340.721 Epidemiologic Inference in Public Health I

PRE-Activity Questions: Observational Studies: Body Composition & Colon Cancer

The Activities provide experience in applying epidemiologic methods, interpreting findings, and drawing inferences. Activities will be discussed during the LiveTalks. Students are expected to work with their assigned Course Group prior to the start of each LiveTalk.

Prior to each Activity, students are to complete the corresponding set of PRE-Activity Questions. Each set of PRE-Activity Questions consists of 10 graded multiple choice questions. The graded multiple choice questions are to be completed via CoursePlus by the date and time listed in CoursePlus. PRE-Activity Questions prepare you for a productive and collaborative experience during the Activities.

Expectations for the PRE-Activity Questions

1. *Individually, read and attempt to answer all PRE-Activity Questions.*
2. *"Meet" or communicate with fellow students discuss challenging concepts, questions and compare answers. You may refer to their course materials and are strongly encouraged to collaborate with fellow students to complete the PRE-Activity Questions.*
3. *PRE-Activity Questions are due to Courseplus by the date listed on the syllabus. Although group collaboration is encouraged to complete the PRE-Activity Questions, each student must individually submit the PRE-Activity Questions.* ***Without exception, no credit will be given for submitting the PRE-Activity Questions after the due date****. The lowest PRE-Activity grade will be dropped when calculating the overall course grade.*

Motivation
In this assignment, you will evaluate two observational designs: cohort studies and case-control studies. Some motivating questions to think about are: What are the strengths of the cohort study design? Case-control studies? Are there potential biases inherent in each study design? How do you know if something is a cause? Can you apportion disease to a particular cause? What assumptions do you make when you do so?

This assignment corresponds to:
Lectures: Epidemiologic Study Design I & II; Measures of Association I & II
Readings: Gordis text (5th ed.) Chapter 9, 10, 13

Introduction
In this assignment you will examine two studies of the association between body composition and cancer, particularly considering the advantages and disadvantages of their study designs, and the measures of disease frequency and association used in each study.

In Part I, you will answer questions referring to a large cohort study of the association between body mass index and cancer. In Part II, questions will refer to a case-control study addressing the same research question.

Concepts Covered:
- Case-control and cohort study designs
- Study population
- Selection of controls
- Matching
- Measurement and Information bias
- Calculation of odds ratios and relative risks
- Causal guidelines
- Attributable risk
- Population attributable risk

Learning Objectives:
1. Compare and contrast case-control and cohort study designs.
2. Evaluate case definition, selection of cases and selection of controls.
3. Calculate odds ratios and relative risks
4. Identify potential biases in study design.
5. Calculate attributable risk and population attributable risk.
6. Apply causal guidelines.

I. Obesity and Cancer Risk in the United States – A Prospective Cohort Study

Reference: Calle, Rodriguez, Walker-Thurmond et al. Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults. *NEJM* .2003; 348:1625-1638.

According to the Centers for Disease Control and Prevention (CDC), a growing obesity epidemic is threatening the health of millions of Americans in the United States. Data from the Behavioral Risk Factor Surveillance System (BRFSS) provide evidence that the prevalence of obesity has increased from 12% in 1991 to almost 21% in 2001. In response to these observations, the causes and health effects of obesity have become the focus of an enormous research effort. However, despite the intensity of the effort, the causes of the epidemic and the health effects of obesity remain controversial.

The American Cancer Society (ACS) has conducted two prospective cohort studies of cancer mortality: the Cancer Prevention Study I (CPS-I) (1959-1972) and the Cancer Prevention Study II (CPS-II) which recruited participants in 1982 and for which follow-up is ongoing. For the CPS-II, 1184617 participants were enrolled by more than 77000 ACS volunteers in 1982 and completed a confidential mailed questionnaire at baseline.

The CPS-II included participants from 50 states, the District of Columbia, Puerto Rico and Guam and 93% of the study group were white. Participants in both the CPS-I and CPS-II were older, more educated, more likely to be married and more often in the middle class than the general U.S. population.

In 2003, investigators used the CPS-II data to characterize the effect of excess body weight on the risk of death from cancer. In the baseline questionnaire, "participants were asked their current weight, their weight one year previously, and height (without shoes)."[1] Deaths were ascertained by personal inquiries made by the ACS volunteers and linkage to the National Death Index (NDI), a central index of death record information maintained by the National Center for Health Statistics. Death certificates were obtained for 98.8% of deaths.

Body mass index was classified to correspond with the Centers for Disease Control and Prevention's proposed categories, as follows:

Body mass index (BMI) in kg/m^2	**CDC Weight Status Category**
< 18.5	Underweight
18.5 – 24.9	Normal range
25.0 – 29.9	Overweight
≥ 30.0	Obese

[1] Calle EE, Rodriguez D, Walker-Thurmond K, Thun MJ. Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults. NEJM 2003;348:1625-1638.

The body mass index, originally proposed in the 19th Century by Quetelet, provides a height-independent measure of obesity. It is calculated as weight (in kilograms) divided by height (in meters) squared.

