

## Sample size calculation

Sample size for pair-matched studies, the total number of pairs:  $M \cong m/(p_0q_1 + p_1q_0)$  [41],

where  $m = \frac{[Z_{\alpha/2} + Z_{\beta}\sqrt{P(1-P)}]^2}{(P - 1/2)^2}$ ; where m represents the number of exposure discordant

pairs (b+c);  $P = OR/(1 + OR)$ ;  $p_0$  and  $p_1$  represent the proportion of the exposure factor in control and case groups, respectively;  $p_1 = p_0OR/[1 + p_0(OR - 1)]$ ;  $q_0 = 1 - p_0$ ,  $q_1 = 1 - p_1$ .

According to previous finding, we assumed  $p_0 = 15\%$ ,  $OR = 2.16$  [27]. We assumed a level of significance of  $\alpha = 0.05$  ( $Z_{\alpha/2} = 1.96$ ) and the power of the test as  $\beta = 0.1$  for 90% power ( $Z_{\beta} = 1.28$ ). The corresponding sample size per group based on a 1:1 ratio was 272 subjects (i.e. Cases=272 and Controls =272). The estimated required sample size was 544 subjects.

The present study was based on multiple controls per case with a ratio between cases and controls of 1:4 resulting in a sample size of cases 170 subjects and controls 680 subjects. The estimated required sample size was 850 subjects as a crude approximation. After adjusting the variance inflation factor (VIF) [42] the partial correlation coefficient = 0.4. The numbers of cases were 203 subjects, and controls were 812. The total sample size was 1015 as a multiple model.

For this present study we collected data of 210 cases and 840 control subjects, so the total sample size was 1050 as is appropriate for an analysis.