

meta regress — Meta-analysis regression

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Description

`meta regress` performs meta-analysis regression, or meta-regression, which is a linear regression of the study effect sizes on study-level covariates (moderators). Meta-regression investigates whether between-study heterogeneity can be explained by one or more moderators. You can think of meta-regression as a standard meta-analysis that incorporates moderators into the model. `meta regress` performs both random-effects and fixed-effects meta-regression.

Quick start

Perform meta-regression of the effect size, `_meta_es`, on covariate (moderator) `x1`

```
meta regress x1
```

As above, but assume a DerSimonian–Laird random-effects method instead of the method declared by either `meta set` or `meta esize`

```
meta regress x1, random(dlaird)
```

Add a factor variable `a`, and request a Knapp–Hartung adjustment to the standard errors of coefficients

```
meta regress x1 i.a, random(dlaird) se(khartung)
```

Perform a sensitivity analysis by assuming a fixed value of 0.2 for the between-study variance τ^2

```
meta regress x1 i.a, tau2(0.2)
```

Menu

Statistics > Meta-analysis

Syntax

Meta-regression using meta-analysis model as declared with meta set or meta esize

```
meta regress moderators [if] [in] [, reopts options]
```

Random-effects meta-regression

```
meta regress moderators [if] [in], random[ (remethod) ] [reopts options]
```

Fixed-effects meta-regression

```
meta regress moderators [if] [in], fixed [multiplicative options]
```

Constant-only meta-regression

```
meta regress _cons [if] [in] [, modelopts]
```

<i>reopts</i>	Description
<u>tau2</u> (#)	sensitivity meta-analysis using a fixed value of between-study variance τ^2
<u>i2</u> (#)	sensitivity meta-analysis using a fixed value of heterogeneity statistic I_{res}^2
<u>se</u> (<i>seadj</i>)	adjust standard errors of the coefficients

<i>options</i>	Description
Model	
<u>noconstant</u>	suppress constant term
<u>tdistribution</u>	report <i>t</i> tests instead of <i>z</i> tests for the coefficients
Reporting	
<u>level</u> (#)	set confidence level; default is as declared for meta-analysis
<u>noheader</u>	suppress output header
[<u>no</u>] <u>metashow</u>	display or suppress meta settings in the output
<u>display_options</u>	control columns and column formats, row spacing, line width, display of omitted variables and base and empty cells, and factor-variable labeling
Maximization	
<u>maximize_options</u>	control the maximization process; seldom used
<u>coeflegend</u>	display legend instead of statistics

moderators may contain factor variables; see [U] 11.4.3 **Factor variables**.

coeflegend does not appear in the dialog box.

See [U] 20 **Estimation and postestimation commands** for more capabilities of estimation commands.

<i>remethod</i>	Description
<code>rem1</code>	restricted maximum likelihood; the default
<code>mle</code>	maximum likelihood
<code>ebayes</code>	empirical Bayes
<code>dlaird</code>	DerSimonian–Laird
<code>sjonkman</code>	Sidik–Jonkman
<code>hedges</code>	Hedges
<code>hschmidt</code>	Hunter–Schmidt

modelopts is any option except `noconstant`.

Options

Model

`noconstant`; see [R] [Estimation options](#). This option is not allowed with constant-only meta-regression.

Options `random()` and `fixed`, when specified with `meta regress`, temporarily override the global model declared by `meta set` or `meta esize` during the computation. Options `random()` and `fixed` may not be combined. If these options are omitted, the declared meta-analysis model is assumed; see [Declaring a meta-analysis model](#) in [META] [meta data](#). Also see [Meta-analysis models](#) in [META] [Intro](#).

`random` and `random(remethod)` specify that a random-effects model be assumed for meta-regression; see [Random-effects model](#) in [META] [Intro](#).

remethod specifies the type of estimator for the between-study variance τ^2 . *remethod* is one of `rem1`, `mle`, `ebayes`, `dlaird`, `sjonkman`, `hedges`, or `hschmidt`. `random` is a synonym for `random(rem1)`. See [Options](#) in [META] [meta esize](#) for more information.

`fixed` specifies that a fixed-effects model be assumed for meta-regression; see [Fixed-effects model](#) in [META] [Intro](#). It uses the inverse-variance estimation method; see [Meta-analysis estimation methods](#) in [META] [Intro](#).

reopts are `tau2(#)`, `i2(#)`, and `se(khartung[, truncated])`. These options are used with random-effects meta-regression.

`tau2(#)` specifies the value of the between-study variance parameter, τ^2 , to use for the random-effects meta-regression. This option is useful for exploring the sensitivity of the results to different levels of between-study heterogeneity. Only one of `tau2()` or `i2()` may be specified.

`i2(#)` specifies the value of the residual heterogeneity statistic I^2_{res} (as a percentage) to use for the random-effects meta-regression. This option is useful for exploring the sensitivity of the results to different levels of between-study heterogeneity. Only one of `i2()` or `tau2()` may be specified.

`se(seadj)` specifies that the adjustment *seadj* be applied to the standard errors of the coefficients. Additionally, the tests of significance of the coefficients are based on a Student's *t* distribution instead of the normal distribution.

seadj is `khartung[, truncated]`. Adjustment `khartung` specifies that the Knapp–Hartung adjustment (Hartung and Knapp 2001a, 2001b; Knapp and Hartung 2003), also known as the Sidik–Jonkman adjustment (Sidik and Jonkman 2002), be applied to the standard errors of the coefficients. `hknapp` and `sjonkman` are synonyms for `khartung`. `truncated` specifies

that the truncated Knapp–Hartung adjustment (Knapp and Hartung 2003), also known as the modified Knapp–Hartung adjustment, be used.

`multiplicative` performs a fixed-effects meta-regression that accounts for residual heterogeneity by including a multiplicative variance parameter ϕ . ϕ is referred to as an “(over)dispersion parameter”. See [Introduction](#) for details.

