Lab 9- Instructors guide

Effect Modification

Goal: To practice skills used for characterizing the joint effect of two or more causes of a disease

Additive and multiplicative models – the case of leuX

Background

Scientists in Epidoria suspect that smoking exotic cigars (imported from the neighboring nation of Biosoria) may be causally linked to a specific blood disease (leuX). leuX may also be related to environmental factors in Biosoria. The two nations conduct a joint study to evaluate the relationship. Results from the study are summarized in Table 1. Age adjustment is not necessary, since both countries have identical age distributions.

Table 1. Incidence of leuX per 100,000 persons per year, by country of residence and cigar smoking status

	Country	
Cigar smoking	Epidoria	Biosoria
Smoke cigars	40	120
Do not smoke	10	90

Questions

1. Calculate the incidence density ratio associated with cigar smoking within each country. Do the data suggest that cigar exposure is a risk factor for leuX? Do the data suggest effect modification by country of residence?

   IDR for Epidoria = 40/10 = 4

   IDR for Biosoria = 120/90 = 1.33

   There is an association between leuX and cigar smoking. The association is stronger in Epidoria. The data for cigar smoking and country do not fit a multiplicative model (because the country-specific rate ratios differ), i.e., there appears to be effect modification with respect to a multiplicative model.

2. Calculate the incidence density difference within each country. Assuming that smoking Biosorian cigars is causally related to leuX, which country has the greater attributable risk?

IDD for Epidoria = 40/100,000 – 10/100,000 = 30/100,000

IDD for Biosoria = 120/100,000 – 90/100,000 = 30/100,000

The IDD is the same for both countries. The rates for both exposed and unexposed persons in Biosoria are greater than the corresponding rates in Epidoria, so that even with a smaller rate ratio in Biosoria it has the same rate difference as Epidoria.

3. Formulate an expression for the joint effect on leuX morbidity from smoking Biosorian cigars and country of residence, based on an additive model. Determine whether the rates in Table 1 fit this model. For convenience, use the group with the lowest rate (non-smoking Epidorians) as the reference or "baseline" level.

Additive model for expected joint IDD:

$$\mathbf{IDD}_{\text{joint}} = \mathbf{IDD}_{\text{cigars}\,|\,\text{Epidoria}} + \mathbf{IDD}_{\text{country}\,|\,\text{Nonsmoking}}$$

$$= (40/100{,}000 - 10/100{,}000) + (90/100{,}000 - 10/100{,}000) = 110/100{,}000$$

Observed IDD from cigars and Biosoria $= \mathbf{IDD}_{\text{cigars}\,|\,\text{Biosoria}} = 120/100{,}000 - 10/100{,}000$

$= 110/100{,}000$. The data from table 1 fit an additive model for joint risk.

4. Formulate an expression for the joint effect on leuX morbidity from smoking Biosorian cigars and country of residence, based on a multiplicative model. Determine whether the rates in Table 1 fit this model. Use the same reference group.

Multiplicative model for expected joint IDD:

$$\mathbf{IDR}_{\text{joint}} = \mathbf{IDR}_{\text{cigars}\,|\,\text{Epidoria}} \times \mathbf{IDR}_{\text{Biosoria}\,|\,\text{Nonsmoking}}$$

$$= (40/100{,}000) / (10/100{,}000) \times (90/100{,}000) / (10/100{,}000) = 36$$

Observed IDR from cigars and Biosoria $= \mathbf{IDD}_{\text{cigars}\,|\,\text{Biosoria}}$

$$= (120/100{,}000)/(10/100{,}000) = 12$$

The data from table 1 do <u>not</u> fit a multiplicative model for joint risk.

5. Assuming that the observed associations are causal, briefly interpret these data with respect to synergism and possible public health implications.

Low birth weight, maternal age, and smoking

Low-weight births are a major public health concern. Cigarette smoking may be responsible for 17-26% of low-weight births in the U.S. Maternal age is also an important factor. In order to investigate the magnitude of the effect of cigarette smoking during pregnancy on birth weight at different maternal ages, Fox et al. (Steven H. Fox, Thomas D. Koepsell, Janet R. Daling. Birth weight and smoking during pregnancy – effect modification by maternal age. *Am J Epidemiol* 1994;139:1008-15) analyzed birth certificate data for 347,650 singleton births during 1984-1988 in Washington State. 4.39 percent of these births were low weight (less than 2,500 g). Prevalence of smoking was 24.7% overall. Smoking was associated with higher parity, poorer prenatal care, and being unmarried; these associations were stronger for older women.

