Confounding

Goal: To familiarize students with the factors associated with confounding and methods of stratified analysis for evaluation of confounding.

Background

In the small island nation of Epidoria, a team of reproductive epidemiologists has been studying the relationship between very low birth weight and risk of cognitive, motor, and behavioral problems. Five years ago these investigators initiated a cohort study. Using birth certificate files and delivery room entry logs, these investigators attempted to identify all full-term births in Epidoria over a 6-month period. The investigators enrolled all low birth weight babies and a representative sample of normal birth weight babies into their study. The investigators then examined the children every year until age 3 years. During the last examination, the investigators administered a standardized developmental screening test to assess personal-social, language, and motor-adaptive skills. Based on this test, the investigators classified the children into two groups: normal development and delayed development.

The results from the study were:

	Birth weight		
Development	Low	Normal	Total
Delayed	140	77	217
Normal	220	283	503
Total	360	360	720

1. Calculate the crude cumulative incidence ratio for the primary exposure (low birth weight).

2. To take account of the possibility that environmental lead exposure might confound the relationship between birth weight and developmental status, blood lead levels were determined from blood samples collected at the age 3-year visit. Elevated lead levels (> 10 μg/dL) were found in 173 of the low birth weight children (88 of whom had delayed development according to their screening test). Elevated lead levels were also found in 72 of the normal birth weight children (24 of whom had delayed development). Diagram several plausible sets of relationships among birth weight, blood lead level, and delayed development. In which ones could blood lead confound the association between low birth weight and delayed development?

3. Carry out a stratified analysis of birth weight and developmental delay, controlling for blood lead level. Create 2 x 2 tables for each stratum, estimate the CIR for each stratum, and interpret the results in comparison with the crude CIR from question 1.

4. Is there evidence of an association between the confounder (blood lead level) and the primary exposure (low birth weight)? To determine this association would you use (a) the entire cohort of children, (b) only those children with delayed development, or (c) only those children with normal development? Why? If there is an association, are low birth weight children more or less likely to have elevated blood lead levels?

5. Is there an association between the confounder (blood lead level) and the outcome (delayed development)? To determine this association would you use

a) the entire cohort of children,
b) only those children with low birth weight, or
c) only those children with normal birth weight?

Why?

6. Using all of the above information, do you think blood lead level is a confounder of the association between low birth weight and delayed development in this study population?

7. What changes in the study design would have avoided the potential confounding effects blood lead level? What are the advantages and disadvantages of these alternatives?