.6.4 Meta-regression

If studies are divided into subgroups (see Section 9.6.2), this may be viewed as an investigation of how a categorical study characteristic is associated with the intervention effects in the meta-analysis. For example, studies in which allocation sequence concealment was adequate may yield different results from those in which it was inadequate. Here, allocation sequence concealment, being either adequate or inadequate, is a categorical characteristic at the study level. Meta-regression is an extension to subgroup analyses that allows the effect of continuous, as well as categorical, characteristics to be investigated, and in principle allows the effects of multiple factors to be investigated simultaneously (although this is rarely possible due to inadequate numbers of studies) (Thompson 2002). Meta-regression should generally not be considered when there are fewer than ten studies in a meta-analysis.

Meta-regressions are similar in essence to simple regressions, in which an outcome variable is predicted according to the values of one or more explanatory variables. In meta-regression, the outcome variable is the effect estimate (for example, a mean difference, a risk difference, a log odds ratio or a log risk ratio). The explanatory variables are characteristics of studies that might influence the size of intervention effect. These are often called ‘potential effect modifiers’ or covariates. Meta-regressions usually differ from simple regressions in two ways. First, larger studies have more influence on the relationship than smaller studies, since studies are weighted by the precision of their respective effect estimate. Second, it is wise to allow for the residual heterogeneity among intervention effects not modelled by the explanatory variables. This gives rise to the term ‘random-effects meta-regression’, since the extra variability is incorporated in the same way as in a random-effects meta-analysis (Thompson 1999).

The regression coefficient obtained from a meta-regression analysis will describe how the outcome variable (the intervention effect) changes with a unit increase in the explanatory variable (the potential effect modifier). The statistical significance of the regression coefficient is a test of whether there is a linear relationship between intervention effect and the explanatory variable. If the intervention effect is a ratio measure, the log-transformed value of the intervention effect should always be used in the regression model (see Section 9.2.7), and the exponential of the regression coefficient will give an estimate of the relative change in intervention effect with a unit increase in the explanatory variable.

Meta-regression can also be used to investigate differences for categorical explanatory variables as done in subgroup analyses. If there are J subgroups membership of particular subgroups is indicated by using J – 1 dummy variables (which can only take values of zero or one) in the meta-regression model (as in standard linear regression modelling). The regression coefficients will estimate how the intervention effect in each subgroup differs from a nominated reference subgroup. The P value of each regression coefficient will indicate whether this difference is statistically significant.

Meta-regression may be performed using the ‘metareg’ macro available for the Stata statistical package.

estimate se zval pval ci.lb ci.ub

intrcpt 27.2523 6.4346 4.2353 <.0001 14.6407 39.8640 \*\*\*

Sample -0.2262 0.7442 -0.3039 0.7612 -1.6848 1.2324

Race -0.2459 1.0337 -0.2379 0.8120 -2.2719 1.7802

Age -0.2851 0.0676 -4.2150 <.0001 -0.4176 -0.1525 \*\*\*

Methods -0.4784 0.2549 -1.8770 0.0605 -0.9780 0.0211 .

MultiTarge -0.8721 0.7377 -1.1822 0.2371 -2.3179 0.5737

Aim 1.2613 0.4850 2.6004 0.0093 0.3106 2.2119 \*\*

GenderM2F -8.8095 3.6289 -2.4276 0.0152 -15.9221 -1.6969 \*

Country -0.1633 0.2554 -0.6394 0.5226 -0.6639 0.3373