UNIVERSITY OF LONDON

GOLDSMITHS' COLLEGE

B. Sc. Examination 2003

STATISTICS

ST53011A (ST319) Medical Statistics

Duration: 2 hours 15 minutes

Date and time:

Answer any FOUR questions.

Full marks can be obtained for complete answers to FOUR questions.

WHITE, YEATS & SKIPWORTH: Tables for Statisticians to be provided.

Electronic calculators may be used. The make and model should be specified on the script. The calculator must not be programmed prior to the examination. Calculators which display graphics, text or algebraic equations are not allowed.

NOTE: Full details of all calculations are to be shown; pre-programmed statistical tests and procedures on a calculator, apart from mean and standard deviation, must not be used.

Question 1 A trial reported in the *British Medical Journal* is described as a Randomised Controlled Double Blinded trial.

(a) Explain what is meant by this. [5]

(b) What biases can be introduced if the trial is not Double Blinded? [5]

(c) Why is randomisation preferred to a systematic assignment (such as using the birth date of the patient)? [5]

(d) What is meant by the biased coin method of randomisation? Why is it used? [5]

(e) What are the advantages and disadvantages of using historical controls? [5]

Question 2 Write a protocol for carrying out a trial for a new drug designed to relieve pain after minor surgery.

You should include at least the following in the protocol: the objectives of the trial, eligibility criteria for inclusion in the trial; trial design; randomisation; baseline data to be collected; sample size; data recording; statistical analysis. [25]

Question 3 (a) What are the disadvantages of carrying out small phase III clinical trials? [4]

(b) A study is to be carried out at a clinic to investigate the effectiveness of supervised exercise for patients with mild asthma. The control group will be given advice on doing exercise. The main outcome measure will be the proportion of patients reporting less wheeziness after two months. It is thought that in the control group this measure will be 10%. The study organisers will use a one-sided test with significance level 0.025 and wish a power of 0.95 to detect an improvement in the measure for the supervised group to 30%.

(i) Derive and evaluate an expression for the number of patients required for each treatment group. [13]

(ii) The researcher involved in the study realises that with current numbers of patients attending the clinic with mild asthma it would take five years to recruit enough patients onto the trial. Discuss the possible options open to the researcher and the disadvantages of each. [8]

Question 4 The following table gives the number of days free from pain for patients suffering from chronic back pain treated with one of two drugs given by a one-off injection. Patients marked with an asterisk were still free from pain at the time recorded.

Drug A	2	4	5*	6	9	9	12*	13	15*	17*
Drug B	3	6	8	10*	12*	14	15*	15*	16	18*

(a) Calculate the Kaplan-Meier survival curves for drugs A and B and sketch them on the same plot. [10]

(b) Find a 95% confidence interval for the probability of being pain free after 9 days for drug A. [5]

(c) Carry out a logrank test to see if there is a difference in the two drugs. [10]

Question 5 (a) What are the advantages and disadvantages of a *cross-over design* relative to a *parallel group design* in a clinical trial to compare two treatments? [5]

(b) In a small trial to assess a new anti-depressant drug, each of sixteen patients received a month's treatment with the drug and a month's treatment with a placebo, the order of receiving the treatments being selected at random. Depression scores were recorded at the end of the treatment period. The scores, which fall in the range from 0 (no depression) to 30, are tabulated below; they may be assumed to be normally distributed

Group A (drug/placebo)		Group B (placebo/drug)	
Period 1	Period 2	Period 1	Period 2
11	19	20	14
11	15	16	16
22	28	22	16
19	21	6	3
7	13	16	14
7	9	11	8
6	12	24	23
8	9	12	7

Is there evidence for (i) a period effect, (ii) a treatment $\times$ period interaction, (iii) a treatment effect? [16]

(c) Discuss problems in the interpretation of these results. [4]

Question 6 Observational studies often result in a 2×2 table of the following form.

		Disease		
		Present	Absent	Total
Risk	Present	a	b	$a+b$
Factor	Absent	c	d	$c+d$
	Total	$a+c$	$b+d$	$a+b+c+d$

(a) Describe what is meant by a retrospective observational study. Which totals in the 2×2 table does it fix? [4]

(b) Describe what is meant by a prospective observational study. Which totals in the 2×2 table does it fix? [4]

(c) Define the relative risk. For which of these types of observational study can it be estimated? [3]

(d) Define the odds ratio. [2]

(e) In what circumstances is the estimated odds ratio a good approximation to the estimated relative risk? [2]

(f) Explain how to calculate a confidence interval for the odds ratio. [6]

(g) How should you amend the confidence interval if you have data from a retrospective study with *matched* cases and controls? [4]