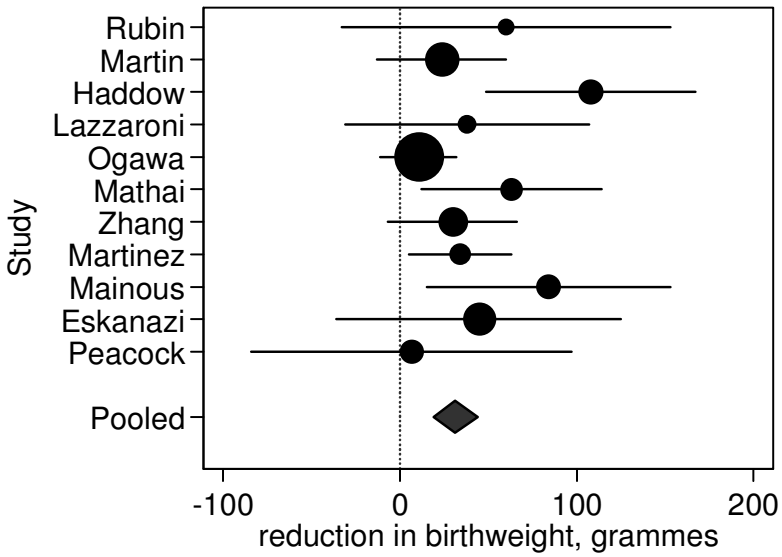
University of York Department of Health Sciences

M.Sc. Module: Systematic Reviews

Suggested answers: Bias in meta-analysis

a) *What could the authors of the meta-analysis do about this?* They had to find some way to treat the estimates as equivalent. They decided to convert both rates to g per 10 cigarettes per day. A pack of 20 cigarettes per day is typical of a smoker's consumption and we might suppose that the partner of a smoker might spend half their waking time in the smoker's company. Thus 10 cigarettes per day might plausibly be considered typical exposure.

b) *How might this figure be improved to better represent the data?* We could make the points proportional to the total sample size for the comparison, to emphasise the large studies. We could also make the pooled estimate more distinctive, by using a lozenge shape:



c) *Why can publication bias be a problem in meta-analysis?* Publication bias is the process by which studies that report positive results are more likely to be published and published more prominently than studies that report negative results.

d) *What kind of graphs are these and for what is each used?* The first figure shows a Galbraith plot, a plot of the difference/standard error against standard error. It is useful for looking for heterogeneity. In this case there is one study outside the limits, otherwise the studies are fairly evenly distributed within them, suggesting little departure from homogeneity. The second figure is a funnel plot. In this case the estimate is plotted against the sample size. The distribution about the central line representing the pooled estimate should be symmetrical. Here there appears to be a lack of small studies with small or negative differences. The bottom of the funnel is missing.

e) *Is publication bias likely to be a problem in this study?* Publication bias is likely to be a problem here. There have been many studies of birthweight and many may have collected data on smoking by the parents. Some of these may not have analysed for passive smoking, others may have analysed for it but either not published it at all or published it with little prominence, as many potential risk factors would be considered.

In these studies, low prominence is more likely if the difference is small, negative, or not significant. Hence publication bias might be expected. The funnel plot shows a lack of studies in small sample, negative results end, where they would be expected if the meta-analysis estimate is correct. Hence we may be missing studies which would lower the overall effect.

f) *What do these tests do and what conclusions would we draw?* These are tests for publication bias in the sense of a relationship between the magnitude of the outcome and the size of the study or precision of the estimate. The Begg test is not powerful for such a small number of studies. We do not have evidence of publication bias from this test, although, of course, absence of evidence is not evidence of absence and publication bias may be present. The Eggar test has been criticised for being biased and it is hard to believe that testing twice and taking the lower P value is a good idea. The evidence for publication bias produced is unconvincing as a result.

g) *What is the purpose of this test and what does the result encourage us to do?* In a meta-analysis, we assume that there is some overall common difference, which we want to estimate. We call this a fixed effects model. The test for heterogeneity is asking whether it is OK to assume that the population difference is the same for all studies. If so, we can estimate the difference ignoring any variation between studies, as in this case. If the test is significant, we cannot assume that there is a common difference which all the studies estimate. The population difference is not constant, but varies from study to study. We call this a random effects model. We could estimate the mean difference across a population of study populations. We would have to assume that these studies were carried out in a representative (i.e. can be treated as random) sample of all possible populations. The confidence interval using a random effects model would be much wider.

h) *What can we conclude from this?* We can conclude that we estimate the effect of passive smoking on birthweight to be between 19 and 44 g.

i) *How does the possible publication bias influence our conclusions?* The effect of the possible publication bias would be to make these over-estimates. It seems fair to conclude that the effect of passive smoking, if any, on birthweight must be small.

j) *Do you agree with this conclusion?* The authors hope that you agree with their interpretation. The possible bias in the meta-analysis means that the estimate is, if anything, likely to be an over-estimate.