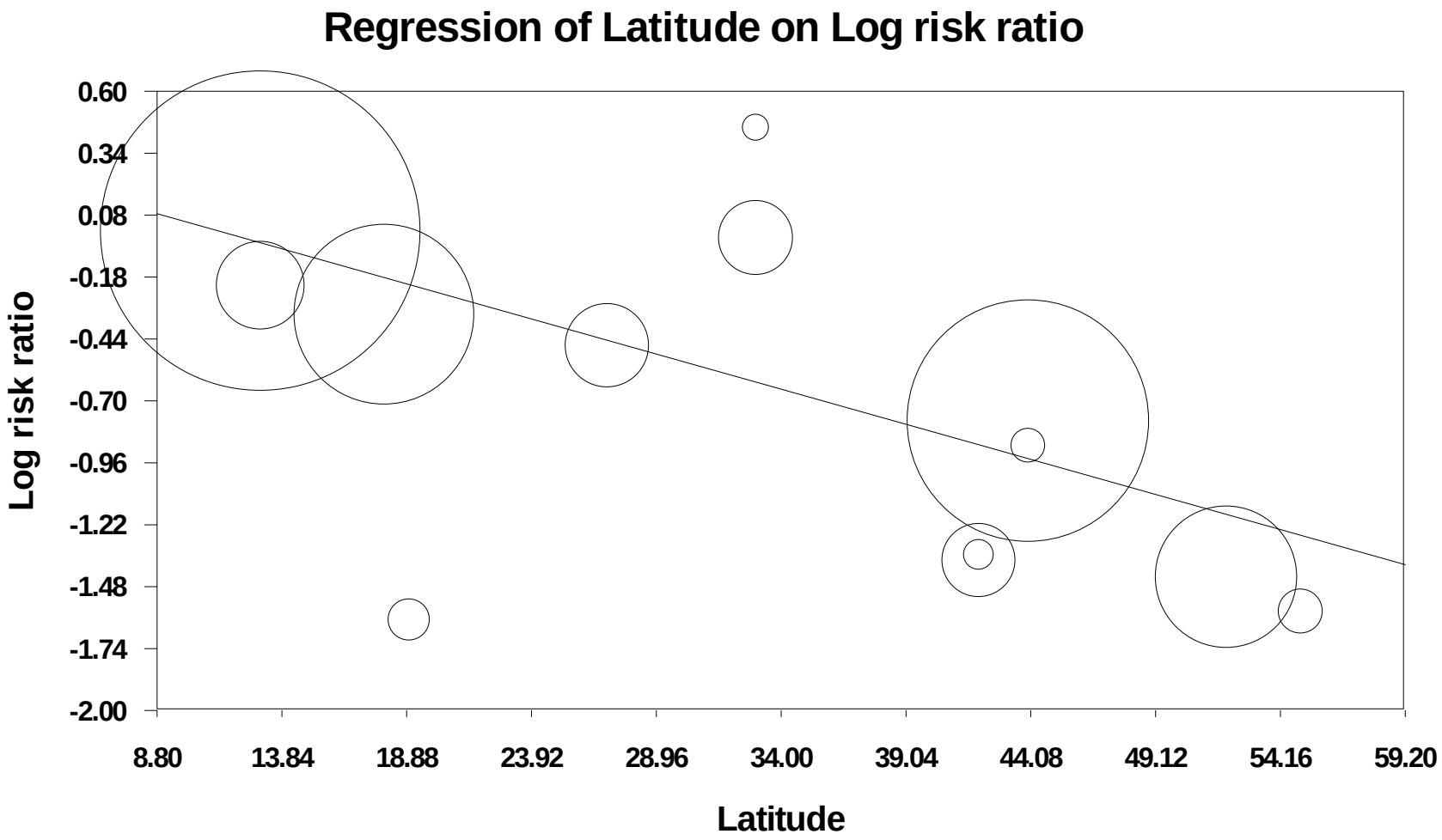
Agenda

- Meta-regression
  - In-class activity
- Complex data structures
  - In-class activity

