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Design and analysis of clinical trials

For pass (godkänt) 15 scores, for excellent (väl godkänt) 25 scores

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1. A treatment consists in giving each patient two drugs A and B. Each drug can be given in three different of doses. We suspect that each drug has an effect of its own on some primary efficacy variable of interest but also that the two drugs can interact with each other. Propose a (statistical) model for this primary variable. Discuss how you would analyze data arising from such a situation. (4 scores)
2. What are the most important elements of the clinical study protocol? Discuss the two most important ones. (4 scores)
3. Discuss the difference between observational and randomization studies. What is the main point of using randomization? Discuss two randomization methods. Define and discuss blinding. (3 scores)
4. Discuss how the problem of testing equality of proportions of "success" in two different groups can be treated using three different approaches: (i) directly (ii) as a problem of independence (iii) using logistic regression. (5 scores)
5. In a survival study aiming at comparing two drugs, the following data was obtained when using proc phreg in SAS. Discuss. (3 scores)

variable	DF	Parameter estimate	Standard error	Wald chi square	Pr > chi square	Risk ratio
drug	1	-1.5	0.63	4.46	0.035	0.262

6. To plan a survival study aiming at comparing a new treatment with placebo, we proceed in two steps: finding the number of events, d, and using this to find the number, n, of patients required. Plan such a study assuming a significance level of 5%, and equal numbers in both groups and a power of 80% if the 10 years survivals in the two groups are 0.6 and 0.3 respectively. (4 scores)

7. How would you design a study to test the hypothesis $H_0: p=0.5$ against $H_1: p>0.5$? Use normal approximation and assume some values for α and β . (3 scores)
8. Cancer trials are special. Describe very shortly how a clinical cancer program looks like (a couple of meanings on each phase). Write some more about Phase I including two possible designs. (4 scores)