Multicausality: Effect modification - Assignment
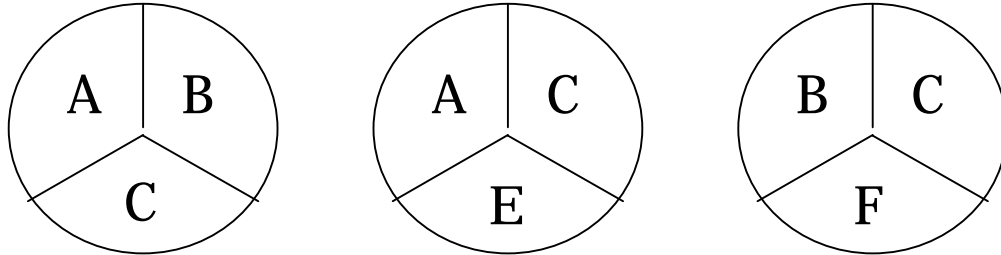
1. Answer the following questions based on the Rothman-style diagram for the etiology of "incidensititis"

   a.   Which component cause is a necessary cause?

   b.   Which two component causes have both modifying and independent (of each other) effects?

   c.   If the population prevalence of C is very high, prevalence of E and F are very low, and prevalence of A is less than that of B, which will be perceived as the "stronger" cause, E or F?

   d.   What are some implications of a situation like the above for studying the incidence of "incidensititis"?

2. Evaluate the joint effect of cigarette smoking and asbestos exposure on the lung cancer rate of the following groups of workers.

Incidence of Lung Cancer Per 100,000 person-years

Asbestos exposure	Nonsmokers	Smokers
No	10	100
Yes	20	400

Select <u>one best interpretation</u> based on these data, and write a brief justification for your choice.

A. Synergism apparently exists in these data because the joint effect of smoking and asbestos exposure is greater than the effect of smoking alone or of asbestos alone.

B. Smoking appears to have a synergistic effect and also to be a confounder, since smoking is associated with asbestos exposure and is a proven risk factor for lung cancer.

C. Smoking appears to have a synergistic effect because the rate ratio of lung cancer among smoking asbestos workers is greater than what would be expected on the basis of the individual rate ratios of smoking alone and of asbestos alone.

D. Smoking appears to have synergistic effect because the excess rate (RR-1) for smoking and asbestos together is greater than the sum of the excess rates for smoking alone and asbestos alone.

E. From these data, it is not possible to evaluate synergism since we do not know the distribution of smoking habits among smokers who are exposed to asbestos and among those who are not.

3. Consider the following data based on the Royal College of General Practitioners Oral Contraceptive Study (1977).

Mortality rates per 100,000 women-years from cardiovascular disease (ICD 390-458) by smoking habit at entry and oral contraceptive use (Standardized by age, social class, and parity).

Cigarette smoking status	Oral Contraceptive Status	
	User	Non User
Non-Smoker	13.8	3.0
Smoker	39.5	8.9

a. Formulate an expression for the joint effect of oral contraceptive use (OC) and smoking on cardiovascular disease mortality, based on an <u>additive</u> model, and determine whether the rates in the above table fit such a model (do not do any statistical tests).

b. Formulate an expression for the joint effect of oral contraceptive use and smoking on cardiovascular disease mortality, based on a <u>multiplicative</u> model, and determine whether the rates in the above table fit such a model (do not do any statistical tests).

c. In commenting on the mortality rates for OC and smoking, a prominent epidemiologist remarked that "the relative risk for oral contraceptive users, compared to non-users, is the same for smokers and non-smokers." Other observers have characterized the relationship as synergistic. Briefly discuss the issues underlying the assessment of synergism in the above data.

4. Several studies have shown a synergistic effect between smoking and drinking in their relation to oral cancer. Consider these hypothetical data:

Yearly Incidence Rates per 100,000 at Risk

	Drinker	Non-Drinker
Smoker	100	40
Non-smoker	15	10

   a. Draw a diagram using Rothman's "causal pies" to show pathways by which oral cancer occurs.

   b. Assuming that there are 100,000 smoker/drinkers, 100,000 smoker/non-drinkers, 100,000 drinker/non-smokers and 100,000 non-drinker/non-smokers, how many cases of oral cancer would be prevented in one year if (only) smoking were eliminated?

   c. How many cases of oral cancer would be eliminated if (**only**) drinking were eliminated?

   d. How many cases of oral cancer would be prevented if **both** smoking and drinking were eliminated?

   e. How many cases of oral cancer can be attributed to **each** causal pathway you have identified in part a.?

   f. Explain why the answers to b. and c. do not sum to the answer in d.

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5. Walker (*International Journal of Epidemiology* 1980; 10:81) suggests a measure to estimate the proportion of cases due to the synergism between two factors, which he calls the etiologic fraction due to interaction $EF_{(AxB)}$.

$$EF_{(AxB)} = \frac{\text{Observed rate for A and B together} - \text{Expected rate if there were no synergy}}{\text{Observed rate for A and B together}}$$

a. For the data in question 9, what is the observed rate for oral cancer among the smokers and drinkers?

b. What rate would you expect to see if there is no synergism between smoking and drinking?

c. Calculate the EF_{AxB}.

d. Suggest a public health application for this result.

(Thanks to Stephen Kritchevsky, Ph.D., for questions 4 and 5.)