`tdistribution` reports t tests instead of z tests for the coefficients. This option is useful, for instance, when `meta regress` is used to conduct a regression-based test for funnel-plot asymmetry. Traditionally, the test statistic from this test is compared with critical values from a Student’s t distribution instead of the default normal distribution. This option may not be combined with option `se()`.

Reporting

`level(#)` specifies the confidence level, as a percentage, for confidence intervals. The default is as declared for the meta-analysis session; see [Declaring a confidence level for meta-analysis](#) in [\[META\] meta data](#). Also see option `level()` in [\[META\] meta set](#).

`noheader` suppresses the output header, either at estimation or upon replay.

`metashow` and `nometashow` display or suppress the meta setting information. By default, this information is displayed at the top of the output. You can also specify `nometashow` with `meta update` to suppress the meta setting output for the entire meta-analysis session.

display_options: `nocl`, `nopvalues`, `noomitted`, `vsquish`, `noemptycells`, `baselevels`, `allbaselevels`, `nofvlabel`, `fvwrap(#)`, `fvwrapon(style)`, `cformat(%fmt)`, `pformat(%fmt)`, `sformat(%fmt)`, and `nolstretch`; see [\[R\] Estimation options](#).

Maximization

maximize_options: `iterate(#)`, `tolerance(#)`, `nrtolerance(#)`, `nonrtolerance` (see [\[R\] Maximize](#)), `from(#)`, and `showtrace`. These options control the iterative estimation of the between-study variance parameter, τ^2 , with random-effects methods `reml`, `mle`, and `ebayes`. These options are seldom used.

`from(#)` specifies the initial value for τ^2 during estimation. By default, the initial value for τ^2 is the noniterative Hedges estimator.

`showtrace` displays the iteration log that contains the estimated parameter τ^2 , its relative difference with the value from the previous iteration, and the scaled gradient.

The following option is available with `meta regress` but is not shown in the dialog box:

`coeflegend`; see [\[R\] Estimation options](#).

Remarks and examples

[stata.com](http://www.stata.com)

Remarks are presented under the following headings:

[Introduction](#)

[Examples of using meta regress](#)

Introduction

Meta-regression is a regression performed in the context of meta-analysis. It is used to study the relationship between study effect sizes and covariates. Meta-regression is analogous to standard regression used when individual data are available, but in meta-regression, the observations are the studies, the outcome of interest is the effect size, and the covariates are recorded at the study level. The study-level covariates in meta-regression are known as moderators. Several examples of moderators include study location, study test environment, drug administration method. For a general overview and discussions about meta-regression, see [Berlin and Antman \(1992\)](#), [Berkey et al. \(1995\)](#), and [Thompson and Higgins \(2002\)](#).

The goal of meta-regression is to explore and explain the between-study heterogeneity as a function of moderators. Two types of regression models, fixed-effects (FE) and random-effects (RE), are available. An FE meta-regression assumes that all heterogeneity between study effect sizes can be accounted for by the included moderators. An RE meta-regression accounts for potential additional variability unexplained by the included moderators, also known as residual heterogeneity. Because a common-effect meta-analysis model implies no study heterogeneity, it is not applicable to meta-regression, except in a less interesting case of a constant-only model, which is equivalent to the standard common-effect meta-analysis; see [\[META\] meta summarize](#).

`meta regress` fits meta-regression. Use the `random()` option to fit an RE meta-regression and the `fixed` option to fit an FE meta-regression. Also see [Default meta-analysis model and method](#) in [\[META\] meta data](#) to learn about the default regression model used by `meta regress`.

For the j th study, let $\hat{\theta}_j$ denote the effect size, $\hat{\sigma}_j^2$ its variance, and \mathbf{x}_j be a $1 \times p$ vector of moderators with the corresponding unknown $p \times 1$ coefficient vector β .

An FE meta-regression ([Greenland 1987](#)) is given by

$$\hat{\theta}_j = \mathbf{x}_j\beta + \epsilon_j, \text{ weighted by } w_j = \frac{1}{\hat{\sigma}_j^2}, \text{ where } \epsilon_j \sim N(0, \hat{\sigma}_j^2)$$

Residual heterogeneity may be incorporated into an FE meta-regression via a multiplicative factor, ϕ , applied to each of the variances $\hat{\sigma}_j^2$. This leads to a multiplicative meta-regression or FE meta-regression with multiplicative dispersion parameter ([Thompson and Sharp 1999](#))

$$\hat{\theta}_j = \mathbf{x}_j\beta + \epsilon_j^\phi, \text{ weighted by } w_j = \frac{1}{\hat{\sigma}_j^2}, \text{ where } \epsilon_j^\phi \sim N(0, \hat{\sigma}_j^2\phi)$$

This regression model may be specified by the combination of `fixed` and `multiplicative` options.

Another method of incorporating residual heterogeneity is to include an additive between-study variance component, τ^2 , that leads to an RE meta-regression ([Berkey et al. 1995](#)), also known as a mixed model in the meta-analysis literature:

$$\hat{\theta}_j = \mathbf{x}_j\beta + \epsilon_j^* = \mathbf{x}_j\beta + u_j + \epsilon_j, \text{ weighted by } w_j^* = \frac{1}{\hat{\sigma}_j^2 + \hat{\tau}^2}, \text{ where } \epsilon_j^* \sim N(0, \hat{\sigma}_j^2 + \tau^2)$$

As we mentioned earlier, an RE meta-regression assumes that the moderators explain only part of the heterogeneity, and a random-effects term $u_j \sim N(0, \tau^2)$ is used to account for the remainder.

Harbord and Higgins (2016) point out that some authors (Thompson and Sharp 1999; Higgins and Thompson 2004) argue that an FE meta-regression should not be used because, in practice, the included moderators rarely capture all the between-study heterogeneity and that the failure of the FE regression to capture the extra between-study heterogeneity can lead to excessive type I errors. Also, the results from an FE meta-regression, including its multiplicative version, may not be generalized to populations from which the observed studies are a sample (Konstantopoulos and Hedges 2009). If you do not specify a meta-analysis model with `meta set` or `meta esize` during declaration, an RE meta-regression will be assumed by `meta regress`.

