Multicausality: Effect modification - Assignment solutions

1.

a. C - because it is a component of all three sufficient causes of "incidensititis." C is a necessary cause since "incidensititis" cannot occur in the absence of C.

b. A and B - Modification implies that two component causes are members of the same sufficient cause for "incidensititis." Independence implies that two component causes are members of different sufficient causes for "incidensititis." Both A and B fulfill these requirements.

c. F will appear as the stronger cause. Since C will be present in most people, and the prevalence of B is greater than the prevalence of A, people with F will be more likely to develop incidensititis than will people with E.

d. The most important implication for our purposes is the need to control the other factors when studying the effect of A. If our A and not-A groups differ with respect to B, C, and E, then the disease rates observed could be due to the latter factors, rather than to A. Moreover, the effect of A will appear to differ from study to study unless these other factors are taken into account.

It is also interesting to note that the multiplicity of sufficient causes imply different "etiologic routes" to incidensititis. So, for example, a person could acquire incidensititis through the first sufficient cause and never have either component cause E or F. Thus, cases of incidensititis will be heterogenous with regard to the etiology of their disease. The only common (necessary) cause is C, which must be present for disease occurrence.

2. 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.

3.

a. Under an additive model, we expect that the joint effect of the two factors will be equal to the sum of the excess risk from each factor separately, i.e.,

Expected Rate Difference (RD) of OC and SMK together =

$$\text{Expected } RD_{OC,SMK} = RD_{OC,\overline{SMK}} + RD_{\overline{OC},SMK}$$

(or equivalently, the rate for persons exposed to both factors together is expected to be equal to the rate for those exposed to neither plus the increase associated with the first factor alone plus the increase associated with the second factor alone):

$$\text{Expected } R_{OC,SMK} = R_{neither} + (R_{OC,\overline{SMK}} - R_{neither}) + (R_{\overline{OC},SMK} - R_{neither})$$

$$= R_{OC,\overline{SMK}} + R_{\overline{OC},SMK} - R_{neither}$$

In the data from the table,

$$\text{Expected } R_{OC,SMK} = 13.8 + 8.9 - 3.0 = 19.7$$

Observed $R_{OC,SMK}$ = 39.5 per 100,000 women-years.

Or,

$$\underline{\text{Expected}} \text{ excess risk } (RR - 1) \\ (\text{of OC alone + SMK alone}) = \left(\frac{13.8}{3.0} - 1\right) + \left(\frac{8.9}{3.0} - 1\right)$$

$$\underline{\text{Observed}} \text{ excess risk } (RR - 1) \\ (\text{of OC alone + SMK alone}) = \left(\frac{39.5}{3.0} - 1\right)$$

The large discrepancy between expected and observed rates indicates that the data do not fit an additive model.

b. Under a multiplicative model, we expect the joint effect of the two factors to be equal to the product of the risk (or rate) ratios for each factor separately, i.e.:

Expected Rate Ratio (RR) for OC and SMK together,

$$RR_{OC,SMK} = (RR_{OC,\overline{SMK}})\,(RR_{\overline{OC},SMK})$$

or equivalently, the risk or rate (R) for OC and SMK together is:

$$\text{Expected } R_{OC,SMK} = \frac{(R_{OC,SMK})(R_{OC,SMK})}{R_{OC,SMK}}$$

In these data,

$$\text{Expected } RR_{OC,SMK} = \frac{(13.8)\,(9.9)}{3.0} = 40.9$$

$$\text{Observed } RR_{OC,SMK} = 39.5$$

or,

$$\text{Expected } RR_{OC,SMK} = RR_{OC,SMK} \times RR_{OC,SMK}$$

$$= \frac{13.8}{3.0} \times \frac{8.9}{3.0} = 13.6$$

$$\text{Observed } RR_{OC,SMK} = \frac{39.5}{3.0} = 13.2$$

The very close agreement for the observed rate and that expected under a multiplicative model suggests that the relationship among OC, SMK, and cardiovascular mortality is multiplicative.

c. Both positions can be supported. It is correct that the relative risk for OC users is the same for smokers and nonsmokers, indicating that the data fit a multiplicative model. An analysis stratified by smoking status will show no effect modification of the association between OC and CVD.

