Clinical Biostatistics

Suggested answers to examination, Wednesday 21st June 2006

1. *In the Abstract, the authors say that 'The adjusted odds ratio for SIDS associated with using a dummy during the last sleep was 0.08 (95% confidence interval 0.03 to 0.21)'. What is an odds ratio and how can it be interpreted in this study?* Odds is the number of subjects experiencing the event divided by the number not experiencing the event (or the probability of the event divided by one minus the probability of the event). An odds ratio is the odds of the event (dummy) in one group (cases) divided by the odds in the other group (controls). As this is a case control study and the case definition, SIDS, is rare in the population, we can interpret the odds ratio as an estimate of the relative risk of SIDS if a dummy is used compared to when no dummy is used.

2. *What is meant by '95% confidence interval 0.03 to 0.21' and what can we conclude from it?* This is a 95% confidence interval for the odds ratio of dummy use for SIDS cases in the population. From the sample, we estimate that in the population the odds ratio is between 0.03 and 0.21. A 95% confidence interval is calculated so that for 95% of possible samples the confidence interval would include the difference for the population. Hence we conclude that the odds ratio is estimated to be between 0.03 and 0.21 in the population. As this does not include 1.00, the value the odds ratio would have if there were no relationship between SIDS and dummy use, we can conclude that the odds ratio is highly significant.

3. *In the Table, the symbol '§' is used to indicate 'P<0.05'. What does 'P<0.05' mean? What can we conclude about this for glucose?* This is the result of a significance test. It is asking whether the data are consistent with the null hypothesis that, in the population from which these children come, the mean blood glucose concentration would be the same for children receiving school dinners and home meals. P is the probability of observing a difference as far from zero as this if the null hypothesis were true. We can conclude that there is evidence that the difference in the population is not zero.

4. *What is the relationship between the P values and the confidence intervals in the Table?* The P value will be less than 0.05 if the 95% confidence interval does not include the value the difference would have if the null hypothesis were true, which is zero. Hence the difference is significant and P<0.05 whenever the confidence interval for the difference does not include zero.

5. *In the Table, the means and mean differences are adjusted for age, sex, town, ethnicity, and school. What does 'adjusted' mean and what method would be used to do this? What assumptions about the data would be required?* A regression equation has been fitted to the data predicting the outcome variable from meal type, age, sex, town, ethnicity, and school. This predicts the mean of the outcome variable for any combination of these factors. The coefficient of the meal type is the difference in the mean of the outcome variable between children receiving school dinners and home meals for children who are alike in age, sex, town, ethnicity, and school. The method here would be ordinary least squares multiple regression, because the outcome variables are quantitative and continuous. The assumptions are that the observations are independent and that

the deviations from the prediction should have a Normal distribution with uniform variance.

6. *For folate, we are given geometric means and percentage differences. What is a geometric mean and why might the authors have used this method? Why are percentage differences given for folate, rather than the difference in µmol/l? Why is no standard deviation given for folate?* The geometric mean of *n* numbers is found by multiplying them all together and taking the *n*th root of the product. The authors have used this because they have analysed a logarithmic transformation of folate. The will have done this because folate had a positively skew distribution and the log transformation made it more like a Normal distribution. When we antilog the difference for the transformed folate and its confidence interval, we get the ratio of the two geometric means and a confidence interval for this. This ratio has then been turned into a percentage difference, for example –10.8% will have come from the ratio 0.892. No standard deviation is given because although we can transform the mean back from the transformed scale, we cannot transform the standard deviation back.

7. *In Table 3, for the combined estimate of smoking cessation, we are given four relative risks. What is a relative risk? How might these be interpreted here?* A relative is the ratio of the proportion of women having the characteristic in the intervention group divided by the proportion having the characteristic in the control group. A relative risk greater than one means that a greater proportion of women in the intervention group had the characteristic than in the control group, so more women in the intervention quit or remained the same, more women in the control group cut down or increased their smoking.

8. *In Table 3, for the combined estimate of smoking cessation, there are two chi-squared tests: χ^2 for trend 0.93, P=0.34, χ^2 non-linear 9.08, P=0.01 (2 df). What is the chi-squared test for trend and what can we conclude from it? What is the non-linear term and what can we conclude?* We use these tests when the variables are ordered categories, which smoking cessation is, from quit through cut down and stay the same to increase. The chi-squared test for trend tests the null hypothesis that there is no linear trend in the table, i.e. that the proportion of women in the control group does not increase or decrease steadily from quit to increase. We can conclude that there is no evidence that there is a linear trend, hence no evidence that the intervention tended to decrease or to increase smoking. The non-linear term tests whether there is any relationship which cannot be explained as a linear trend. This is significant, showing that there was evidence of a treatment effect, but that the effect was inconsistent, women in the intervention group tending to quit or remain the same while women in the control group tended to reduce or increase their smoking.

9. *The authors report that these results were unchanged after logistic regression was used to adjust for age, level of deprivation, living with a partner, having previous children, smoking level before pregnancy, and cutting down before enrolment. What is logistic regression and what does 'adjustment' mean? Why might it be done in a randomised trial?* Logistic regression is a method of regression used when the outcome variable is a dichotomous variable. Here the outcome variable was smoking more, yes or no. Adjustment means that we find the odds ratio for the intervention for women with any given characteristics of age, level of deprivation, living with a partner, having previous children, smoking

level before pregnancy, and cutting down before enrolment. We would do it in a randomised trial to reduce the variability in the outcome variable by adjusted for things which are related to it. This should improve the estimate of the treatment effect.

10. *In Table 4, we are given means and standard deviations for serum cotinine. What could we conclude about the distribution of serum cotinine and why?* Serum cotinine has a positively skew distribution. We know this because it must be positive and the standard deviation is greater than half the standard deviation. If the distribution were symmetrical, we would expect a few observations, about 2.5%, to be below the mean minus two standard deviations. This is negative, so there cannot be any such observations and the mean must be positively skew.

11. *What method could be used to calculate the 95% confidence intervals for the difference in mean cotinine? What assumptions would be required and do you think that these data would meet them?* We could use the large sample Normal distribution method or z method for the difference between two means. This would require the observations to be independent and the sample to be large enough for the standard deviations to be well estimated, at least 50 in each group. The data meet these assumptions easily. These are all different women and there is no matching involved in the design, so they are independent. The sample are both greater than 300 in size. The authors actually say a two sample t test in the methods section, which would be equivalent in such a large sample. Assumptions are a Normal distribution and equal variances in the population, unless the Satterthwaite version is used in which case the variances may differ.

12. *What could we conclude from the confidence interval for the difference in mean cotinine at enrolment?* The women were randomised into the two groups, so they are taken from the same population. It follows that the intervention and control samples come from populations with the same mean cotinine. Hence we know that the difference is zero in the population. There is no point in calculating the confidence interval and we can conclude nothing.