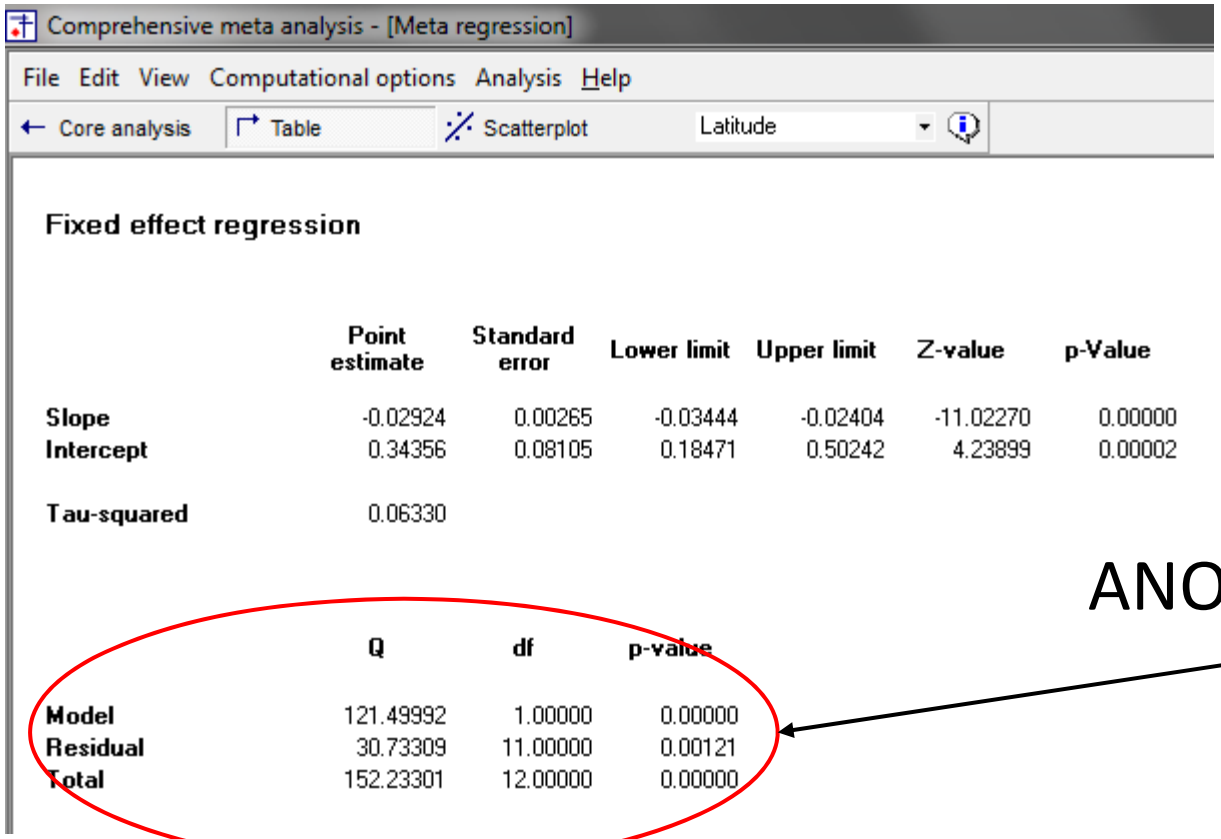
Meta-Regression

- Used to estimate the impact/influence of categorical and/or continuous covariates (moderators) on effect sizes or to predict effect sizes in studies with specific characteristics
- A ratio of 10:1 (studies to covariates) is recommended

Fixed-Effect Model



Fixed-Effect Model



Fixed effect regression

	Point estimate	Standard error	Lower limit	Upper limit	Z-value	p-Value
Slope	-0.02924	0.00265	-0.03444	-0.02404	-11.02270	0.00000
Intercept	0.34356	0.08105	0.18471	0.50242	4.23899	0.00002
Tau-squared	0.06330					

	Q	df	p-value
Model	121.49992	1.00000	0.00000
Residual	30.73309	11.00000	0.00121
Total	152.23301	12.00000	0.00000