Meta-regression can also be considered an extension of subgroup analysis (see `meta summarize`, `subgroup()` in [META] `meta summarize`) to include continuous moderators in addition to the categorical ones. In particular, an FE meta-regression with the subgroup variable specified as a factor variable (see [U] 11.4.3 **Factor variables**) is equivalent to the FE subgroup analysis on that variable.

It is recommended that you have at least 10 studies per moderator to perform meta-regression (Borenstein et al. 2009, chap. 20). Otherwise, you may not be able to estimate the effects of moderators reliably. For more recommendations regarding meta-regression, see Schmidt and Hunter (2015, chap. 9), Deeks, Macaskill, and Irwig (2005), Harbord and Higgins (2016), Sharp (2016), and Thompson and Higgins (2002).

Examples of using meta regress

Consider a dataset from Colditz et al. (1994) of clinical trials that explore the efficacy of a Bacillus Calmette-Guérin (BCG) vaccine in the prevention of tuberculosis (TB). This dataset was introduced in *Efficacy of BCG vaccine against tuberculosis (bcg.dta)* of [META] `meta`. In this section, we use its declared version and focus on the demonstration of various options of `meta regress` and explanation of its output.

```
. use https://www.stata-press.com/data/r16/bcgset
(Efficacy of BCG vaccine against tuberculosis; set with -meta esize-)
. meta query, short
-> meta esize npost nnegt npsc nnegc, esize(lnrratio) studylabel(study1b1)
Effect-size label:  Log Risk-Ratio
Effect-size type:  lnrratio
Effect size:      _meta_es
Std. Err.:       _meta_se
Model:           Random-effects
Method:          REML
```

`meta query, short` reminds us about the main settings of the declaration step. Our data were declared by using `meta esize` with variables `npost`, `nnegt`, `npsc`, and `nnegc` representing the summary data from 2×2 tables, which record the numbers of positive and negative TB cases in the treatment and control groups. The computed effect sizes are log risk-ratios; their values and standard errors are stored in the respective **system variables** `_meta_es` and `_meta_se`. The `study1b1` variable supplies the study labels to be used in the output. The declared meta-analysis model is the default random-effects model with the REML estimation method.

Examples are presented under the following headings:

Example 1: Random-effects meta-regression

Example 2: Sidik–Jonkman random-effects method

Example 3: Truncated Knapp–Hartung standard-error adjustment

Example 4: Sensitivity meta-analysis

Example 5: Fixed-effects meta-regression

Example 6: Multiplicative meta-regression

Example 7: Constant-only model

► Example 1: Random-effects meta-regression

In [example 8](#) of [\[META\] meta](#), following [Berkey et al. \(1995\)](#), we fit a meta-regression with a centered absolute latitude, `latitude_c`, as the moderator to address heterogeneity. Let's refit this model here and focus on the specification and output from `meta regress`.

```
. meta regress latitude_c
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Random-effects meta-regression                Number of obs =          13
Method: REML                                Residual heterogeneity:
                                          tau2 = .07635
                                          I2 (%) = 68.39
                                          H2 = 3.16
                                          R-squared (%) = 75.63
Wald chi2(1) = 16.36
Prob > chi2 = 0.0001
```

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
latitude_c	-.0291017	.0071953	-4.04	0.000	-.0432043 - .0149991
_cons	-.7223204	.1076535	-6.71	0.000	-.9333174 - .5113234

Test of residual homogeneity: $Q_{res} = \text{chi2}(11) = 30.73$ Prob > $Q_{res} = 0.0012$

Unlike with many Stata regression commands, we do not specify the dependent variable with `meta regress`. The command includes it automatically from the declared [meta settings](#). `meta regress` provides a short summary of the settings, which you can suppress with the `nometashow` option. [System variable](#) `_meta_es` contains the effect sizes and is thus used as the dependent variable. [System variable](#) `_meta_se` contains effect-size standard errors; it is used to construct the weights for the regression.

The header includes the information about the meta-analysis model and reports various summaries such as heterogeneity statistics and the model test. For example, the results are based on 13 studies. The reported I^2_{res} statistic is 68%, which still suggests moderate heterogeneity, using the categorization of [Higgins et al. \(2003\)](#), even after including `latitude_c` as the moderator. In other words, 68% of the variability in the residuals is still attributed to the between-study variation, whereas only 32% is attributed to the within-study variation. The adjusted R^2 statistic can be used to assess the proportion of between-study variance explained by the covariates; see (4) in [Methods and formulas](#) for its definition used in the meta-analysis literature. Here roughly 76% of the between-study variance is explained by the covariate `latitude_c`.

The output header also displays a model test that all coefficients other than the intercept are equal to zero based on the χ^2 distribution with $p - 1$ degrees of freedom. In our example, the χ^2 test statistic is 16.36 with a p -value of 0.0001. We have only one moderator, so the results of the model test in our example are equivalent to the z test (χ^2 value equals squared z value) of the coefficient of `latitude_c` reported in the output table.

The regression coefficient for `latitude_c` is -0.029 , which means that every one degree of latitude corresponds to a decrease of 0.0291 units in log risk-ratio. The intercept, $\widehat{\beta}_0$, is -0.722 , which means that the overall risk ratio at the mean latitude (`latitude_c = 0` corresponds to `latitude` ≈ 33.46) is $\exp(-0.722) = 0.46$. Both of these coefficients are statistically significantly different from zero based on the reported z tests.

Finally, a test of residual homogeneity is reported at the bottom of the output. The test statistic Q_{res} is 30.73 with a p -value of 0.0012, which suggests the presence of heterogeneity among the residuals.



