Confounding

Introduction

You have learned that random error and bias must be considered as possible explanations for an observed association between an exposure and disease. This week we will examine the role of confounding. Unlike random error or bias, confounding is a property of the study population, and occurs when the effect of an exposure on an outcome is mixed together with the effect of a third variable. The following exercise will examine the properties of confounders and describe methods to adjust for confounding through both study design and analysis. (Please see Aschengrau & Seage Chapter 11 for more information).

Good luck and have fun!

Next »

Welcome Module Index Glossary Epiville Chamber of Commerce About this site Requirements

Confounding

Learning Objectives

A. Basic elements of confounding

1. Define confounding and distinguish it from bias and chance error
2. Identify three criteria a variable must fulfill to be a confounder in an epidemiological study
3. Diagram the relationship of a confounder with exposure and outcome

B. Explain methods to adjust for confounding

1. Describe ways of handling confounding at the design phase of a study
    a. Randomization

b. Restriction

c. Matching

2. Describe ways of handling confounding at the analysis phase of a study
   a. Stratification
   b. Multivariate adjustment techniques

C. Describe how to evaluate potential confounding in epidemiological data

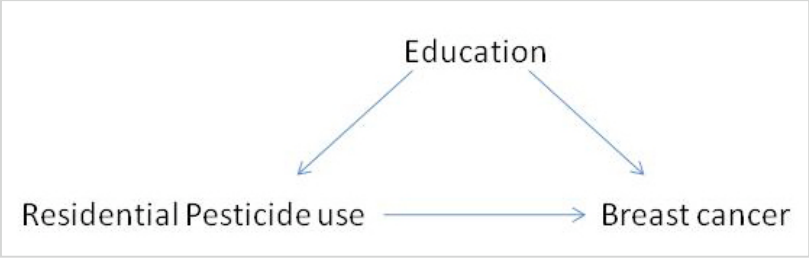
1. Explain the difference between a crude and adjusted effect estimate
2. Discuss what is meant by "residual" confounding

« Previous || Next »

Confounding

Student Role

For this exercise, we will pay special attention to evaluation of confounding in Teitelbaum et al. 2007. In their study of the association between residential pesticide use and breast cancer, they critically examined the potential confounding role of education. The causal model visually representing the investigators' hypothesis about the effect of education on the pesticide-breast cancer risk is presented below.



Work through this interactive exercise which demonstrates the "mixing of effects" when confounding is present in the data, using the example of coffee drinking as a potential risk factor for low birth weight and the mixing of effects that occurs between coffee drinking and smoking.

« Previous || Next »

Confounding

Design Questions

1. Education, a marker of socioeconomic status, was one of the potential confounders considered in the study of pesticide use and breast cancer in Teitelbaum et al. (2007). Please explain why education was considered to be a potential confounder:

a. Education is associated with high exposure to pesticide use. Those with higher education may have larger homes with more lawns and gardens in need of pesticide application to enhance their landscape's appearance. Further, more advanced education is associated with a higher risk of breast cancer (hypothesized to operate via a host of factors, including older age at having a first child), and is not in the causal pathway of interest between pesticide use and breast cancer (pesticide use is not hypothesized to cause education).

b. Education is in the causal path between pesticide use and breast cancer. All variables in the causal pathway are potential confounders regardless of their association with exposure and outcome.

c. Although education is not associated with pesticide use, advanced education is associated with a higher risk of breast cancer (hypothesized to operate via a host of factors, including older age at having a first child). Moreover, it is not in the causal pathway of interest between pesticide use and breast cancer (pesticide use is not hypothesized to cause education).

2. Would confounding due to education still be a problem if the investigators were able to conduct a cohort study instead of a case-control study?

a. Confounding would not be a problem in a cohort study

b. Confounding would still pose a problem in a cohort study

c. Confounding would be minimal in a cohort study compared to a case-control study

3. How was potential confounding by age handled in the design stage of the study?

a. Randomization of subjects into cases and controls

b. Restriction of cases and controls within a narrow age category

c. Matching controls to cases on age

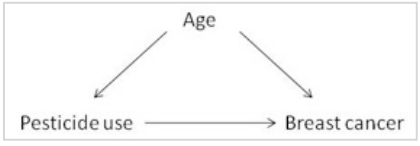
« Previous || Next »