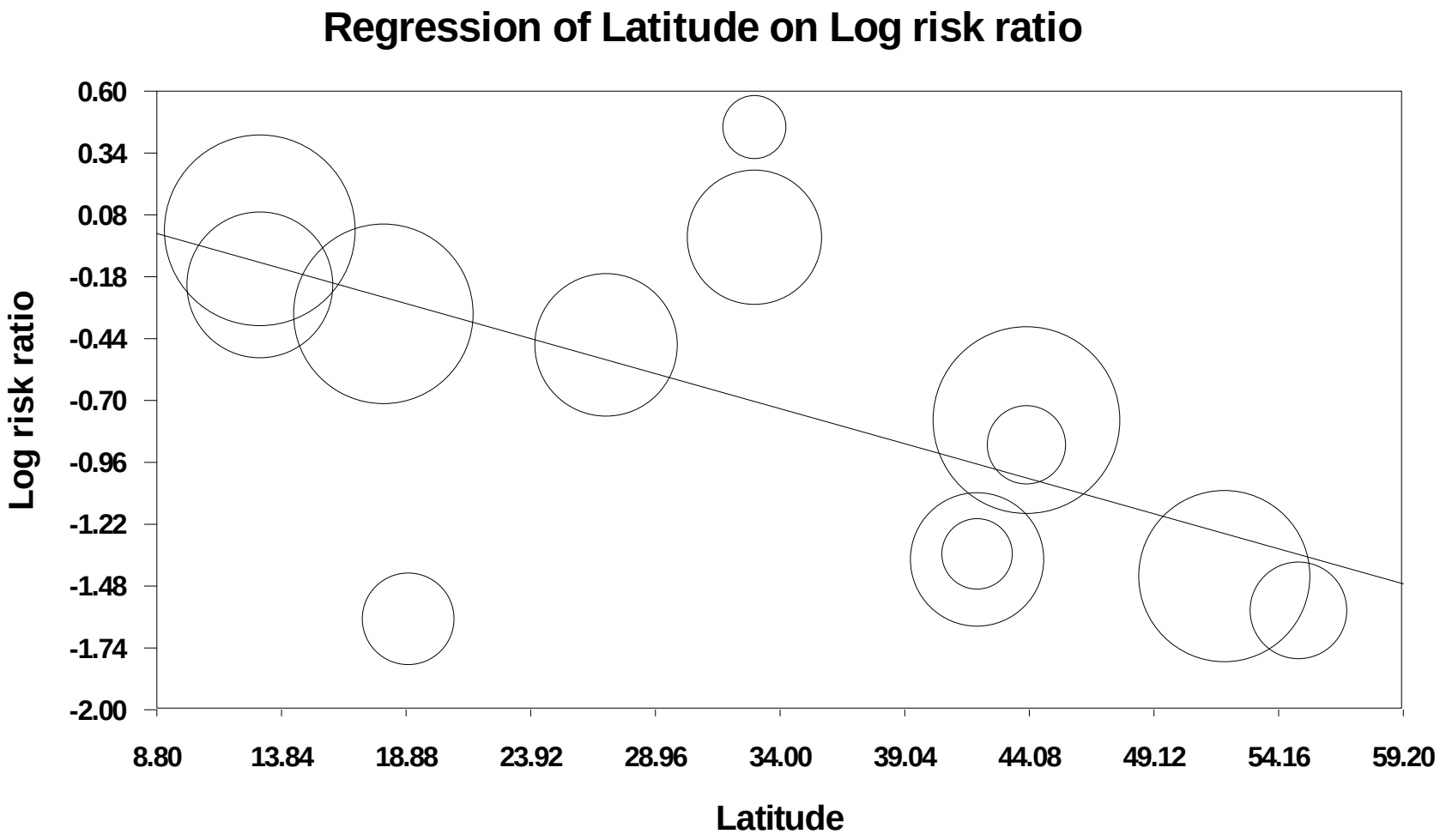
ANOVA information

Fixed-Effect Model ANOVA Table

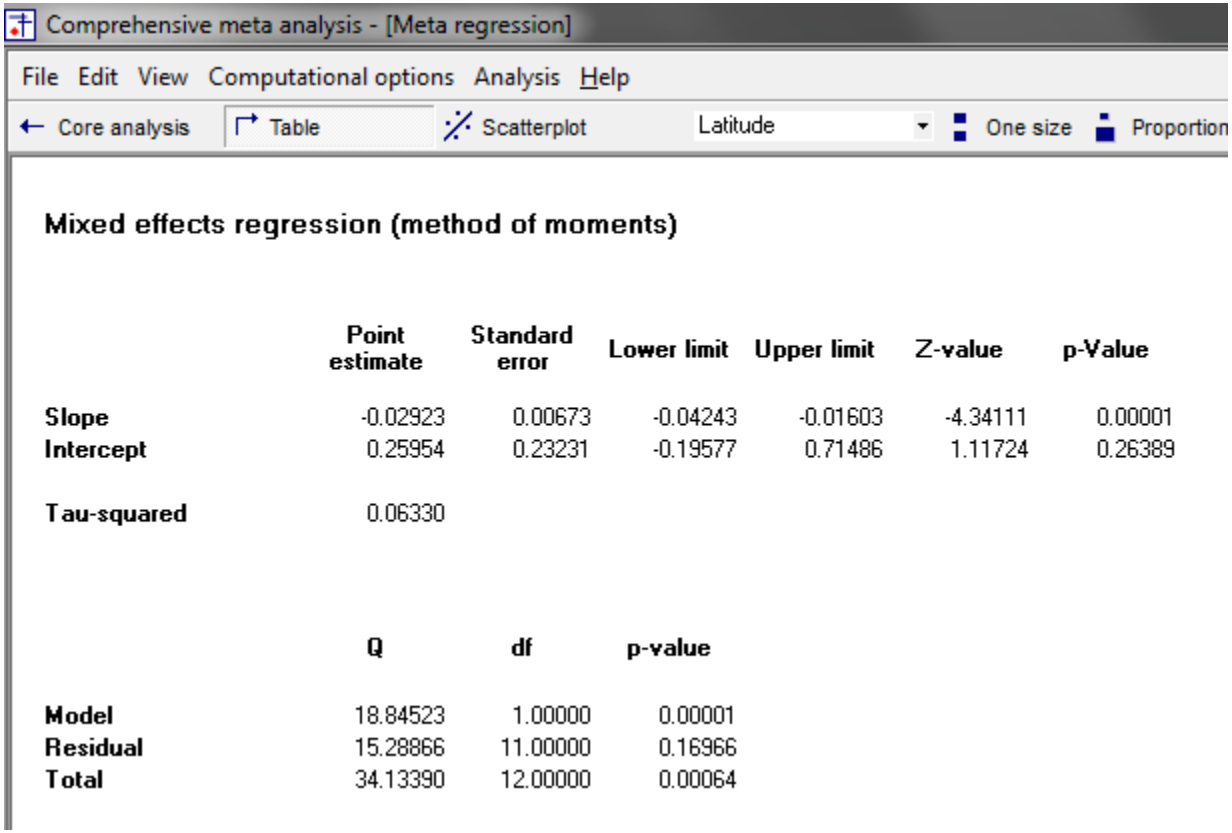
	Q	df	p
Model (Q_{model})	121.49992	1	0.00000
Residual (Q_{resid})	30.73309	11	0.00121
Total (Q)	152.23301	12	0.00000

- $Q = 152.233, df = 12, p = 0.000$, means that the total variance is greater than would be expected based on within-study error
- $Q_{model} = 121.499, df = 1, p = 0.000$, means that the relationship between the covariate and the effect is greater than would be expected by chance
- $Q_{resid} = 30.733, df = 11, p = 0.001$, means that even with the covariate in the model, some of the between-studies variance is unexplained

Random-Effects Model



Random-Effects Model



Mixed effects regression (method of moments)

	Point estimate	Standard error	Lower limit	Upper limit	Z-value	p-Value
Slope	-0.02923	0.00673	-0.04243	-0.01603	-4.34111	0.00001
Intercept	0.25954	0.23231	-0.19577	0.71486	1.11724	0.26389
Tau-squared	0.06330					

	Q	df	p-value
Model	18.84523	1.00000	0.00001
Residual	15.28866	11.00000	0.16966
Total	34.13390	12.00000	0.00064

Random-Effects Model Fit

- Tests of the model
  - Simultaneous test that all coefficients (excluding intercept) are zero
    - Q^*_{model}, df, p
  - Goodness of fit test that all unexplained variance is zero
    - T^2, Q_{resid}, df, p