□ Technical note

Heterogeneity statistics I^2_{res} and H^2_{res} , reported under **Residual heterogeneity:** in the header, are extensions of the corresponding statistics I^2 and H^2 from standard meta-analysis to meta-regression (Higgins and Thompson 2002). They measure the remaining between-study heterogeneity among the residuals after adjusting for the variability due to moderators. Similarly, the test of residual homogeneity based on the Q_{res} statistic is the extension of the standard meta-analysis homogeneity test based on the Cochran's Q statistic to meta-regression. See [Residual heterogeneity measures](#) and [Residual homogeneity test](#) in *Methods and formulas*.



▷ Example 2: Sidik–Jonkman random-effects method

Continuing with [example 1](#), let's demonstrate the use of a different RE method, for instance, the Sidik–Jonkman method, instead of the default REML method.

```
. meta regress latitude_c, random(sjonkman)
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Random-effects meta-regression
Method: Sidik-Jonkman

Number of obs =      13
Residual heterogeneity:
      tau2 =      .2318
      I2 (%) =     86.79
      H2 =       7.57
      R-squared (%) = 32.90
Wald chi2(1) =      6.50
Prob > chi2 =      0.0108
```

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
latitude_c	-.0280714	.0110142	-2.55	0.011	-.0496589	-.0064838
_cons	-.7410395	.1602117	-4.63	0.000	-1.055049	-.4270304

```
Test of residual homogeneity: Q_res = chi2(11) = 30.73  Prob > Q_res = 0.0012
```

The estimate of the regression coefficient for `latitude_c` is -0.028 and is similar to the REML estimate of -0.029 , but the standard errors are quite different: 0.011 versus 0.007. Recall that REML assumes that the error distribution is normal, whereas the Sidik–Jonkman estimator does not. Thus, its standard-error estimates are likely to be larger than those from REML. The estimates of the between-study variance, τ^2 , are also very different: 0.23 compared with the REML estimate of 0.08.



▶ Example 3: Truncated Knapp–Hartung standard-error adjustment

Continuing with [example 1](#), let's use an alternative standard-error computation sometimes used in practice—the truncated Knapp–Hartung method.

```
. meta regress latitude_c, se(khartung, truncated)
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Random-effects meta-regression                Number of obs =      13
Method: REML                                Residual heterogeneity:
SE adjustment: Truncated Knapp-Hartung      tau2 = .07635
                                             I2 (%) = 68.39
                                             H2 = 3.16
                                             R-squared (%) = 75.63
Model F(1,11) = 12.59
Prob > F = 0.0046
```

_meta_es	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
latitude_c	-.0291017	.0082014	-3.55	0.005	-.0471529	-.0110505
_cons	-.7223204	.1227061	-5.89	0.000	-.9923946	-.4522462

Test of residual homogeneity: $Q_{\text{res}} = \text{chi2}(11) = 30.73$ Prob > $Q_{\text{res}} = 0.0012$

The reported standard errors are larger than those from [example 1](#). This is expected because the Knapp–Hartung adjustment incorporates the uncertainty in estimating τ^2 in the standard-error computation. Also, the inferences for the tests of coefficients and the model test are now based on the Student's t and F distributions, respectively, instead of the default normal and χ^2 distributions.

◀

▶ Example 4: Sensitivity meta-analysis

We can perform sensitivity analysis to explore the impact of the various levels of heterogeneity on the regression results. Continuing with [example 1](#), let's fit a meta-regression assuming that the residual heterogeneity statistic I_{res}^2 equals 90%.

```
. meta regress latitude_c, i2(90)
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Random-effects meta-regression                Number of obs =      13
Method: User-specified I2                    Residual heterogeneity:
                                             tau2 = .3176
                                             I2 (%) = 90.00
                                             H2 = 10.00
Wald chi2(1) = 4.89
Prob > chi2 = 0.0269
```

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
latitude_c	-.0277589	.0125474	-2.21	0.027	-.0523514	-.0031664
_cons	-.7443082	.1812664	-4.11	0.000	-1.099584	-.3890326

Test of residual homogeneity: $Q_{\text{res}} = \text{chi2}(11) = 30.73$ Prob > $Q_{\text{res}} = 0.0012$

The estimate of the coefficient for `latitude_c` is now -0.028 with a standard-error estimate of 0.01 .

Let's now fit a meta-regression assuming the between-study variance of 0.01.

```
. meta regress latitude_c, tau2(0.01)
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Random-effects meta-regression
Method: User-specified tau2

Number of obs =      13
Residual heterogeneity:
      tau2 =      .01
      I2 (%) =     22.08
      H2 =      1.28
Wald chi2(1) =     57.62
Prob > chi2 =     0.0000
```

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
latitude_c	-.0295601	.0038942	-7.59	0.000	-.0371926 - .0219277
_cons	-.6767043	.0617892	-10.95	0.000	-.7978089 - .5555998

Test of residual homogeneity: $Q_{res} = \text{chi2}(11) = 30.73$ Prob > $Q_{res} = 0.0012$

The specified value of τ^2 corresponds to the I^2_{res} value of 22.08%. The coefficient estimate is now -0.03 with a standard error of 0.004.

In both sensitivity analyses, `latitude_c` remained a statistically significant moderator for the log risk-ratios.

◀

▶ Example 5: Fixed-effects meta-regression

Instead of an RE meta-regression as in [example 1](#), we can use the `fixed` option to fit an FE meta-regression. The use of an FE meta-regression is usually discouraged in the meta-analysis literature because it assumes that all between-study heterogeneity is accounted for by the specified moderators ([Harbord and Higgins 2016](#); [Thompson and Sharp 1999](#); [Higgins and Thompson 2004](#)). This is often an unrealistic assumption in meta-analysis. We fit this model in our example for the purpose of demonstration.

```
. meta regress latitude_c, fixed
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Fixed-effects meta-regression
Method: Inverse-variance

Number of obs =      13
Wald chi2(1) =     121.50
Prob > chi2 =     0.0000
```

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]
latitude_c	-.0292369	.0026524	-11.02	0.000	-.0344356 - .0240383
_cons	-.6347482	.0445446	-14.25	0.000	-.7220541 - .5474423

Because the FE regression assumes no additional residual heterogeneity, the residual heterogeneity statistics and the residual homogeneity test are not reported with `meta regress, fixed`.

