JOMO KENYATTA UNIVERSITY OF AGRICULTURE AND TECHNOLOGY

UNIVERSITY EXAMINATIONS 2023/2024

EXAMINATION FOR THE DEGREE OF MASTER OF SCIENCE IN EPIDEMIOLOGICAL & BIOSTATISTICS

PEH 3103: EPIDEMIOLOGICAL METHODS

DATE: AUGUST 2023   **TIME: 3 HOURS**

INSTRUCTIONS: ANSWER ANY **FOUR** QUESTIONS

1) Read the following abstract and answer the questions that follow:

Background: Male circumcision reduces the risk of human immunodeficiency virus infection in men. We assessed the effect of male circumcision on the incidence and natural history of human papillomavirus (HPV) in a study in Kisumu, Kenya.
Methods: Sexually active, 18–24-year-old men provided penile exfoliated cells for HPV DNA testing every six months for two years. HPV DNA was detected via GP5+/6+ PCR in glans/coronal sulcus and in shaft samples. HPV incidence and persistence were assessed by intent-to-treat analyses.
Results: 2,193 men participated (1,096 randomized to circumcision; 1,097 controls). HPV prevalence was 50% at baseline for both groups and dropped to 23.7% at 24 months in the circumcision group, and 41.0% in control group. Incident infection of any HPV type over 24 months was lower among men in the circumcision group than in the control group (hazard ratio [HR], 0.61; 95% confidence interval [CI], 0.52, 0.72). Clearance rate of any HPV infection over 24 months was higher in the circumcision group than in the control group (HR, 1.87; 95% CI, 1.49, 2.34). Lower HPV point-prevalence, lower HPV incidence, and higher HPV clearance in the circumcision group were observed in glans but not in shaft samples.
Conclusion: Male circumcision reduced the risk of HPV acquisition and reinfection, and increased HPV clearance in the glans.

[*Jennifer S. Smith et al. / Cancer Epidemiol. Biomarkers Prev. 2021 Jun; 30(6): 1139–1148.*]

(a) What type of epidemiologic study design was employed by the investigators? *(2 Marks)*

(b) In the methods sections of the journal article the authors say that, *"some of the participants were recruited from sexually transmitted infection (STI) clinics"*. How might this bias the study results and what measures would you put in place to prevent this bias? *(5 Marks)*

(c) In the abstract (above) the authors say that, *"HPV incidence and persistence were assessed by intent-to-treat analyses"*. What do they mean by this? *(3 Marks)*

(d) Although loss to follow-up was not described in the abstract, it is possible that it took place in this study. Outline three possible measures you would take to reduce loss to follow up if you were invited to participate as an investigator in such a study. *(6 Marks)*

(e) The investigators might have chosen to recruit 18-24 year-old male participants and then request them to provide penile exfoliated cells for HPV DNA testing as they determined their circumcision status. What study design would this be? *(3 Marks)*

(f) <u>Outline</u> the advantages and disadvantages which might have arisen if the study design ((e) above) was used. *(6 Marks)*

2) Water chlorination and the use of chlorine-based disinfectants which end up in surface and underground water has been linked to colorectal cancer. You intend to study this within Kiambu County for your Master's degree thesis. You will get the incidence of colorectal cancer for the year 2023 for each Kiambu Sub-county from the National Cancer registry and then measure the average Chlorine concentration in water in each Sub-county (by taking the mean chlorine concentration in tap water or water in containers in a random sample of homes per sub-county). You will compare the incident colorectal cancer between the sub-counties based on the mean chlorine concentration in their water.

    (a) What features make this an ecological study? *(4 Marks)*

    (b) What difficulties might you encounter in the implementation of your study? *(8 Marks)*

    (c) <u>Briefly</u> described two (2) situations (with examples) which demonstrate that an ecological study may on occasion lead to more accurate conclusions than studies using individual level data? *(8 Marks)*

    (d) <u>Briefly</u> describe one major disadvantage of ecological studies compared to other epidemiological study designs. *(5 Marks)*

3) The table below shows the results of a case-control study done at 3 public universities in Kenya to see if consumption of *cannabis sativa* among undergraduate students was associated with depression (exposure status was determined using a self-administered questionnaire and the outcome status was ascertained by a study psychiatrist):

Cannabis Consumption	Depression	
	Yes	No
Yes	81	77
No	125	335

An epidemiology Masters student was interested in this study and found out that some blood and urine samples had been taken and stored for possible future analysis. After examining the urine samples for presence of cannabis he found that 20% of students (both cases and controls) who had reported no consumption of cannabis had positive urine samples for cannabis. He thus made a new table correctly classifying the students using their new exposure status.

