



TECHNICAL UNIVERSITY OF MOMBASA

FACULTY OF APPLIED AND HEALTH SCIENCES

DEPARTMENT OF ENVIRONMENT & HEALTH SCIENCES

UNIVERSITY EXAMINATION FOR:

MASTER OF PUBLIC HEALTH

APH 5114: EPIDEMIOLOGY IN PRACTICE

END OF SEMESTER EXAMINATION

SERIES: AUGUST 2019

TIME: 3HOURS

DATE: Pick Date Jul 2019

Instructions to Candidates

You should have the following for this examination

-Answer Booklet, examination pass and student ID

This paper consists of Choose No choose Sect/Quest. Attempt Choose instruction.

Answer question ONE (COMPULSORY) and any other three questions

Do not write on the question paper.

QUESTION ONE (30 MARKS)

- a) Please read the following abstract (adapted from O'Reilly EJ, Mirzaei F, Forman MR, Ascherio A. Diethylstilbestrol exposure in utero and depression in women. *Am J Epidemiol.* 2010;171(8):876-82) and answer the corresponding questions:

Background: Diethylstilbestrol (DES) is an estrogenic endocrine disruptor with long-term health effects, possibly including depression, following exposure in utero. **Methods:** The association between in utero DES exposure and depression was assessed among participants in the Nurses' Health Study II who were followed from 1995 to 2005. **Results:** 76,240 women were eligible for inclusion in this study. DES exposure was reported by 1,612 (2.2%) women. Incident depression (first use of antidepressants among women who also reported depressive symptoms) during follow-up was reported by 19.7% of women exposed to DES and 15.9% of women unexposed to DES (OR = 1.41, 95% CI: 1.22, 1.63). **Conclusions:** These results suggest that the neurophysiologic effects of in utero exposure to DES could lead to an increased risk of depression in adult life.

- i. What is the study design? What is the study population? (2 marks)
- ii. Interpret "OR = 1.41." Are these exposure odds or disease odds? Why? (2 marks)
- iii. What would have been a more appropriate relative measure for the investigators to calculate given the type of data collected? (2 marks)
- iv. Under what conditions does the Odds Ratio approximate this measure? (2 marks)

- b) A 46-year-old man is currently enrolled in a Phase 2 study of a drug for severe diabetic neuropathy. While the study is ongoing, a new drug becomes commercially available that may have equal or greater benefit to the subject. What would you do as an investigator? (4 marks)
- c) State which method to control for confounding is being used in the following scenarios. In each scenario, exercise is the exposure, myocardial infarction is the disease, and gender is the confounder (3 marks).
- A study of exercise and myocardial infarction that is limited to men
 - A case-control study of exercise and myocardial infarction that includes men and women. Controls are selected so that the proportions of male and female subjects groups are identical
 - A study of exercise and myocardial infarction that includes men and women. The study determines the relative risk separately for men and for women and compares these with the crude relative risk.
- d) A group of investigators proposes to investigate genetic factors that may increase risks for esophageal cancer. Genetic factors in esophageal cancer are not well understood and esophageal cancer occurs in many racial and ethnic populations. The investigators propose to collect DNA from cheek swabs and administer a risk factor questionnaire. Both cancer patients and age-matched controls will be included. The investigators have access to a predominantly Caucasian sample, and have no plans to recruit participants outside of their available pool. Is this an acceptable strategy? (4 marks)
- e) A prospective cohort study was conducted to determine the risk of heart attack among men with varying levels of baldness. Second-year master of public health students conducted visual baldness assessments at the start of the study (which was before any heart attacks had occurred). Four levels of baldness were coded: none, minimal, moderate, and severe. The follow-up rate was 100% for 5 years. State 3 potential biases that were surely avoided in this study? (6 marks)
- f) A researcher seeks to improve treatment for severe migraines that are partially responsive to oral medication. He proposes to test whether acupuncture, in addition to a sufferer's oral medication, is more effective treatment than oral medication alone. Because women are three times more likely to experience migraines than men, he proposes to enrol three times as many women as men. They will be recruited from racially and ethnically diverse communities. Does this study design fulfil the principle of justice? (5 marks)

QUESTION TWO (30 MARKS)

A double-blind study was conducted at 33 centers in seven countries to determine whether supplementation with folic acid or a mixture of seven other vitamins around the time of conception can prevent neural tube defects (NTDs). 1817 women were randomized to one of four groups: folic acid, other vitamins, both, or neither. There were no significant differences among the groups in age and outcome of previous pregnancies. The trial was stopped after one year because a significant protective effect of folic acid was seen. When all women allocated to receive folic acid were compared to all women not receiving folic acid, the measure of association was 0.28 (95% CI: 0.12-0.71). The analysis was repeated excluding women who reported that they had stopped taking their folic acid capsules and investigators found a measure of association of 0.21 (95% CI: 0.07; 0.62). The measure of association for NTDs among women allocated to the "other vitamin" groups compared with those not receiving other vitamins nor folic acid? was 0.80 (95% CI: 0.37-1.72). The measure of association for the "other vitamin" groups, excluding those who stopped taking capsules, was 0.93 (95% CI: 0.41-2.12) [Adapted from: MRC Vitamin Study Research Group, *The Lancet* 1991;338:131-7].