The coefficient estimates are similar to those from [example 1](#), but standard errors from the FE regression are smaller. This is because the FE regression does not account for the residual heterogeneity that is not explained by the included moderators.

Considering the presence of residual heterogeneity in these data, we should go back to our RE analysis or explore the multiplicative meta-regression, which we demonstrate in [example 6](#).



► Example 6: Multiplicative meta-regression

An FE meta-regression in [example 5](#) does not account for residual heterogeneity. An extension of this regression model that does, known as a multiplicative meta-regression (see [Introduction](#) and [Methods and formulas](#)), has been considered in the meta-analysis literature. An RE meta-regression is the preferred analysis these days, but we provide the multiplicative meta-regression for completeness.

Continuing with [example 5](#), we add the multiplicative option to fit an FE meta-regression with a multiplicative dispersion parameter ϕ .

```
. meta regress latitude_c, fixed multiplicative
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Fixed-effects meta-regression
Error: Multiplicative
Method: Inverse-variance

Number of obs =      13
Dispersion phi =     2.79
Wald chi2(1)  =     43.49
Prob > chi2   =     0.0000
```

_meta_es	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
latitude_c	-.0292369	.0044335	-6.59	0.000	-.0379265	-.0205474
_cons	-.6347482	.0744564	-8.53	0.000	-.7806801	-.4888163

```
Test of residual homogeneity: Q_res = chi2(11) = 30.73  Prob > Q_res = 0.0012
```

The estimate of the dispersion parameter, reported in the header as Dispersion phi, is 2.79. It is greater than 1, which suggests the presence of residual heterogeneity in these data. The coefficient estimates are the same as those in [example 5](#), but the standard errors are about two times larger.



► Example 7: Constant-only model

The primary use of `meta regress` is to fit meta-regression models containing moderators. You can also fit a constant-only model (without moderators), although this is less common in the context of meta-regression.

To fit a constant-only model with many regression estimation commands, you simply omit the covariates in the command specification. This would not work with `meta regress` because, without the dependent-variable specification, we would have to type

```
. meta regress
```

which means replaying previous estimation results consistently across Stata. The above will either issue an error that previous estimation results are not found or redisplay the results from the previous `meta regress` specification.

Instead, to fit a constant-only model with `meta regress`, you specify the designator `_cons` following the command name.

```
. meta regress _cons
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se

Random-effects meta-regression
Method: REML
Number of obs =      13
Residual heterogeneity:
      tau2 =    .3132
      I2 (%) =   92.22
      H2 =    12.86
Wald chi2(0) =      .
Prob > chi2 =      .
```

<code>_meta_es</code>	Coef.	Std. Err.	z	P> z	[95% Conf. Interval]	
<code>_cons</code>	-.7145323	.1797815	-3.97	0.000	-1.066898	-.362167

Test of residual homogeneity: $Q_{res} = \text{chi2}(12) = 152.23$ Prob > $Q_{res} = 0.0000$

Note that the estimated value of $\hat{\tau}^2$ is now 0.313, whereas in [example 1](#) it was 0.076. That is, the inclusion of covariate `latitude_c` in [example 1](#) reduced $\hat{\tau}^2$ from 0.313 to 0.076 for a relative reduction of $(0.313 - 0.076)/0.313 \approx 76\%$.

The reason a constant-only meta-regression is not as common is because it produces the same results as a standard meta-analysis.

```
. meta summarize, nostudies
      Effect-size label:  Log Risk-Ratio
      Effect size:      _meta_es
      Std. Err.:       _meta_se
      Study label:     studylbl

Meta-analysis summary
Random-effects model
Method: REML
Number of studies =    13
Heterogeneity:
      tau2 =   0.3132
      I2 (%) =   92.22
      H2 =    12.86
```

theta: Overall Log Risk-Ratio

	Estimate	Std. Err.	z	P> z	[95% Conf. Interval]	
theta	-.7145323	.1797815	-3.97	0.000	-1.066898	-.362167

Test of homogeneity: $Q = \text{chi2}(12) = 152.23$ Prob > $Q = 0.0000$

See [\[META\] meta summarize](#) for details.

Stored results

`meta regress` stores the following in `e()`:

Scalars

<code>e(N)</code>	number of observations (studies)
<code>e(df_m)</code>	model degrees of freedom
<code>e(df_r)</code>	residual degrees of freedom
<code>e(chi2)</code>	model χ^2 Wald test statistic
<code>e(F)</code>	model F statistic
<code>e(p)</code>	p -value for model test
<code>e(phi)</code>	dispersion parameter
<code>e(tau2)</code>	between-study variance
<code>e(I2_res)</code>	I^2_{res} heterogeneity statistic
<code>e(H2_res)</code>	H^2_{res} heterogeneity statistic
<code>e(R2)</code>	R^2 heterogeneity measure
<code>e(Q_res)</code>	Cochran's Q residual homogeneity test statistic
<code>e(df_Q_res)</code>	degrees of freedom for residual homogeneity test
<code>e(p_Q_res)</code>	p -value for residual homogeneity test
<code>e(seadj)</code>	standard-error adjustment
<code>e(level)</code>	confidence level for CIs
<code>e(converged)</code>	1 if converged, 0 otherwise (with iterative random-effects methods)