The following figures display (1) prevalences of low birth weight in relation to maternal age and smoking and (2) differences and ratios of these prevalences. Discuss the relationship among the prevalence of low weight births, maternal age, and maternal smoking. Is the effect of smoking modified by maternal age? Suggest some possible explanations for the observed patterns and consider implications for prevention.

Possible explanations (from Fox, Koepsell, and Daling):

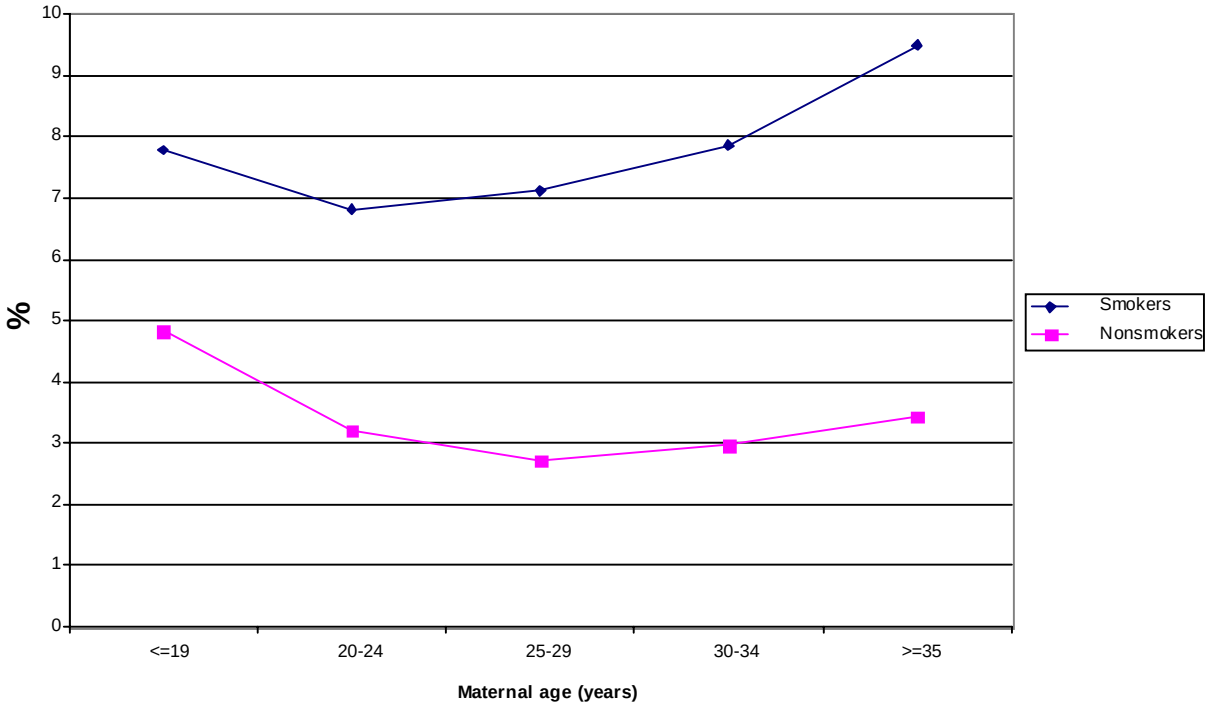
1. Susceptibility to effect of smoking increases with age. Decline in cardiovascular reserve with age could mean that cardiovascular system of older mothers is less able to compensate for hypoxia due to carbon monoxide or vasoconstriction from smoking. Capacity to metabolize nicotine might decline with age.

2. Measurement of exposure - smoking has been measured as "yes" versus "no", but older smokers may smoke more. Also, cumulative exposure over years might increase the effect of smoking.

3. Smoking could be a marker for unmeasured factors, e.g., other unhealthy habits, exposures, behavior, SES, not adequately controlled. If smoking is a more reliable marker in older women, the apparent effect would increase with age. The relatively small numbers of women in their 30's and 40's who smoke during pregnancy "might more purely reflect such characteristics". Or, smoking might mediate factors whose effects that are modified by maternal age, e.g., prepregnancy weight or pregnancy weight gain.

Implications - "if causal, from a public policy standpoint, "although smokers over age 35 years constitute only a small fraction of the women who smoke during pregnancy (4.2% in Washing State), they might be the ones for whose babies smoking cessation would make the most difference. . . . consider directing intensive efforts toward pregnant smokers in older age groups." p1014]

Low birth weight and maternal smoking (Fox, Koepsell, and Daling, AJE 1994)



Ratios and differences of low birth weight prevalence by maternal smoking and age