Item 12b. Methods for additional analyses, such as subgroup analyses and adjusted analyses

Examples—“Proportions of patients responding were compared between treatment groups with the Mantel Haenszel χ2 test, adjusted for the stratification variable, methotrexate use.”

“Pre-specified subgroup analyses according to antioxidant treatment assignment(s), presence or absence of prior CVD, dietary folic acid intake, smoking, diabetes, aspirin, hormone therapy, and multivitamin use were performed using stratified Cox proportional hazards models. These analyses used baseline exposure assessments and were restricted to participants with nonmissing subgroup data at baseline.”

Explanation—As is the case for primary analyses, the method of subgroup analysis should be clearly specified. The strongest analyses are those that look for evidence of a difference in treatment effect in complementary subgroups (for example, older and younger participants), a comparison known as a test of interaction. A common but misleading approach is to compare P values for separate analyses of the treatment effect in each group. It is incorrect to infer a subgroup effect (interaction) from one significant and one non-significant P value. Such inferences have a high false positive rate. Because of the high risk for spurious findings, subgroup analyses are often discouraged. Post hoc subgroup comparisons (analyses done after looking at the data) are especially likely not to be confirmed by further studies. Such analyses do not have great credibility. In some studies, imbalances in participant characteristics are adjusted for by using some form of multiple regression analysis. Although the need for adjustment is much less in RCTs than in epidemiological studies, an adjusted analysis may be sensible, especially if one or more variables is thought to be prognostic. Ideally, adjusted analyses should be specified in the study protocol (see item 24). For example, adjustment is often recommended for any stratification variables (see item 8b) on the principle that the analysis strategy should follow the design. In RCTs, the decision to adjust should not be determined by whether baseline differences are statistically significant (see item 16). The rationale for any adjusted analyses and the statistical methods used should be specified. Authors should clarify the choice of variables that were adjusted for, indicate how continuous variables were handled, and specify whether the analysis was planned or suggested by the data. Reviews of published studies show that reporting of adjusted analyses is inadequate with regard to all of these aspects.