Macros

<code>e(cmd)</code>	<code>meta regress</code>
<code>e(cmdline)</code>	command as typed
<code>e(depvar)</code>	name of dependent variable, <code>_meta_es</code>
<code>e(indepvars)</code>	names of independent variables (moderators)
<code>e(title)</code>	title in estimation output
<code>e(model)</code>	meta-analysis model
<code>e(method)</code>	meta-analysis estimation method
<code>e(seadjtype)</code>	type of standard-error adjustment
<code>e(properties)</code>	<code>b V</code>
<code>e(estat_cmd)</code>	program used to implement <code>estat</code>
<code>e(predict)</code>	program used to implement <code>predict</code>
<code>e(marginsok)</code>	predictions allowed by <code>margins</code>
<code>e(marginsnotok)</code>	predictions disallowed by <code>margins</code>
<code>e(marginsdefault)</code>	default <code>predict()</code> specification for <code>margins</code>
<code>e(asbalanced)</code>	factor variables <code>fvset</code> as <code>asbalanced</code>
<code>e(asobserved)</code>	factor variables <code>fvset</code> as <code>asobserved</code>

Matrices

<code>e(b)</code>	coefficient vector
<code>e(V)</code>	variance–covariance matrix of the estimators

Functions

<code>e(sample)</code>	marks estimation sample
------------------------	-------------------------

In addition to the above, the following is stored in `r()`:

Matrices

<code>r(table)</code>	matrix containing the coefficients with their standard errors, test statistics, p -values, and confidence intervals
-----------------------	---

Note that results stored in `r()` are updated when the command is replayed and will be replaced when any `r`-class command is run after the estimation command.

`meta regress` also creates a system variable, `_meta_regweight`, that contains meta-regression weights.

Methods and formulas

Methods and formulas are presented under the following headings:

Fixed-effects meta-regression
Random-effects meta-regression
Iterative methods for computing $\hat{\tau}^2$
Noniterative methods for computing $\hat{\tau}^2$
Knapp–Hartung standard-error adjustment
Residual homogeneity test
Residual heterogeneity measures

Fixed-effects meta-regression

For an overview of estimation methods used by meta-regression, see [Berkey et al. \(1995\)](#), [Sidik and Jonkman \(2005\)](#), and [Viechtbauer et al. \(2015\)](#).

Consider an FE meta-analysis, where $\hat{\theta}_j \sim N(\theta_j, \hat{\sigma}_j^2)$, θ_j is the true effect size for study j , $\hat{\theta}_j$ is the estimated effect size, and $\hat{\sigma}_j^2$ is the variance of $\hat{\theta}_j$. In an FE meta-regression ([Greenland 1987](#)), the study-specific mean, θ_j , is expressed as

$$\theta_j = \beta_0 + \beta_1 x_{1j} + \cdots + \beta_{p-1} x_{p-1,j} = \mathbf{x}_j \boldsymbol{\beta}$$

where $\mathbf{x}_j = (1, x_{1j}, \dots, x_{p-1,j})$ is a $1 \times p$ vector of categorical and continuous moderators (covariates) and $\boldsymbol{\beta}$ is a $p \times 1$ vector of regression coefficients to be estimated.

Defining $K \times p$ matrix $\mathbf{X} = (\mathbf{x}'_1, \mathbf{x}'_2, \dots, \mathbf{x}'_K)'$ and $\hat{\boldsymbol{\theta}} = (\hat{\theta}_1, \hat{\theta}_2, \dots, \hat{\theta}_K)'$. Let $w_j = 1/\hat{\sigma}_j^2$ be the weight associated with study j in an FE meta-analysis. The vector of estimated regression coefficients is

$$\hat{\boldsymbol{\beta}} = (\mathbf{X}' \mathbf{W} \mathbf{X})^{-1} \mathbf{X}' \mathbf{W} \hat{\boldsymbol{\theta}}$$

where $\mathbf{W} = \text{diag}(w_1, w_2, \dots, w_K)$.

The above FE regression does not account for residual heterogeneity. This can lead to coefficient standard errors that are too small. [Thompson and Sharp \(1999\)](#) incorporated residual heterogeneity into the model by including a multiplicative variance parameter:

$$\hat{\theta}_j \sim N(\mathbf{x}_j \boldsymbol{\beta}, \phi \sigma_j^2)$$

For a multiplicative FE meta-regression, \mathbf{W} in the above is replaced with $\mathbf{W}^\phi = \text{diag}(w_1^\phi, w_2^\phi, \dots, w_K^\phi)$, where the weights are defined as $w_j^\phi = 1/(\hat{\phi} \hat{\sigma}_j^2)$. $\hat{\phi}$ is estimated as the mean squared error from the weighted linear regression with weights proportional to $1/\hat{\sigma}_j^2$.

Next, we present another method of incorporating residual heterogeneity by including an additive between-study variance parameter.

Random-effects meta-regression

An RE meta-regression (Berkey et al. 1995) model may be expressed as

$$\hat{\theta}_j = \mathbf{x}_j \boldsymbol{\beta} + u_j + \epsilon_j \quad u_j \sim N(0, \tau^2) \quad \epsilon_j \sim N(0, \hat{\sigma}_j^2)$$

All algorithms for RE meta-regression first estimate the between-study variance, τ^2 . The regression coefficients are then estimated via weighted least squares,

$$\hat{\boldsymbol{\beta}}^* = (\mathbf{X}' \mathbf{W}^* \mathbf{X})^{-1} \mathbf{X}' \mathbf{W}^* \hat{\boldsymbol{\theta}}$$

where $\mathbf{W}^* = \text{diag}(w_1^*, w_2^*, \dots, w_K^*)$ and $w_j^* = 1/(\hat{\sigma}_j^2 + \tau^2)$.

All the estimators of τ^2 can be expressed in terms of the matrix

$$\mathbf{P} = \mathbf{A} - \mathbf{A} \mathbf{X} (\mathbf{X}' \mathbf{A} \mathbf{X})^{-1} \mathbf{X}' \mathbf{A} \quad (1)$$

where \mathbf{A} is a $p \times p$ diagonal weight matrix whose elements depend on the type of estimator (Viechtbauer et al. 2015).

The formulas in the following sections are based on Viechtbauer et al. (2015).

