CHUKA  **UNIVERSITY**

UNIVERSITY EXAMINATIONS

EXAMINATION FOR THE AWARD OF DOCTOR OF PHILOSOPHY IN APPLIED STATISTICS

MATH 954: STATISTICAL METHODS FOR CLINICAL TRIALS

STREAMS: PhD (APPLIED STATS) **TIME: 3 HOURS**

DAY/DATE: WEDNESDAY 14/08/2019 **11.30 A.M - 2.30 P.M.**

INSTRUCTIONS:

- **Answer ANY THREE Questions**.
- **Show ALL your Working Clearly**

QUESTION ONE (20 MARKS)

a) Explain the concept of Randomization in terms of: design- based inference and fixed allocation randomization as they relate to clinical trials. State the advantages and disadvantages of each.

b) Two competing therapies for a particular cancer are to be evaluated by a cohort study in a multi-centric clinical trial. Patients will be randomized to either treatment A or treatment B and will be followed for 5 years after treatment for recurrence of the disease. Treatment A is a new therapy that will be widely used if it can be demonstrated that it halves the risk of recurrence in the first 5 years after treatment (i.e. RR=0.5): 35% recurrence is currently observed in patient who have received treatment B.

(i) How many Patients should be studied in each of the two treatment groups if the investigators wish to be 90% confident of correctly rejecting the null hypothesis (RR 0=1), if it is false, and the test is to be performed at the 5% level of significance?

(ii) Assume that the budget for the study is low, recommend possible directions that a researcher can take. Give reasons.

(iii) What other considerations are necessary while determining the sample size in clinical studies?

QUESTION TWO (20 MARKS)

a) Discuss the four Phases of Clinical Trials in terms of the statistical issues and methods involved in each phase.

b) Discuss five statistical issues that need to be considered in the designing of clinical trials

c) Explain the procedures of drug development and approval

d) Distinguish between cross-over and repeated measures designs

e) Distinguish between clinical trials and multicentre trials

QUESTION THREE (20 MARKS)

a) Discuss five issues that need to be considered before designing a clinical trial

b) The efficacy of BCG vaccine in preventing childhood tuberculosis is in doubt and a study is designed to compare the vaccination coverage rates in a group of people with tuberculosis and a group of controls. Available information indicates that roughly 30% of the controls are not vaccinated. The investigator wishes to have an 80% chance of detecting an odds ratio significantly different from 1 at the 5% level. An odds ratio of 2 would be considered an important difference between the two groups. Give advice to the investigators in terms of:

(i) Exclusion / inclusion criteria
(ii) Number of patients to be involved
(iii) The study design
(iv) Data collection process and sequential monitoring process

QUESTION FOUR (20 MARKS)

a) Discuss two important issues in clinical trials where the primary endpoint of interest is time to an event which are different than most studies.

b) Derive the Greenwood's formula for $Var\ (\hat{S}(t))$ and explain the necessary conditions for its application.

c) The data below shows survival times for ovarian cancer patients

T (days)	No. of subjects at risk	Deaths	Censored
59	26	1	0
115	25	1	0
156	24	1	0
268	23	1	0
329	22	1	0
353	21	1	0
365	20	0	1

377	19	0	1
421	18	0	1
431	17	1	0

Calculate:

(i) Kaplan – Meier estimate for the data
(ii) The median survival time
(iii) Probability of survival and estimate the survival function
(iv) Discuss ethical issues that should be considered when carrying out such a study.

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