Using the information provided in Table 1 below, calculate the colorectal cancer mortality rate per 100,000 person-years at risk during the study by sex and BMI categories. Also calculate the relative risks and attributable risks (*i.e.,* rate differences) of colorectal cancer among overweight (BMI 25 – 29.9 kg/m^2) and obese (BMI ≥30 kg/m^2) individuals as compared to individuals with BMI in the normal range (BMI 18.5 – 24.9 kg/m^2). The answers for BMI category 18.5 – 24.9 kg/m^2 have been provided for you.

For this assignment, 'unexposed' individuals are those with BMI in the 18.5 – 24.9 kg/m^2 range.

$$\text{Relative Risk} = \frac{\text{(Mortality rate among exposed)}}{\text{(Mortality rate among unexposed)}}$$

Attributable Risk = (Mortality rate among exposed) − (Mortality rate among unexposed)

Table 1. Mortality Rates, Relative Risks and Attributable Risks of Colorectal Cancer for Men and Women in the CPS-II Study. Overweight and Obese Individuals Compared to Individuals of Normal Weight.

	BMI Category (kg/m^2)	Person-years[1]	# of Deaths	Mortality Rate[2]	Relative Risk	Attributable Risk
Men						
	18.5 – 24.9	2,414,502	1,292	53.51	1.00	0.0
	25.0 – 29.9	2,810,802	1,811			
	≥30.0	477,004	391			
Women						
	18.5 – 24.9	4,411,689	1,706	38.67	1.00	0.0
	25.0 – 29.9	2,093,829	906			
	≥30.0	732,064	400			

[1] Person-years at risk for each category are calculated by summing up the time each participant in the category spends in the study.

[2] Express the mortality rate as the number of deaths per 100,000 person-years at risk.

Question 1:
What is the mortality rate for men and women who have a BMI ≥30 kg/m^2?

a. Men: 10.9; Women: 43.3
b. Men: 28.5; Women: 16.0
c. Men: 64.3; Women: 1.4
d. Men: 82.0; Women: 54.6

Question 2:
What is the *relative risk* for men and women comparing rates of colorectal cancer among obese (BMI ≥30 kg/m^2) individuals as compared to individuals with BMI in the normal range (BMI 18.5 – 24.9 kg/m^2)?

a. Men: 1.2; Women: 1.1
b. Men: 1.5; Women: 1.4
c. Men: 10.9; Women: 4.6
d. Men: 28.5; Women: 16.0

Question 3:
What is the *attributable risk* for men and women comparing rates of colorectal cancer among obese (BMI ≥30 kg/m^2) individuals as compared to individuals with BMI in the normal range (BMI 18.5 – 24.9 kg/m^2)?

a. Men: 1.2; Women: 1.1
b. Men: 1.5; Women: 1.4
c. Men: 10.9; Women: 4.6
d. Men: 28.5; Women: 16.0

POPULATION ATTRIBUTABLE RISK

$$\text{Population Attributable Risk(\%)} = \frac{\text{(Mortality rate in total population)} - \text{(Mortality rate in unexposed group)}}{\text{(Mortality rate in total population)}} \times 100\%$$

Mortality Rate in Total Population = (Mortality rate in exposed group)(% exposed in population) +
(Mortality rate in non-exposed group)(% non-exposed in population)

<u>Question 4</u>
Using the mortality rates from Table 1, what is the mortality rate among adults who are normal or overweight (BMI <30 kg/m^2)?

<u>HINT:</u> Create a new 2x2 table from the data in Table 1 (the cells for ≥30 kg/m^2 have been completed for you):

BMI Category (kg/m^2)	**Person-years[1]**	**# of Deaths**
≥30	1,209,068	791
<30		

a. 43.9 deaths per 100,000 person-years
b. 48.7 deaths per 100,000 person-years
c. 53.7 deaths per 100,000 person-years
d. 65.4 deaths per 100,000 person-years

Question 5

The prevalence of obesity (BMI ≥30 kg/m^2) among adults in the United States is 30%.[2] Using the mortality rates from Table 1, and considering a comparison of obese (BMI ≥30 kg/m^2) versus normal or overweight (BMI <30 kg/m^2), what is the mortality rate ***in the US population***?

HINT: Use the 2x2 table that was created to answer Question 4:

BMI Category (kg/m^2)	**Person-years[1]**	**# of Deaths**
≥30	1,209,068	791
<30		

a. 43.9 deaths per 100,000 person-years
b. 48.7 deaths per 100,000 person-years
c. 53.7 deaths per 100,000 person-years
d. 65.4 deaths per 100,000 person-years

[2] NCHS. News Release: Obesity Still a Major Problem, New Data Show. October 6, 2004. Available at: http://www.cdc.gov/nchs/pressroom/04facts/obesity.htm

Question 6

Using the mortality rate in the US population that you calculated in Question 5 and the mortality rates from Table 1, and considering a comparison of obese (BMI ≥30 kg/m^2) versus normal or overweight (BMI <30 kg/m^2), what is the *population attributable risk (%)* of death from colorectal cancer for men and women together (*i.e.,* not stratified by sex)?