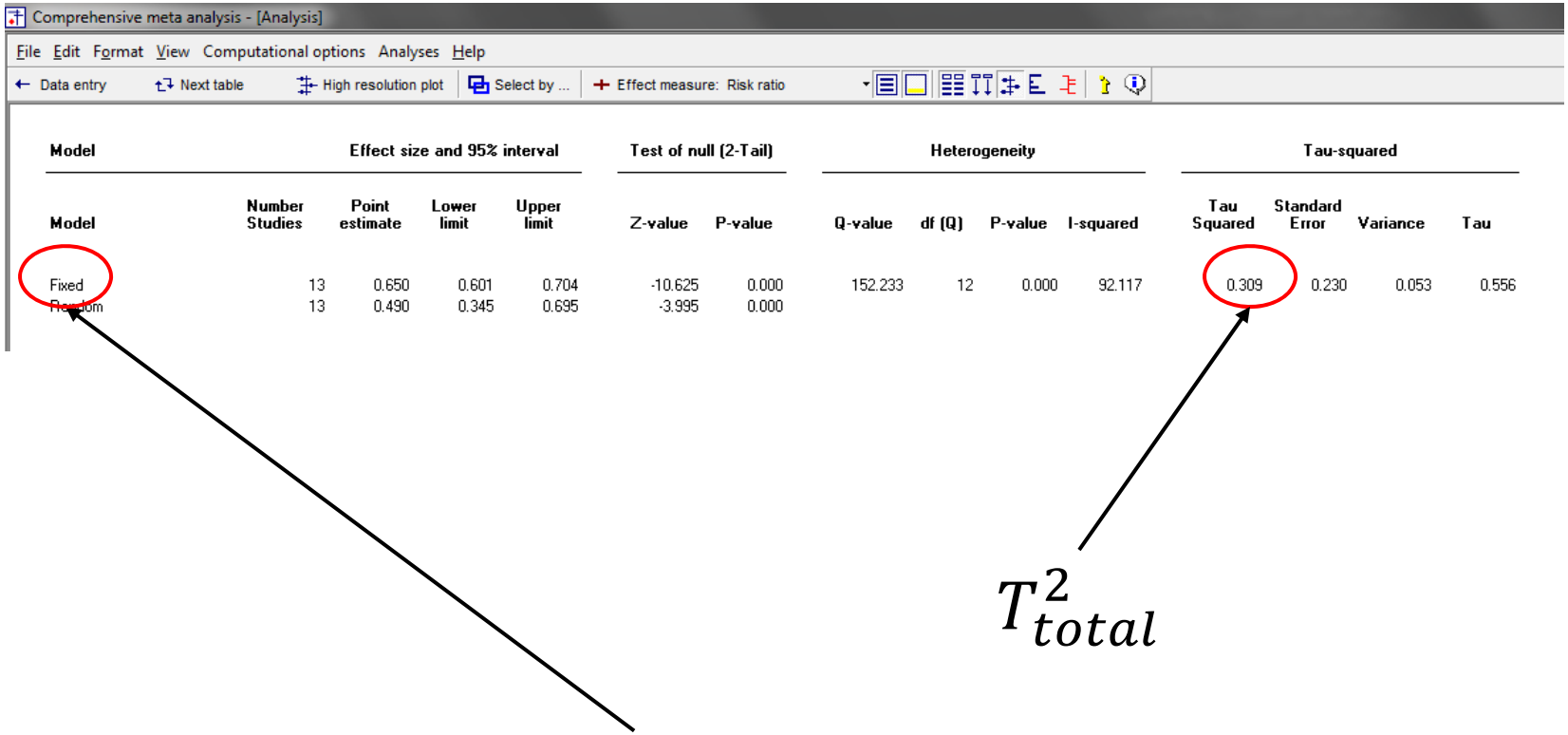
$$=\text{CHIDIST}(Q, df)$$

Proportion of Covariate Explained Variance

- In meta-analysis, the total variance includes both variance within studies and between studies
- Study-level covariates explain only the between-studies portion of the variance

