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## Measuring Confounder Influence

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## Meaning of an Association

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An association obtained from statistics in a random sample can be:

- “**Statistically significant**” if very unlikely when due solely to the influence of chance.
- “**Confounder resistant**” if strongly resistant to nullification by a large confounder

Quantitative measures are needed to be useful!

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## “Resistance” Rules of Thumb

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Sir Richard Doll: No single study is persuasive unless the lower limit of its 95% confidence level falls above a **threefold** increased risk.

“As a general rule of thumb,” says Angell of the New England Journal, “we are looking for a relative risk of **three or more**” before accepting a paper.

Robert Temple, FDA Director of Drug Evaluation, puts it bluntly: “My basic rule is if the relative risk isn’t at least **three or four**, forget it.”

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## Problem of Confounding in Epidemiology

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John Bailar, epidemiologist: “*There is no reliable way of identifying the dividing line.*”

Epidemiologists need an abstract description of confounding that can generate confounder significance and confounder intervals for RR.

This description must handle binary data, be meaningful, useful and easy to understand.

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## “S Confounder” Confounder Resistant

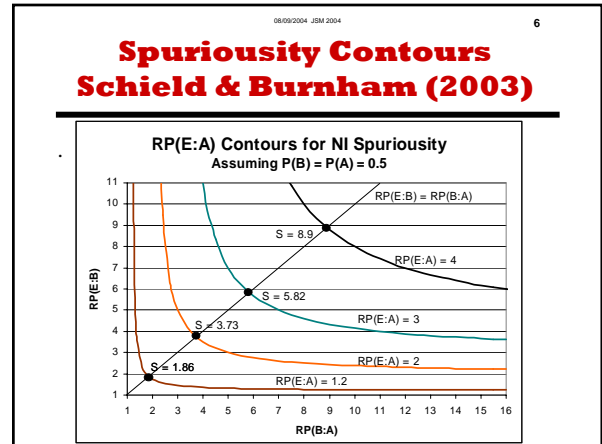
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A is predictor, B is confounder, E is effect.

- \*  $P(B)$  = Prevalence of the confounder.
- $P(A)$  = Prevalence of predictor.
- \*  $RP(E:B)$  = Rel. Prev of effect for confounder
- \*  $RP(B:A)$  = Rel. Prev of confounder for predictor.

An **S confounder** is a binary confounder where  **$RP(B:A) = RP(E:B) = S$  and  $P(B) = P(A)$ .**

An association is “**confounder resistant**” to a size S confounder if it withstands nullification.



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### Algebraic Condition to Resist Nullification

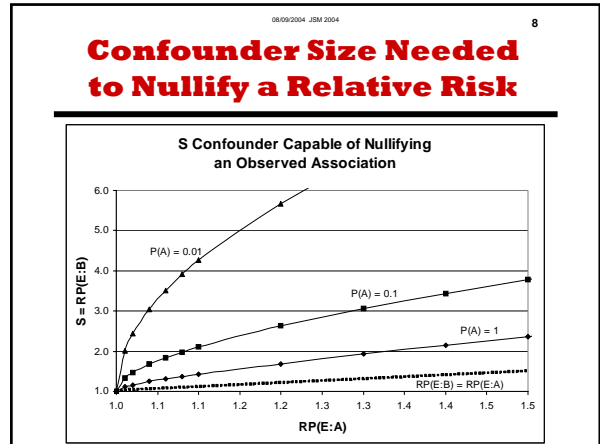
The confounder size,  $S$ , and predictor prevalence,  $P(A)$ , determine the minimum excess relative risk,  $XRP(E:A)$ , that can resist nullification.

$$XRP(E:A) = P(A) \cdot (S - 1)^2 / \{1 + [2P(A) \cdot (S - 1)]\}$$

If the predictor prevalence is 50%, then

$$XRP(E:A) = (S - 1)^2 / (2S)$$

If  $S = 5$ ,  $RP(E:A) = 2.6$ ; if  $S = 6$ ,  $RP(E:A) = 3.1$



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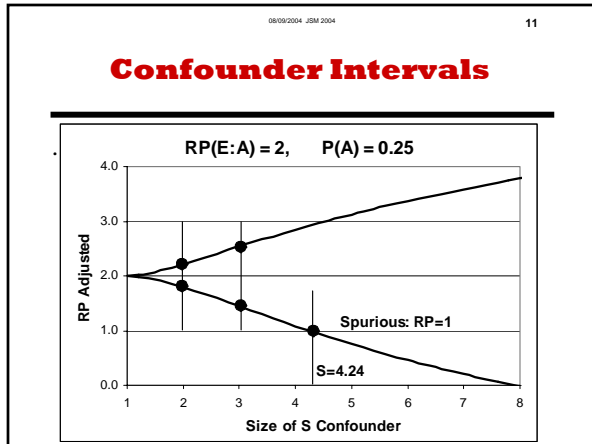
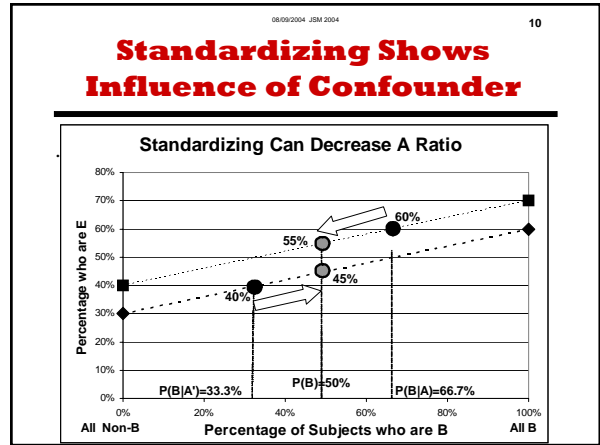
### Confounder Intervals: Influence of Confounder

Lower limit: determined by removing the influence of a confounder where  $RP(B:A) = RP(E:B)$ .

Upper limit: determined by removing the influence of a confounder where  $RP(B:A) = 1/ RP(E:B) = 1/S$ .

Given the size of an  $S$  confounder, the confounder influence can be determined algebraically and illustrated using a standardization diagram.

For a  $S$  confounder of size 2, the confounder interval for  $RP(E:A) = 2$  with  $P(A) = 0.5$  is [1.67, 3.0].



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### Recommendations

Statistical educators should find ways to teach confounder influence in the first course.

Analysts should show confounder susceptibility: either give confounder intervals or identify the  $S$  confounder needed to nullify an association.

Subject experts should set generally accepted confounder sizes for confounder resistance: e.g.,  $S = 6$  for  $P(A) = 50\%$ .