HINT: Use the 2x2 table and calculations from Question 5:

BMI Category (kg/m^2)	**Person-years[1]**	**# of Deaths**
≥30	1,209,068	791
<30		

Calculations from Question 5:

Mortality Rate $_{\text{exposed}}$ (BMI ≥ 30 kg/m^2) =

Mortality Rate $_{\text{unexposed}}$ (BMI < 30 kg/m^2) =

Mortality Rate $_{\text{total population}}$ =

Now, calculate and select the Population Attributable Risk (%) =

a. 9.3%
b. 12.8%
c. 32.9%
d. 49.7%

Question 7

The investigators in this study assessed mortality from cancer as their outcome of interest. However, cancer mortality should be distinguished from cancer incidence.

Under what circumstances would it ***not be necessary*** to distinguish between cancer incidence and cancer mortality? (In other words, under what circumstances would cancer incidence be equivalent to cancer mortality?)

a. A new drug is introduced that improves survival following cancer diagnosis
b. Case fatality from cancer is high
c. The cancer progresses very slowly and most people who develop the cancer will die from another cause
d. It is never necessary to distinguish cancer incidence from cancer mortality

II. Obesity and Cancer Risk in Canada – A Population-Based Case-Control Study

Reference: Pan, S.Y., Johnson, K.C., Ugnat, A.M., et al. Association of Obesity and Cancer Risk in Canada. *Am J Epidemiol* 2004;159:259–268

Between 1994 and 1997, Health Canada, in collaboration with provincial cancer registries, initiated the National Enhanced Cancer Surveillance System (NECSS) study. The NECSS is a population-based case-control study designed primarily to investigate the relationship between environmental risk factors and cancer. The study population consisted of 21,022 people with one of 19 types of cancer diagnosed over the 4 year period along with 5,039 population controls. Cases were identified through the provincial cancer registries as individuals aged 20-76 years with histologically confirmed primary cancer. Controls were matched to cases on age, sex and geographical (provinces) distributions. Controls were identified through provincial health insurance plans, random digit dialing, and population databases. All study participants were mailed questionnaires and asked to provide information on demographic factors, diet and risk behaviors. (Pan, S.Y., Johnson, K.C., Ugnat, A.M., et al. Association of Obesity and Cancer Risk in Canada. Am J Epidemiol 2004;159:259–268).

$$\text{Odds Ratio} = \frac{\text{(Odds of exposure among cases)}}{\text{(Odds of exposure among controls)}}$$

Table 2. Odds Ratios for Colon Cancer by Level of Obesity for Men and Women in a Canadian Case-Control Study – Overweight and Obese Individuals in Comparison to non-Overweight/Obese Individuals

BMI Category (kg/m^2)	Cases	Controls	Odds Ratio
18.5 - < 25 (reference group)	634	2,420	1.0
25 - <30	726	1,886	______
≥30	367	706	______

Question 8

Which of the following answer choices best describes the study population?

a. Adults living in Canada between 1994 and 1997
b. Adults in Canada with histologically confirmed primary cancer diagnosed between 1994 and 1997
c. 5,039 adults in Canada who did not have cancer but were matched to 21,022 adults who did have cancer on age, sex and geographical location
d. 21,022 people from Canada with one of 19 types of cancer diagnosed between 1994 and 1997 along with 5,039 population controls

Question 9

Given the data in Table 2, calculate odds ratios for colon cancer for those in the Overweight (25-30 kg/m^2) and Obese (≥30 kg/m^2) BMI categories, compared to those with a BMI less than 25 kg/m2 (unexposed reference group). (Hint: Create a separate 2x2 table for each odds ratio.)

Overweight vs. Normal Weight:

BMI Category (kg/m^2)	Cases	Controls
25 - <30		
18.5 - < 25		

Obese vs. Normal Weight:

BMI Category (kg/m^2)	Cases	Controls
≥30		
18.5 - < 25		

a. Overweight: 1.4; Obese: 1.5
b. Overweight: 1.5; Obese: 2.0
c. Overweight: 2.0; Obese: 1.4
d. Overweight: 2.4; Obese: 1.5

You decide to conduct your own case-control study to further investigate the relationship between obesity and colon cancer. You identify 248 incident cases of colon cancer among patients at Johns Hopkins Hospital and 248 hospital controls individually matched on age and sex. You find that there are 35 matched pairs in which both cases and controls are obese, 102 pairs in which both cases and controls are not obese, 32 pairs in which the control was obese and the case was not, and 79 pairs in which the case was obese and the control was not. Recall that the odds ratio for matched pairs is calculated as the ratio of discordant case-control pairs.

$$\text{Odds Ratio (matched pairs)} = \frac{\text{Number of pairs in which the } \textit{case} \text{ was exposed but the } \textit{control} \text{ was not}}{\text{Number of pairs in which the } \textit{control} \text{ was exposed but the } \textit{case} \text{ was not}}$$

Create a 2x2 table for this matched case-control study:

		Controls	
		Exposed	Not exposed
Cases	Exposed		
	Not exposed		

Question 10

What is the matched pairs odds ratio?

a. 1.3
b. 1.5
c. 2.3
d. 2.5