    (a) Calculate the crude odds ratio for the initial study and state in clear terms the relationship between consumption of cannabis and depression (*show your work*) *(5 Marks)*

    (b) Make a 2x2 table showing the new exposure status for the cases and controls (*show your work*) *(7 Marks)*

    (c) Calculate the crude odds ratio for the new Masters student analysis and state in clear terms the relationship between consumption of cannabis and depression. *(5 Marks)*

    (d) What type of misclassification was there in the initial study and what effect did this misclassification have on the odds ratio? *(3 Marks)*

    (e) How would you ensure that such misclassification does not occur in a similar future study? *(5 Marks)*

4) Your epidemiology classmate conducts a case-control study to assess whether male gender is a risk factor for Malaria infection. She gets a positive result but before writing a journal article she gives her results to your epidemiology unit lecturer for advice. The lecturer stratifies the results using a third variable which your classmate had keenly recorded in her data. The results, stratified on the third variable, are summarized below:

Third Variable Present

	Cases	Controls
Males	278	79
Females	58	17

Third Variable Absent

	Cases	Controls
Males	113	165
Females	173	261

(a) Calculate the crude odds ratio and the two stratum-specific odds ratios. Show your calculations. *(12 Marks)*

(b) Based upon these calculations, would you conclude that the "critical third factor" is a confounder in the relationship between male gender and Malaria infection? Why or why not? *(4 Marks)*

(c) Would you conclude that the "critical third factor" is an effect modifier in the relationship between male gender and Malaria infection? Why or why not? *(4 Marks)*

(d) What do you think the factor that your lecturer used to create the stratified tables was? Justify your choice. *(3 Marks)*

(e) State in clear terms how your chosen third variable affects the relationship between male gender and Malaria infection. *(2 Marks)*

5) Muscle strength declines with advancing age. Preliminary evidence suggests that part of the loss of muscle strength might be due to the progressing deficiency of vitamin D. Your mentor decides to carry out a study where she will recruit sample of participants above 65 years and follow them up for 5 years for the outcome i.e. muscle strength is measured in mean grip strength.

(a) Briefly outline a study plan to address this research question with a prospective cohort study. *(10 Marks)*

(b) An alternative plan would be to compare evidence of vitamin D deficiency in elderly people who record poor muscle strength with that of elderly people who have good muscle strength. Compared with this "case control" approach, briefly outline the advantages and the disadvantages of your prospective cohort study. *(6 Marks)*

(c) Could the cohort study be designed as a retrospective cohort study and how would this affect your advantages and disadvantages? *(4 Marks)*

(d) Outline five (5) possible confounding factors in this cohort study and for each outline a reason as to why you think they are strong confounders. *(5 Marks)*

6) Read the following abstract and answer the questions that follow:

Background: Breast cancer is rare in men, and information on its causes is very limited from studies that have generally been small. Adult obesity has been shown as a risk factor, but more detailed anthropometric relations have not been investigated.

Methods: We conducted an interview-based case-control study of breast cancer in men in England and Wales including 1998 cases incident during 2005-2017 at ages younger than 80 years and 1597 male controls, with questions asked about a range of anthropometric variables at several ages. All tests of statistical significance were 2-sided.

Results: Risk of breast cancer statistically significantly increased with increasing body mass index (BMI) at ages 20 (odds ratio [OR] = 1.07, 95% confidence interval [CI] = 1.02 to 1.12 per 2-unit change in BMI), 40 (OR = 1.11, 95% CI = 1.07 to 1.16), and 60 (OR = 1.14, 95% CI = 1.09 to 1.19) years, but there was also an indication of raised risk for the lowest BMIs. Large waist circumference 5 years before interview was more strongly associated than was BMI with risk, and each showed independent associations. Associations were similar for invasive and in situ tumours separately and stronger for HER2-positive than HER2-negative tumours. Of the tumours, 99% were oestrogen receptor positive.

Conclusions: Obesity at all adult ages, particularly recent abdominal obesity, is associated with raised risk of breast cancer in men, probably because of the conversion of testosterone to oestrogen by aromatase in adipose tissue. The association is particularly strong for HER2-expressing tumours.

[Anthony J Swerdlow et al. / JNCI Cancer Spectr. 2021 Oct; 5(5).]

(a) Is this a primary or secondary study base? <u>Briefly</u> describe the study base? *(5 Marks)*

(b) In the methods sections of the journal article the authors say that, *"male nonblood relatives of the cases were recruited as controls"*.
    i. What might be the reason why they used this method of control selection? *(3 Marks)*
    ii. How might this bias the study results and what measures would you have put in place to prevent this bias? *(5 Marks)*
    iii. Do you think a similar bias could have arisen in the selection of cases? How? *(3 Marks)*

(c) In the abstract (above) the authors say that, *"Large waist circumference 5 years before interview was more strongly associated than was BMI with risk, and each showed independent associations."*. What might be the reason for this? *(3 Marks)*

(d) Discuss recall bias in relation to this study. *(6 Marks)*