Worksheet 3 MAS367
Crossovers, subgroups and protocols

1.
The following data are from an AB/BA crossover trial on patients with mild to acute bronchial asthma. The two treatments are labelled A and B respectively. The following table gives the forced expiratory volumes in one second (FEV_1s) in litres. Patients were randomized to receive the drugs in the order A then B or B then A (Data from Patel, 1983, *Communications in Statistics*, 12, 2693-2712).

Patient	FEV_1 in period 1(l)	FEV_1 in period 2(l)	Order (1=AB, 2=BA)
1	1.28	1.33	1
2	1.60	2.21	1
3	2.46	2.43	1
4	1.41	1.81	1
5	1.40	0.85	1
6	1.12	1.20	1
7	3.06	1.38	2
8	2.68	2.10	2
9	2.60	2.32	2
10	1.48	1.30	2
11	2.08	2.34	2
12	2.72	2.48	2

(The data can be downloaded in a Minitab worksheet from http://www.mas.ncl.ac.uk/~njnsm/mas367/tutor.htm)

Analyse the above data, assuming that there is no carryover effect of treatment, carefully defining the statistical model you use. Make sure that your analysis includes a test of the null hypothesis that there is no difference in the mean treatment effect when treated with A or B.
Provide a hypothesis test of the assumption that there is no carryover effect and comment on it usefulness.

2.

In a clinical trial of children aged less than 15, the null hypothesis of no treatment effect is tested separately in each of four disjoint subgroups: boys under 10, girls under 10, boys over 10 and girls over 10. Assuming that there is no treatment effect in any subgroup, what is mean number of tests that will yield $P<0.05$? What is the variance of this figure?

How would these two values differ if the subgroups were no longer disjoint, say children under 10, children over 10, boy and girls?

3.

	Allocated to Surgical Treatment		Allocated to Medical Treatment	
	Actually received surgical treatment	Actually received medical treatment	Actually received surgical treatment	Actually received medical treatment
Number of patients	369	26	48	323
Number dying within two years	15	6	2	27

Test the null hypothesis that the proportion of patients surviving for two years is the same for the two treatments using:

i) those who received the allocated treatment;
ii) the groups as formed by randomization.

Give P-values and confidence intervals for the difference in proportions. Explain what each comparison measures, making sure that you outline clearly the benefits and limitations of each.