Iterative methods for computing $\hat{\tau}^2$

The three estimators described below do not have a closed-form solution, and an iterative algorithm is needed to obtain an estimate of τ^2 . The Fisher scoring algorithm, described below, is used to estimate τ^2 .

All three estimators start with an initial estimate of τ^2 based on the Hedges estimator, $\hat{\tau}_0^2 = \hat{\tau}_{\text{HE}}^2$, but you can specify your own initial estimate in the `from()` option. The estimate is then updated at each iteration via the formula,

$$\hat{\tau}_{\text{new}}^2 = \hat{\tau}_{\text{current}}^2 + \delta$$

where δ is a function of $\hat{\tau}_{\text{current}}^2$ and its functional form depends on the estimation method.

The iteration terminates when `reldif`($\hat{\tau}_{\text{new}}^2, \hat{\tau}_{\text{current}}^2$) is less than `tolerance()` and the scaled gradient, computed based on the log-likelihood functions provided below, is less than `nrtolerance()`; see [R] [Maximize](#).

The MLE of τ^2 is the value that maximizes the log-likelihood function (Hardy and Thompson 1996)

$$\ln L_{\text{ML}}(\tau^2) = -\frac{1}{2} \left\{ K \ln(2\pi) + \ln |\tau^2 \mathbf{I} + \mathbf{W}^{-1}| + \hat{\boldsymbol{\theta}}' \mathbf{P} \hat{\boldsymbol{\theta}} \right\}$$

The MLE formula for δ is

$$\delta_{\text{MLE}} = \frac{\hat{\boldsymbol{\theta}}' \mathbf{P} \mathbf{P} \hat{\boldsymbol{\theta}} - \text{tr}(\mathbf{W}^*)}{\text{tr}(\mathbf{W}^* \mathbf{W}^*)}$$

The MLE estimator of τ^2 does not incorporate the uncertainty about the unknown regression coefficients $\boldsymbol{\beta}$ and thus can be negatively biased.

The REML estimate of τ^2 is the value that maximizes the restricted log-likelihood function,

$$\ln L_{\text{REML}}(\tau^2) = \ln L_{\text{ML}}(\tau^2) - \frac{1}{2} \ln \left| \sum_{j=1}^K \frac{1}{\tau^2 + \hat{\sigma}_j^2} \mathbf{x}'_j \mathbf{x}_j \right| + \frac{p}{2} \ln(2\pi)$$

and the REML formula for δ is

$$\delta_{\text{REML}} = \frac{\hat{\boldsymbol{\theta}}' \mathbf{P} \mathbf{P} \hat{\boldsymbol{\theta}} - \text{tr}(\mathbf{P})}{\text{tr}(\mathbf{P} \mathbf{P})}$$

The empirical Bayes estimator for τ^2 was introduced by [Morris \(1983\)](#) and was first used in the meta-analytic context by [Berkey et al. \(1995\)](#). This estimator is also known as the Paule–Mandel estimator ([Paule and Mandel 1982](#)). The empirical Bayes formula for δ is

$$\delta_{\text{EB}} = \frac{K/(K-p) \hat{\boldsymbol{\theta}}' \mathbf{P} \hat{\boldsymbol{\theta}} - K}{\text{tr}(\mathbf{W}^*)}$$

For the three above estimators, $\mathbf{A} = \mathbf{W}^*$ in the definition of the \mathbf{P} matrix from (1).

Noniterative methods for computing $\hat{\tau}^2$

This section describes noniterative methods, which have closed-form expressions.

The method-of-moments estimator of τ^2 ([DuMouchel and Harris \[1983, eq. 3.12\]](#); also see [Raudenbush \[2009, eq. 16.43\]](#)), which can be viewed as an extension of the [DerSimonian–Laird estimator](#) from the RE meta-analysis to meta-regression, is

$$\begin{aligned} \hat{\tau}_{\text{DL}}^2 &= \frac{\hat{\boldsymbol{\theta}}' \mathbf{P} \hat{\boldsymbol{\theta}} - (K-p)}{\text{tr}(\mathbf{P})} \\ &= \frac{Q_{\text{res}} - (K-p)}{\text{tr}(\mathbf{W}) - \text{tr} \left\{ \mathbf{W} \mathbf{X} (\mathbf{X}' \mathbf{W} \mathbf{X})^{-1} \mathbf{X}' \mathbf{W} \right\}} = \frac{Q_{\text{res}} - (K-p)}{\sum_{j=1}^K w_j (1-h_j)} \end{aligned} \quad (2)$$

where \mathbf{P} is defined in (1) with $\mathbf{A} = \mathbf{W}$, h_j is the j th diagonal element of the “hat” matrix $\mathbf{X}(\mathbf{X}' \mathbf{W} \mathbf{X})^{-1} \mathbf{X}' \mathbf{W}$, and Q_{res} is defined in (3).

For a constant-only model, when $p = 1$, (2) reduces to the [DerSimonian–Laird estimator](#) from [Noniterative methods](#) in [\[META\] meta summarize](#).

[Hedges \(1983\)](#) used OLS to provide a method of moments estimator of $\hat{\tau}^2$ for the RE meta-analysis. In the context of meta-regression, the extension of the [Hedges’s \(HE\) estimator](#) introduced by [Raudenbush \(2009, eq. 16.41\)](#) is

$$\begin{aligned} \hat{\tau}_{\text{HE}}^2 &= \frac{\hat{\boldsymbol{\theta}}' \mathbf{P} \hat{\boldsymbol{\theta}} - \text{tr}(\mathbf{P} \mathbf{W}^{-1})}{K-p} \\ &= \frac{\sum_{j=1}^K \left(\hat{\theta}_j - \mathbf{x}_j \hat{\boldsymbol{\beta}}_{\text{ols}} \right)^2 - \sum_{j=1}^K \hat{\sigma}_j^2 (1-h_j^{\text{ols}})}{K-p} \end{aligned}$$

where \mathbf{P} is defined in (1) with $\mathbf{A} = \mathbf{I}$, $\hat{\beta}_{\text{ols}} = (\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'\hat{\theta}$, and h_j^{ols} is the j th diagonal element of the OLS hat matrix $\mathbf{X}(\mathbf{X}'\mathbf{X})^{-1}\mathbf{X}'$.

