SOLUTIONS 9

STRATIFICATION AND MANTEL-HAENSZEL

Q1. The response variable is low birth weight (which corresponds to IUGR as long as we restrict the analysis to term babies), the explanatory variable is parity and the confounding variable is mother's age.

Stratum 1 (`matage2` = 0): RR = 0.293

Stratum 2 (`matage2` = 1): RR = 0.344

Crude RR = 0.369 Summary RR = 0.313

Note that the crude risk ratio (0.369) is closer to 1 than both of the stratum RRs (0.293 and 0.344), ie the association is stronger in each stratum than in the overall table. The summary RR (0.313) is farther from 1 than the crude RR, showing a confounding effect of mother's age. Failing to control for mother's age underestimates the association between parity and low birth weight.

		Birth weight		Total
		Low	Normal	
Mother aged 22 years or less	parity 0	52 (21%)	190 (79%)	242
	parity 1+	7 (6%)	104 (94%)	111
Mother aged 23 years or more	parity 0	12 (26%)	35 (74%)	47
	parity 1+	30 (9%)	312 (91%)	342

The following is a suitable command for obtaining the percentages from STATA:

```
tabulate pargrp lbw if gestwks>=37 & matage2==0, row
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Q2 Combined data: RR = 0.56 Yates $\chi^2 = 8.96$

Village A: RR = 0.85 Yates $\chi^2 = 0.30$
Village B RR = 0.90 Yates $\chi^2 = 0.01$

Crude RR = 0.56 Summary RR = 0.86
M-H Summary $\chi^2 = 0.32$

Data from the villages combined suggests that the use of the bed-nets protects people from the risk of an enlarged spleen. When looked at separately for each village, no such association is seen. Controlling for the confounding variable, village, removed the spurious association between bed-net use and enlarged spleens.

Q3

a) Note that the age-specific odds ratios are greater than the crude OR (with one exception). The fact that adjustment for age resulted in a marked CHANGE in the estimate of the association between the exposure and the outcome suggests that age is likely to be a confounding factor. Note, potential confounding factors CANNOT be determined by the statistical significance of an association with the exposure or with disease. Remember, statistical significance is dependent on the magnitude of the association and also on study size. In a small study, a confounding factor may influence the results although the study is too small to detect a statistically significant association. Conversely, even trivial associations may be significant in a very large study.

b) To begin to evaluate whether the risk of MI associated with OC use is modified by age, the data first can be stratified by logical age groupings as in the table and the OR calculated for each age stratum and compared across strata. This can be considered by 'eyeballing' the data to judge whether there is PATTERN of variation. Decisions about stratification are based on biologic understanding of the condition under study.

Here there appears to be heterogeneity of ORs across age groups. The ORs for the younger age groups are nearly twice as high as for the older age groups. Thus, there may be effect modification by age. Whether interaction is present CAN be tested statistically (unlike confounding for which there is no 'formal test'). Statistical evaluation of interaction is dependent on the model and the reference group selected.

Caution: only large studies have the power to detect interaction. For smaller studies evidence of interaction should be explored and reported as generally it would be obscured if only the single summary estimate were provided.

A given factor can be both, a confounder and an effect modifier, a confounder but not an effect modifier, an effect modifier but not a confounder, or neither. For example, there is a suggestion in the table that age modifies the effect of oral contraceptive use on myocardial infarction. However within each age group there may be some confounding by age which should be adjusted for.

Confounding can be thought of as a NUISANCE effect which distorts the true relationship and must be controlled. Effect modification reflects a TRUE phenomenon of a variation in the relationship between exposure and disease because of the impact of the effect modifier and should be explored and reported. Stratification is used to control confounding and to explore effect modification.