- What type of study design is this (5 marks)
- What type of measure of association was most appropriate for this study? (5 marks)

- c. What is the purpose of masking in randomized studies? What do you think the authors mean by “double blind” in this study? (5 marks)
- d. What are the authors implying when they state that “there were no significant differences among the groups in age and outcome of previous pregnancies?” (5 marks)
- e. What is the difference between efficacy and effectiveness? Do the authors analyses aim to estimate the efficacy or effectiveness of folic acid? (5 marks)]
- f. Comment on whether you think it was ethical to stop the trial after one year (5 marks)

QUESTION THREE (30 MARKS)

The Nuremberg Code established ten directives for Human experimentation. Over the years these directives have been relied on heavily in developing the current research ethics. Discuss the ten Nuremberg Code directives focusing on how they have used shape the research ethics practice

QUESTION FOUR (30 MARKS)

- i. Read the abstract for the paper by Cohn et al. entitled “DDT and Breast Cancer in Young Women: New Data on the Significance of Age at Exposure” and answer the following questions:

Abstract

BACKGROUND: Previous studies of DDT and breast cancer assessed exposure later in life when the breast may not have been vulnerable, after most DDT had been eliminated, and after DDT had been banned. **OBJECTIVES:** We investigated whether DDT exposure in young women during the period of peak DDT use predicts breast cancer. **METHODS:** We conducted a prospective, nested case-control study with a median time to diagnosis of 17 years using blood samples obtained from young women during 1959-1967. Subjects were members of the Child Health and Development Studies, Oakland, California, who provided blood samples 1-3 days after giving birth (mean age, 26 years). Cases (n = 129) developed breast cancer before the age of 50 years. Controls (n = 129) were matched to cases on birth year. Serum was assayed for p,p'-DDT, the active ingredient of DDT; o,p'-DDT, a low concentration contaminant; and p,p'-DDE, the most abundant p,p'-DDT metabolite. **RESULTS:** High levels of serum p,p'-DDT predicted a statistically significant 5-fold increased risk of breast cancer among women who were born after 1931. These women were under 14 years of age in 1945, when DDT came into widespread use, and mostly under 20 years as DDT use peaked. Women who were not exposed to p,p'-DDT before 14 years of age showed no association between p,p'-DDT and breast cancer (p = 0.02 for difference by age). **CONCLUSIONS:** Exposure to p,p'-DDT early in life may increase breast cancer risk. Many U.S. women heavily exposed to DDT in childhood have not yet reached 50 years of age. The public health significance of DDT exposure in early life may be large.

KEYWORDS: breast cancer; child health and development studies; exposure timing; o, p'-DDT; organochlorines; p, p'-DDE; p, p'-DDT; pregnancy; premenopausal

- a. What type of study design did the authors use? (3 marks)
- b. Is this a concurrent or non-concurrent study? Was exposure information collected prospectively or retrospectively? (refer to the Methods Section: Serum assays if necessary) (3 marks)
- c. How did the authors choose the controls (3 marks) ?

- d. For what reason might the authors have chosen to use this method of control selection? (3 marks)
 - e. What does the calculated OR estimate? (3 marks)
 - f. What must be true for the OR to estimate this measure? (3 marks)
- ii. In the early 1980s, studies demonstrated that women who used tampons for menstrual protection were at increased risk of developing Toxic Shock Syndrome (TSS). The cumulative incidence of menstrual TSS today is estimated to be in the range of 1 to 3 per 100,000 women per year. Studies have shown that the risk of tampon-associated TSS is a function of the absorption and chemical composition of the tampons used. Since this finding was published, tampons have changed substantially in their chemical composition and absorption, and it is unknown whether tampons being sold and used today cause an increased risk of menstrual TSS.
- a. If asked to design an epidemiologic study of the association between tampon use and menstrual TSS today, what study design would you choose and why? (4 marks)
 - b. What are potential sources of selection bias in this study? (4 marks)
 - c. What are potential sources of information bias in this study? (4 marks)

QUESTION FIVE (30 MARKS)

Give an account of undue influence in the context of obtaining informed consent for medical research.

QUESTION six (30 MARKS)

Please read the first 3 pages of following article and answer the corresponding questions: Doll R, Hill AB. Lung cancer and other causes of death in relation to smoking. *BMJ* 1956; 1071-81. Though it is not required, we encourage you to read the entire paper if you are interested because it is widely considered one of the seminal papers in epidemiology. **Article provided**

- a. Is the cohort described in this paper open or closed? (4 marks)
- b. What was the exposure and how were subjects classified? What is a disadvantage, if any, of classifying exposure this way? (6 marks)
- c. What was the primary outcome of concern, and how was it determined? (6 marks)
- d. Based on Table 5 in the article, what is the appropriate measure of association for quantifying the relationship between smoking and death? (4 marks)
- e. Using data from Table 5, calculate the measure of association from part d, comparing the rates of deaths due to lung cancer among non-smokers to the rates of death due to lung cancer among all smokers (5 marks)
- f. Interpret the measure calculated in part e (5 marks).