Sidik and Jonkman (2005) proposed the following estimator. Consider an initial estimate of τ^2 ,

$$\hat{\tau}_0^2 = \frac{\sum_{j=1}^K (\hat{\theta}_j - \bar{\theta})^2}{K} \quad \bar{\theta} = \frac{\sum_{j=1}^K \hat{\theta}_j}{K}$$

Then, the estimator is defined as

$$\hat{\tau}_{\text{SJ}}^2 = \frac{\hat{\theta}'\mathbf{P}\hat{\theta}}{K-p} = \frac{\sum_{j=1}^K w_j^{\text{SJ}} (\hat{\theta}_j - \mathbf{x}_j'\hat{\beta}_{\text{SJ}})^2}{K-p}$$

where $w_j^{\text{SJ}} = \hat{\tau}_0^2 / (\hat{\sigma}_j^2 + \hat{\tau}_0^2)$ is a diagonal element of \mathbf{A} from (1), $\hat{\beta}_{\text{SJ}} = (\mathbf{X}'\mathbf{W}^{\text{SJ}}\mathbf{X})^{-1}\mathbf{X}'\mathbf{W}^{\text{SJ}}\hat{\theta}$, and \mathbf{W}^{SJ} is a $K \times K$ diagonal matrix with elements w_j^{SJ} .

The Sidik–Jonkman estimator is not truncated because, theoretically, it should always produce a nonnegative estimate. However, Viechtbauer et al. (2015) point out that, technically, a negative value can be produced in practice in an unlikely case of all $\hat{\theta}_j$'s being identical.

Viechtbauer et al. (2015) provide the following extension for the estimator of τ^2 , which was originally introduced by Schmidt and Hunter (2015) in the context of RE meta-analysis, to meta-regression

$$\hat{\tau}_{\text{HS}}^2 = \frac{\hat{\theta}'\mathbf{P}\hat{\theta} - K}{\text{tr}(\mathbf{W})} = \frac{Q_{\text{res}} - K}{\text{tr}(\mathbf{W})}$$

where \mathbf{P} is defined in (1) with $\mathbf{A} = \mathbf{W}$.

Knapp–Hartung standard-error adjustment

By default, the inference about the regression coefficients and their confidence intervals from meta-regression is based on a normal distribution. The test of the significance of all regression coefficients is based on a χ^2 distribution with $p - 1$ degrees of freedom.

Knapp and Hartung (2003) proposed an adjustment to the standard errors of the estimated regression coefficients to account for the uncertainty in the estimation of τ^2 . They showed that the corresponding tests of individual regression coefficients and their confidence intervals are based on the Student's t distribution with $K - p$ degrees of freedom and that the overall test of significance is based on an F distribution with $p - 1$ numerator and $K - p$ denominator.

The Knapp–Hartung adjustment first calculates the quadratic form,

$$q_{\text{KH}} = \frac{\hat{\theta}'\mathbf{P}\hat{\theta}}{K-p}$$

where \mathbf{P} is defined in (1) with $\mathbf{A} = \mathbf{W}^*$. It then multiplies the regular expressions of the variances of regression coefficients by q_{KH} or, in the case of the truncated Knapp–Hartung adjustment, by $\max(1, q_{\text{KH}})$.

Residual homogeneity test

Consider a test of residual homogeneity, which mathematically translates to $H_0: \tau^2 = 0$ for the random-effects meta-regression and to $H_0: \phi = 1$ for the fixed-effects meta-regression with multiplicative dispersion parameter ϕ . This test is based on the residual weighted sum of squares, Q_{res} ,

$$Q_{\text{res}} = \sum_{j=1}^K w_j \left(\hat{\theta}_j - \mathbf{x}_j \hat{\boldsymbol{\beta}} \right)^2 = \sum_{j=1}^K \left(\frac{\hat{\theta}_j - \mathbf{x}_j \hat{\boldsymbol{\beta}}}{\hat{\sigma}_j} \right)^2 \quad (3)$$

which is a generalization of the heterogeneity test statistic, Q (see [Homogeneity test](#) in [\[META\] meta summarize](#)), to the context of meta-regression.

Under the null hypothesis of residual homogeneity, Q_{res} follows a χ^2 distribution with $K - p$ degrees of freedom (Seber and Lee 2003, sec. 2.4).

Residual heterogeneity measures

The I_{res}^2 statistic represents the percentage of residual between-study variation relative to the total variability. For an RE meta-regression, it is defined by Higgins and Thompson (2002) as

$$I_{\text{res}}^2 = \frac{\hat{\tau}^2}{\hat{\tau}^2 + s^2} \times 100\%$$

where $s^2 = (K - p)/\text{tr}(\mathbf{P})$ and $\mathbf{A} = \mathbf{W}$ is used to define \mathbf{P} . In the meta-regression context, the H^2 statistic is defined as

$$H_{\text{res}}^2 = \frac{\hat{\tau}^2 + s^2}{s^2}$$

Adjusted R^2 (Harbord and Higgins 2016; Borenstein et al. 2009) measures the proportion of the between-study variance that is explained by the moderators. It is defined as

$$R^2 = \frac{\hat{\tau}_c^2 - \hat{\tau}^2}{\hat{\tau}_c^2} \times 100\% \quad (4)$$

where $\hat{\tau}_c^2$ is the between-study variance estimated from a constant-only model.

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Also see

[META] **meta regress postestimation** — Postestimation tools for meta regress

[META] **meta data** — Declare meta-analysis data

[META] **meta summarize** — Summarize meta-analysis data

[META] **meta** — Introduction to meta

[META] **Glossary**

[META] **Intro** — Introduction to meta-analysis

[U] **20 Estimation and postestimation commands**