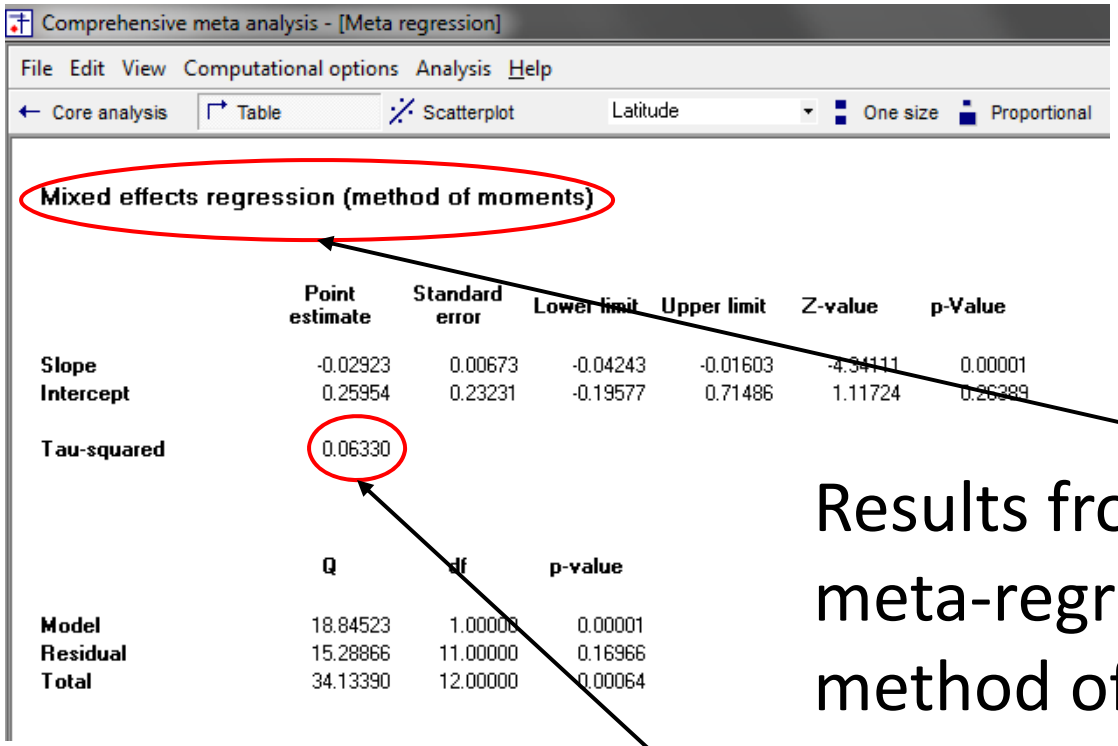
$$R^2 = 1 - \left(\frac{T^2_{unexplained}}{T^2_{total}} \right)$$

Calculating R^2



Use the fixed-effect meta-analysis results (not meta-regression results)

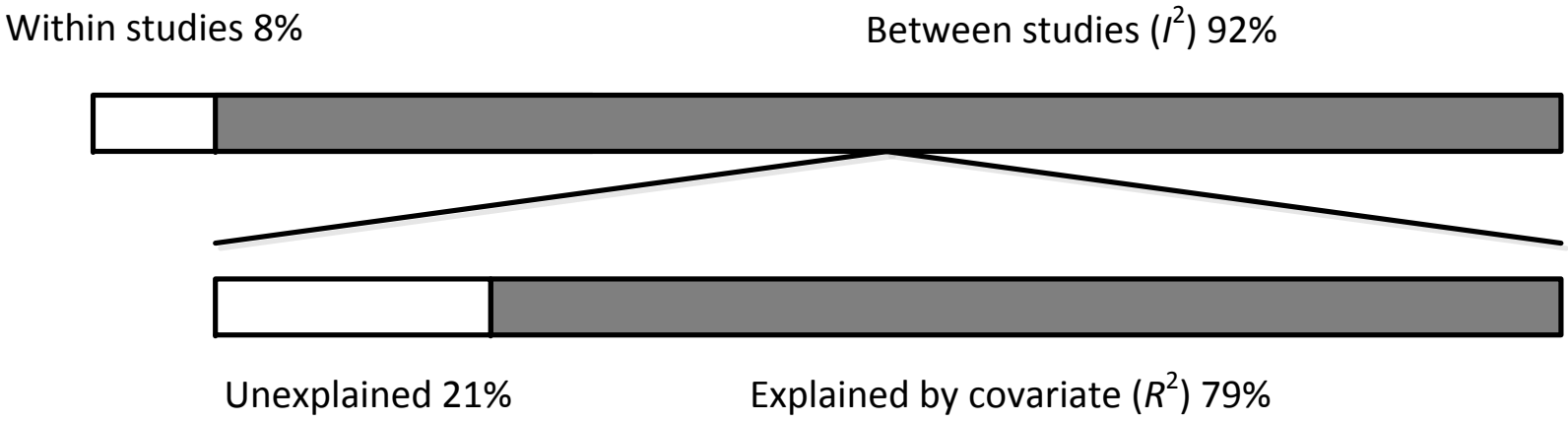
Calculating R^2



Results from random-effects meta-regression using method of moments

$T^2_{unexplained}$

Variance Explained by Covariate



Today's First In-Class Activity

- From the "BCG Meta-Regression.CMA" data set
  - Using a risk ratio as the effect size, conduct a random-effects meta-regression (with method of moments) regressing latitude on the risk ratio
  - Write the regression equation, calculate the Z-test to estimate the impact of the slope, compute the *LL* and *UL* of β, and calculate R^2
  - Interpret and explain the results