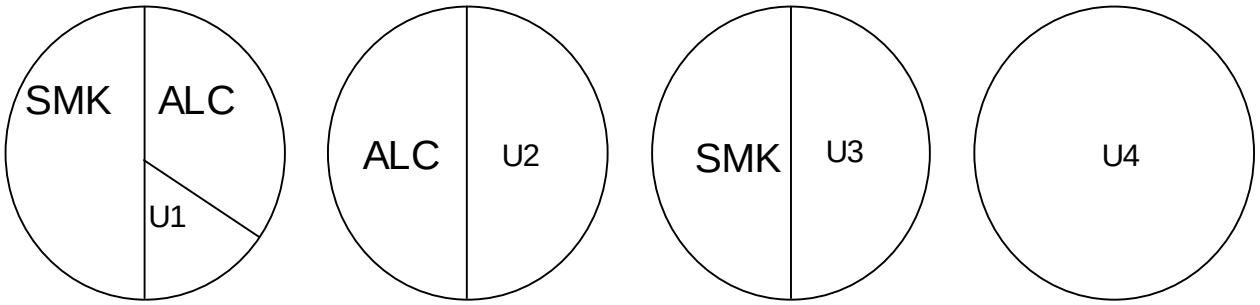
On the other hand, the additive model is more appropriate for assessing public health impact (and individual decision-making). The fact that the joint effect of OC and smoking substantially exceeds the sum of the effects (risk differences) for OC and smoking individually indicates that there the relationship is synergistic in terms of public health

impact. Synergism in this sense implies that if per-person intervention costs are equal, a greater reduction in disease rates will result from focusing on women who both smoke and use OC.

The multiplicative nature of the relationship might suggest that smoking and OC operate on some common element in the pathogenetic process, so that the effects of the one potentiate the effects of the other. However, assessment of biological synergism requires knowledge of biological mechanisms beyond that generally obtainable from epidemiologic data.

4.

a. I II III IV



b. In the Non-drinking group the number of cases would be expected to drop from 40 to 10 (the rate among the non-smokers). The number of cases among the drinkers would be expected to drop from 100 to 15 cases. Thus, (100 - 15) + (40 - 10) = 115 cases would be expected to be prevented through smoking cessation.

c. In the Non-smoking group the number of cases would be expected to drop from 15 to 10 cases, and in the smoking group the number of cases would be expected to drop from 100 to 40 cases. Thus, (15 - 10) + (100 - 40%) = 65 cases could be prevented by abstinence.

d. If both drinking and smoking were eliminated then each cell could be expected to have the same number of cases as in the non-smoking and non-drinking cell. So, (100 - 10) + (40 - 10) + (15 - 10) = 125 cases are prevented by the elimination of smoking and drinking.

e. Ten cases can be attributed to unidentified background factors in pathway IV. For the Smokers-Nondrinkers, 30 cases can be attributed to smoking (pathway III) since 10 of the 40 cases would have occurred in the absence of smoking. Similarly, 5 cases can be attributed

to drinking in the absence of smoking (pathway II). For the Smoker-Drinkers, of the 100 cases, 45 would have been expected to occur either from smoking alone, drinking alone or through unidentified causes (the background rate). Therefore, 55 cases can be attributed to the synergy between smoking and drinking represented by pathway I.

f. In removing either drinking or smoking we prevent not only those cases attributable to the factor alone but also those cases caused by the synergy between the two. Therefore, by removing smoking we prevent 55 of the deaths due to synergy and by removing drinking we prevent the same 55 deaths due to synergy. Of course if we remove both factors we do not prevent the same 55 cases twice. What you have worked through above is an example of non-additivity of attributable risks, which is equivalent to interaction on an additive scale.

5.

a. 100 cases per 100,000 per year.

b. This would be the rate due to smoking + the rate due to drinking + the rate due to unidentified factors. There were 30 cases due to smoking (40 due to the combination of smoking and unidentified factors), 5 due to drinking (15 due to the combination of drinking and unidentified factors), and 10 due to unidentified factors. The expected rate would be: 30 + 5 + 10 = 45 cases per 100,000 people per year. [Note that Rothman's model is based on (or implies) an additive model for combining risks.]

c. EF(Smoking x Drinking) = [(100 - 45) / 100]= .55

d. Since there is such a strong synergism between smoking and drinking health education, physician counseling, and warning labels on both substances should give some attention to the combined effect.