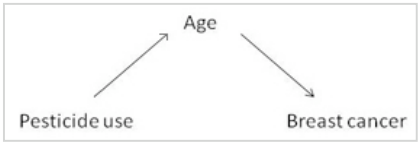
Confounding

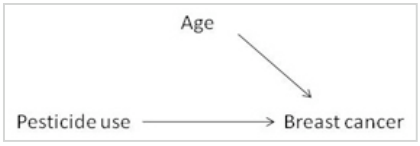
Data Analysis

[Follow this link to learn more about the evaluation of confounding.]
(Note: In the popup window, be sure to scroll down after each correct answer.)

4. Age was a potential confounder in this study. Choose an appropriate diagram representing the relationship of this potential confounder with exposure and outcome.

a.


b.


c.


5. Explain how you would assess whether a potential confounder alters an effect estimate

after adjusting for it in a multivariate model.

a. Look at the crude OR

b. Look at the adjusted ORs

c. Compare the crude OR to the adjusted OR

6. Lawn/garden pesticide use was significantly associated with breast cancer after adjusting for age, level of education, and other combined pest group (OR=1.34, 95% C.I. 1.11-1.63). Given that investigators also determined that a host of other factors (e.g., age of menarche, oral contraceptive use, and family history of breast cancer) did not meet the criteria for confounders, can the authors conclude that they have removed all sources of confounding in the examination of this association?

a. Yes. Investigators have examined all potential risk factors for the outcome, adjusted for necessary confounders, and can be fully confident that their estimate is free of confounding.

b. No. Authors did not adjust for family history of breast cancer, a known risk factor, and thus the association reported may be biased.

c. Yes. Because authors conducted a case-control study, most of the confounding was removed in the design stage of the analysis because cases and controls are comparable on risk factors.

d. No. Investigators can never be fully confident that confounding is eliminated in an observational study.

7. What if, during data analysis, investigators found that use of vitamin supplementation was associated with pesticide use and was an independent risk factor for breast cancer? Should they attempt to control for this potential confounder?

a. Yes, investigators should control for vitamin supplementation as they did for other potential confounders and add this variable to the list of hypothesized confounders in the Methods section of the paper.

b. Yes, investigators should control for vitamin supplementation and describe the process of confounder selection in their Results section.

c. No, it is inappropriate to control for variables if they were not hypothesized as confounders a priori.

8. Suppose investigators wanted to control for education as a potential confounder in the design stage of the analysis. Which of the following would be appropriate to control for education as a potential confounder at the design stage?

a. Create 2x2 tables of pesticide use and breast cancer separately for those with low education, and then for those with high education.

b. Only enroll people in the study who have less than a high school education.

c. Match cases to controls on high vs. low education.

d. Answer choices A and B

e. Answer choices B and C.

9. Teitelbaum et al. (2007) matched cases to controls on age. A more recent study, Itoh et al., (2008), also examined the association between pesticides and breast cancer and matched cases to controls on both age and geographic location. Which study was better at controlling for confounding in the design phase of the study?

a. Teitelbaum et al.'s 2007 study was better because it is best to match cases to controls on as few factors as possible.

b. Itoh et al.'s study was better because it is best to match cases to controls on as many factors as possible.

c. It is not possible to determine whether one study is better than the other at controlling confounding by the number of factors matched.

« Previous || Next »

Confounding

Discussion Questions

Carefully consider the following questions. Write down your answers (1 - 2 paragraphs) for question # 1 within a word document and submit your answers to your seminar leader. Be prepared to discuss all questions during the seminar section.

- Which study design offers the best opportunity to control for confounding -- randomized clinical trial, cohort study, or case-control study? Explain your reasoning and make examples to prove your point.
- Suppose that in the study of pesticide use and breast cancer you wanted to evaluate the hypothesis that pesticide use varies by geographic area. Would you match on geographic area? Please, explain your answer.
- A principle of case-control studies is that controls should be selected independently of exposure status. Under what circumstances would matching violate this principle? What can be done about this type of violation?

Questions for the Intellectually Curious:

Why is it important to distinguish between "confounding" and "confounders"? What does a 95% confidence interval assume about the presence of bias and confounding?

« Previous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