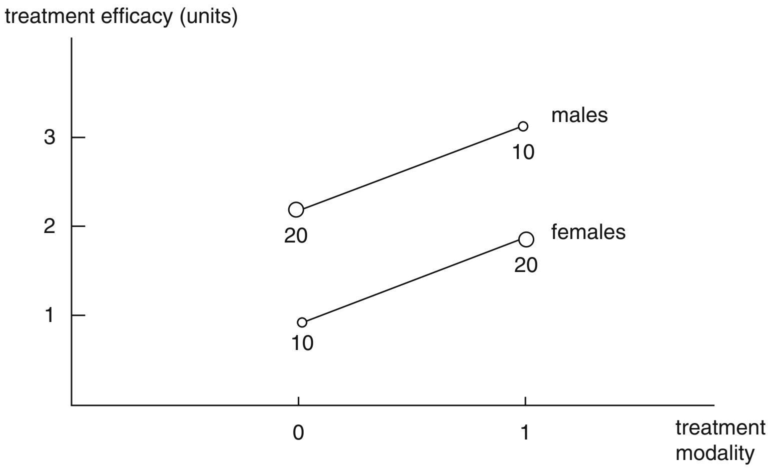
Chapter 17
Confounding



In the above study the treatment effects are better in the males than they are in the females. This difference in efficacy does not influence the overall assessment as long as the numbers of males and females in the treatment comparison are equally distributed. If, however, many females received the new treatment, and many males received the control treatment, a peculiar effect on the overall data analysis is observed as demonstrated by the difference in magnitudes of the circles in the above figure: the overall regression line will become close to horizontal, giving rise to the erroneous conclusion that no difference in efficacy exists between treatment and control. This phenomenon is called confounding, and may have a profound effect on the outcome of the study.

Confounding can be assessed by the method of subclassification. In the above example an overall mean difference between the two treatment modalities is calculated.

For treatment zero

$$\text{Mean effect} \pm \text{standard error (SE)} = 1.5 \text{ units} \pm 0.5 \text{ units}$$

T.J. Cleophas and A.H. Zwinderman, *Statistical Analysis of Clinical Data on a Pocket Calculator: Statistics on a Pocket Calculator*, DOI 10.1007/978-94-007-1211-9_17,

For treatment one

$$\text{Mean effect} \pm \text{SE} = 2.5 \text{ units} \pm 0.6 \text{ units}$$

The mean difference of the two treatments

$$= 1.0 \text{ units} \pm \text{pooled standard error}$$

$$= 1.0 \pm \sqrt{}(0.5^2 + 0.6^2)$$

$$= 1.0 \pm 0.61$$

$$\text{The t-value as calculated} = 1.0 / 0.61 = 1.639$$

With $100 - 2$ (100 patients, 2 groups) = 98 degrees of freedom the p-value of this difference is calculated to be

$$= p > 0.10 \text{ (according to t-table page 21).}$$

In order to assess the possibility of confounding, a weighted mean has to be calculated. The underneath equation is adequate for the purpose.

$$\text{Weighted mean } = \frac{\text{Difference}_{\text{males}} \;/\; \text{its SE}^2 \pm \text{Difference}_{\text{females}} \;/\; \text{its SE}^2}{1/\; \text{SE}^2{}_{\text{males}} + 1/\; \text{SE}^2{}_{\text{females}}}$$

For the males we find means of 2.0 and 3.0 units, for the females 1.0 and 2.0 units. The mean difference for the males and females separately are 1.0 and 1.0 as expected from the above figure. However, the pooled standard errors are different, for the males 0.4, and for the females 0.3 units.

According to the above equation a weighted t-value is calculated

$$\text{Weighted mean} = \frac{(1.0/0.4^2 + 1.0/0.3^2)}{(1/0.4^2 + 1/0.3^2)}$$

$$= 1.0$$

$$\text{Weighted SE}^2\ 1/(1/0.4^2 + 1/0.3^2)$$

$$= 0.576$$

$$\text{Weighted SE} = 0.24$$

$$\text{t-value} = 1.0 / 0.24 = 4.16$$

$$\text{p-value} < 0.001$$

The weighted mean is equal to the unweighted mean. However, its SE is much smaller. It means that after adjustment for confounding a very significant difference is observed.

Other methods for assessing confounding include multiple regression analysis and propensity score assessments. Particularly, with more than a single confounder these two methods are unavoidable, and they can not be carried out on a pocket calculator.