Complex Data Structures

- Main categories of complex data structures
  - Independent subgroups within a study
  - Multiple outcomes or time-points within a study
  - Multiple comparisons within a study
- The first two are (relatively) easily handled in Comprehensive Meta-Analysis 2.0

Independent Subgroups within a Study

- When two or more independent subgroups (each of which contribute unique information) are reported within the same study, the options are
  1. Compare effects between subgroups
     - For two subgroups, Z-test
     - For two or more subgroups, Q-test based on ANOVA
     - Q-test for heterogeneity
  2. Compute a summary effect for all subgroups combined

Combining Across Subgroups

- Option 1a (effect size is computed within subgroups)
  - Treat each subgroup as a separate study
    - Interest is in between-subgroup variation
- Option 1b (effect size is computed within studies)
  - Compute a composite score and use the composite score for each study as the unit of analysis
    - Interest is in between-study variation

Combining Across Subgroups

- Option 2 (ignore subgroup membership)
  - Collapse across subgroups to compute a summary effect size and variance
  - Subgroup membership is considered unimportant and is ignored (and its variance is not part of the summary effect size or standard error)
  - Essentially a main effect meta-analysis

Multiple Outcomes or Time-Points within a Study

- When a study reports data on more than one outcome, or over more than one time-point, where outcomes or time-points are based on the same participants (i.e., dependent), the options are
  1. Compute a composite effect size accounting for the correlation between outcomes or time-points
  2. Compute a difference between outcomes or time-points accounting for the correlation between outcomes or time-points

Combining Outcomes or Time-Points

- The effect size for two outcomes or time-points is computed as

$$\bar{Y} = \frac{1}{2}(Y_1 = Y_2)$$

- With variance of the combined mean

$$V_{\bar{Y}} = \frac{1}{4}(V_{Y_1} + V_{Y_2} + 2r\sqrt{V_{Y_1}}\sqrt{V_{Y_2}}$$

Combining Outcomes or Time-Points

- For more than two outcomes or time-points

$$\bar{Y} = \frac{1}{m}\left(\sum_{j}^{m} Y_j\right)$$

- With variance of

$$V_{\bar{Y}} = \left(\frac{1}{m}\right)^2 \left(\sum_{j=1}^{m} V_i + \sum_{j \neq k} \left(r_{jk}\sqrt{V_{Y_1}}\sqrt{V_{Y_2}}\right)\right)$$

Combining Outcomes or Time-Points

- The problem is that r often is not known (e.g., not reported in a study)
- If r is unknown, the only solution is to use a plausible value or range of values (sensitivity)
  - Similarity (or dissimilarity) of outcomes
  - Time elapsed between time-points and stability of relative scores over time
- By default, Comprehensive Meta-Analysis 2.0 sets r to 1.00 (which may overestimate the variance and underestimate precision)

Comparing Outcomes or Time-Points within a Study

- The effect size for the difference between two outcomes or time-points is computed as

$$Y_{diff} = Y_1 - Y_2$$

- With variance

$$V_{diff} = V_{Y_1} + V_{Y_2} - 2r\sqrt{V_{Y_1}}\sqrt{V_{Y_2}}$$

Comparing Outcomes or Time-Points

- As before, the problem is that r often is not known (e.g., not reported in a study)
- If r is unknown, the only solution is to use a plausible value or range of values (sensitivity)
- By default, Comprehensive Meta-Analysis 2.0 sets r to 0.00 (which may overestimate the variance and underestimate precision of the difference)

Multiple Comparisons within a Study

- When a study reports multiple comparisons between more than two (dependent) groups (e.g., treatment variant *A*, treatment variant *B*, and control group *C*), the options are
  1. Compute a summary effect for the active intervention (combing *A* and *B*) versus control (*C*); the same as option 2 for independent subgroups
  2. Compute a difference for interventions *A* and *B* (ignoring *C*)

Today's Second In-Class Activity

- From the "Complex Data Structures Multiple Outcomes or Time-Points.CMA" data set
  - Conduct fixed-effect analyses (1) using composite effect sizes within studies and (2) treating each outcome as the unit of analysis
  - Interpret and explain both analyses (including all relevant statistical tests)