Multicausality: Confounding - Assignment

1. Some years ago several studies were published showing an association between reserpine (a drug used to lower blood pressure) and breast cancer in women. Since obesity is associated both with breast cancer and with hypertension (elevated blood pressure), the suspicion arose that the association between reserpine and breast cancer could be secondary to the effect of obesity. Assume that a cohort study had been conducted to address this question and produced the following data:

Annual age-adjusted incidence of breast cancer per 100,000 women by body weight and reserpine status

	Reserpine use		
	Yes	No	Total
Obese	12.50	8.30	8.72
Not Obese	6.40	4.10	4.22
Total	10.47	6.14	

Answer the following questions on the basis of the above data (ignore considerations of statistical significance and precision). For each answer cite the most relevant figures from the table, allowing for the possibility that one factor affects the observed relation between the other factor and breast cancer risk.

a. Is reserpine a risk factor for breast cancer?

b. Is obesity a risk factor for breast cancer?

c. Is reserpine use associated with obesity?

d. Is the association between reserpine and breast cancer attributable to obesity?

2. A 20-year retrospective cohort study of the incidence of chronic obstructive pulmonary disease (COPD) was performed in two occupational cohorts with different levels of $S0_2$, copper smelters (high SO_2) and truck maintenance workers (low SO_2). In 1961, when the cohort was defined, 55% of the smelter workers and 55% of the truck shop workers were smokers. The relative risk for COPD due to smoking was 10.5 among the smelters and 3.0 among the truck shop workers. Pulmonary function data taken in 1980 showed that 75% of the smelter workers had low FEV_1 values (<90% predicted) and 33% of the truck shop workers had low FEV_1 values. COPD and low FEV_1 were strongly associated in each cohort. [FEV_1 is forced expiratory volume in one second.]

   a. In the above study, is smoking a likely confounder of the association between COPD and SO_2 exposure (i.e., in smelters vs. truck shop workers)? <u>Briefly</u> discuss (1-3 sentences).

   b. The best reason for not controlling for low FEV_1 as a potential confounder is:

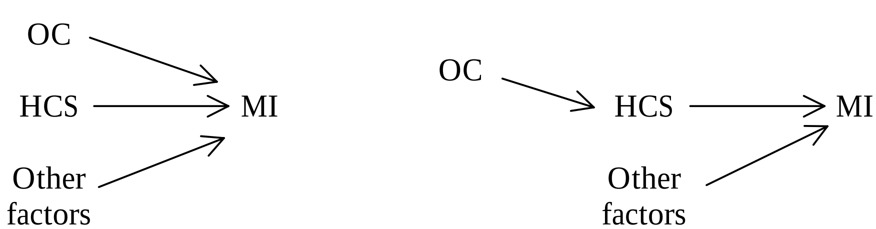
      A. Low FEV_1 is not associated with SO_2 exposure according to the data.

      B. Low FEV_1 is not associated with COPD according to the data.

      C. Low FEV_1 is not an independent risk factor for COPD.

      D. Low FEV_1 is not associated with smoking according to the data.

3. Diagrammed below are two possible causal models involving oral contraceptive use (OC), plasma homocysteine level (HCS) and myocardial infarction (MI). Briefly discuss the implications of the two models with respect to whether HCS would need to be considered as a potential confounder of the relationship between OC and MI.



[arrows show hypothesized causal pathways]

4. The following table, published in the Oxford Family Planning Association Contraceptive Study (Vessey et al.), shows characteristics of individuals at the time of recruitment in to the study. Based on the data presented in the table, discuss three potential sources of bias apparent from the characteristics of the three contraceptive groups. How would these factors be expected to influence the appearance of a causal association between oral contraceptive use and circulatory deaths if no adjustment for the factors were carried out?

Some characteristics of subjects in the three contraceptive groups at time of recruitment

	Method of Contraception in use on Admission		
Characteristic	Oral	Diaphragm	IUD
Percentage aged 25-29 years	56	35	35
Percentage in Social Classes I or II*	39	49	34
Percentage smoking 15 or more cig./day	17	7	12
Mean Quetelet's Index**	2.25	2.26	2.31
Percentage*** with history of:			
Hypertension	0.91	0.67	0.50
Pre-eclamptic toxaemia	12.58	16.26	16.07
Stroke	0.03	0.04	0.30
Rheumatic fever	0.76	0.66	1.04
Rheumatic heart disease	0.09	0.26	0.32
Congenital heart disease	0.12	0.31	0.16
Venous thromboembolism	0.87	4.30	7.96

* Registrar General's classification [Social Class I is highest]

** Weight (g) / height $(cm)_2$.

*** Standardized by indirect method for age and parity. See Vessey, et al.

5. The following questions (from the 1985 EPID 168 second midterm exam) are based on data from Kantor AF, Hartge P, Hoover RN, et al. Urinary tract infection and risk of bladder cancer. *Am J Epidemiol* 1984;119:510-5). In that study, 2982 newly-diagnosed bladder carcinoma patients identified through the U.S. National Cancer Institute SEER (Surveillance, Epidemiology and End Results) Program during a one-year period beginning in December 1977 were interviewed. 5782 population controls from the same geographic areas covered by SEER were selected using an age- and sex-stratified random sample of the general populations, with 2:1 frequency-matching of controls to cases. Information on physician-diagnosed urinary tract infections (UTI) more than one year before interview (and many other factors) was obtained through personal interviews using structured questionnaires in respondents' homes. The following data are from Table 1 in Kantor, Hartge, Hoover et al.:

Table 1
Relative risks (RR) of bladder cancer associated with history of urinary tract infection,* by number of infections; 10 geographic areas of the United States, 1978

	Males				Females			
No. of urinary tract infections	Cases	Controls	RR	95% confidence interval	Cases	Controls	RR	95% confidence interval
0	1758	3642	1.0+		398	979	1.0+	
1 or 2	309	423	1.5	(1.3-1.8)	176	296	1.2	(0.9-1.5)
3+	146	152	2.0	(1.6-2.6)	145	206	2.1	(1.6-2.7)

* Maximum likelihood estimate of relative risk adjusted for race, age, smoking status (never smoked, ex-smoker, current smoker) from stratified analyses.

+ Reference category

a. The sex-specific relative risks for bladder cancer (BC) shown in Table 1 are adjusted for race, age, and smoking status. Which one of the following could be the relative risk of BC risk for 3+ urinary tract infections (UTI) adjusted for race, age, smoking status, and gender? [Choose one best answer]

   A. 1.33

   B. 1.92

   C. 2.05

   D. None of the above.

b. Using the data in Table 1, construct a labeled 2 by 2 table for estimating the crude (with respect to race, age, smoking status, and gender) relative risk for BC in men and women who have a history of 3+ UTI compared to men and women with no history of UTI. Your answer should show the correct formula and substitution.

c. Is gender associated with history of 3+ UTI? Support your answer with the most relevant numbers from Table 1.

d. Is gender a confounder of the association between BC risk and history of 3+ UTI? Support your answer with data from Table 1 and/or your answers to the two preceding questions.