Week 4: Magnitude of Bias due to Confounding

Video 1: Impact of Uncontrolled Confounding on Validity of Point Estimates and Inferential Procedures

EPI202 – Epidemiologic Methods II
Murray A. Mittleman, MD, DrPH
Department of Epidemiology, Harvard TH Chan School of Public Health

HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

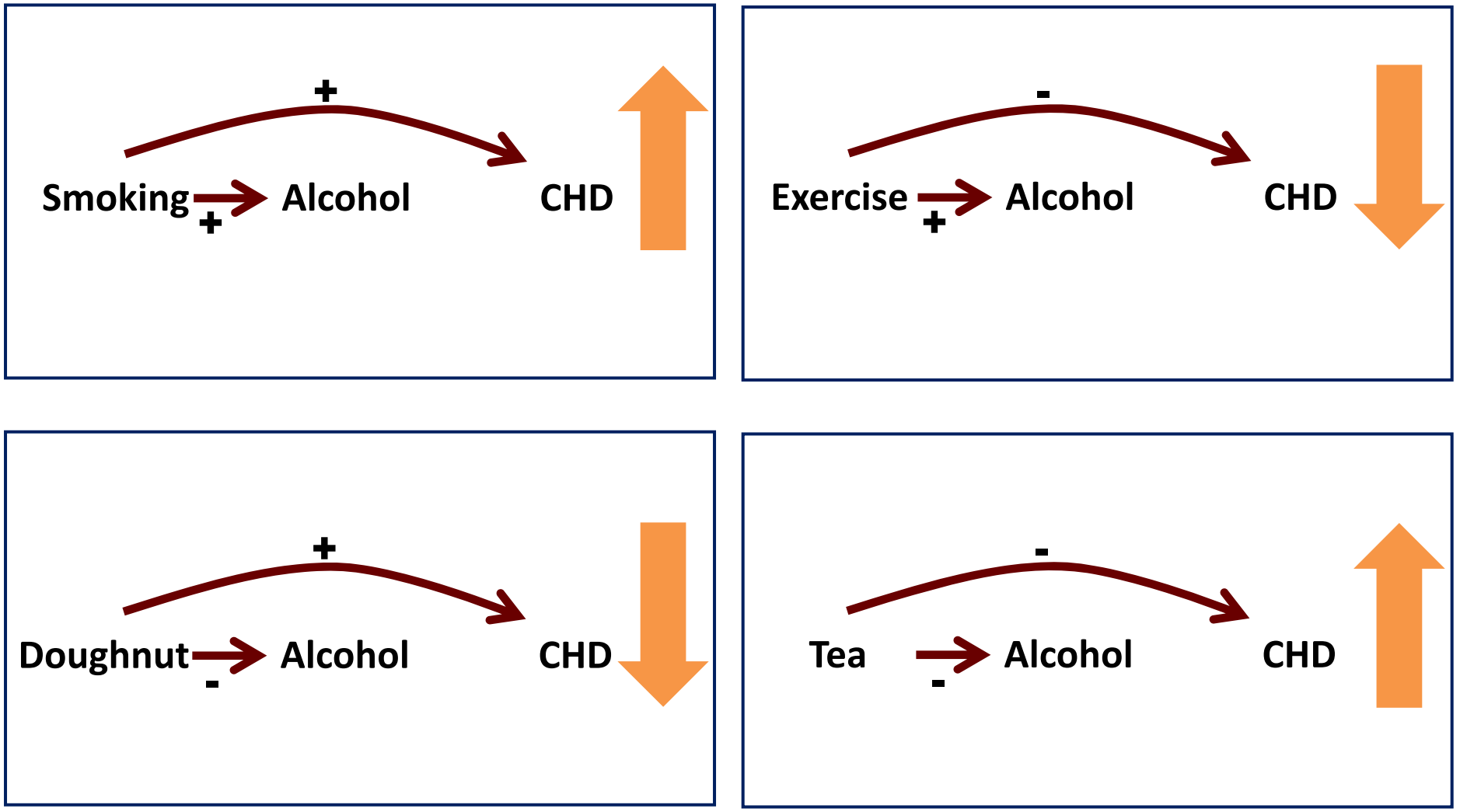
Key Concepts

- Confounding
  - Bias in point estimates
  - Invalid statistical inferences
  - Direction
  - Magnitude

Impact of Confounding on Validity

- Introduces bias into point estimates
- Reduces the validity of statistical inferential procedures and results such as p-values and confidence intervals
- May lead to p-values that are incorrectly too small or too large
- In addition, in a Neyman-Pearson hypothesis testing paradigm, the type I and type II errors (α and β, respectively) may be under- or over- estimated, leading to invalid conclusions.
- May lead to confidence intervals that are
  - incorrectly centered-due to bias in the point estimate
  - of incorrect width-due to bias in the estimate of the variance of the point estimate

Direction of Confounding



Assume exposures and outcomes are binary and there are no other sources of confounding or bias

BREAK

Week 4: Magnitude of Bias due to Confounding

Video 2: Partitioning Crude Associations

EPI202 – Epidemiologic Methods II
Murray A. Mittleman, MD, DrPH
Department of Epidemiology, Harvard TH Chan School of Public Health

HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

Key Concepts

- Confounding
  - Bias in point estimates
  - Invalid statistical inferences
  - Direction
  - Magnitude

Partitioning the Crude RR

- Miettinen presented a conceptual framework of partitioning the crude association into a causal component and spurious component.
- Schlesselman proposes a generic conceptual framework and detailed derivations for the bounds of confounding.
- The observed association can be thought of as arising from two components:
  - the true causal effect
  - the spurious component due to confounding
- This can be written algebraically as:

$$RR_{observed} = RR_{true} * \mathcal{S}$$

where $\mathcal{S}$ represents the spurious component that is due to confounding

Miettinen OS. Components of the crude risk ratio. *Am J Epidemiol*. 1972;96(2):168-72
Schlesselman JJ. Assessing effects of confounding variables. *Am J Epidemiol.* 1978;108:3-8

Magnitude of Bias Due to Uncontrolled Confounding

The extent to which the estimated value of a crude relative risk can be attributed to the effects of a confounding variable is limited by three factors

1. the association between the confounder and the outcome

2. the ratio of prevalence of the confounder in the exposed group divided by the prevalence of the confounder in the unexposed group

3. the prevalence of the confounder

BREAK

Week 4: Magnitude of Bias due to Confounding

Video 3: Assessing Potential Magnitude of Bias due to Uncontrolled Confounding

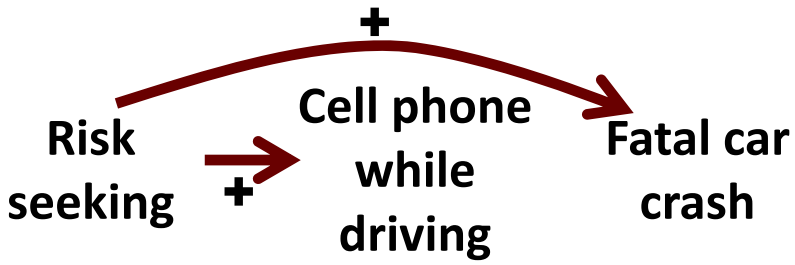
EPI202 – Epidemiologic Methods II
Murray A. Mittleman, MD, DrPH
Department of Epidemiology, Harvard TH Chan School of Public Health

HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

Magnitude of Confounding

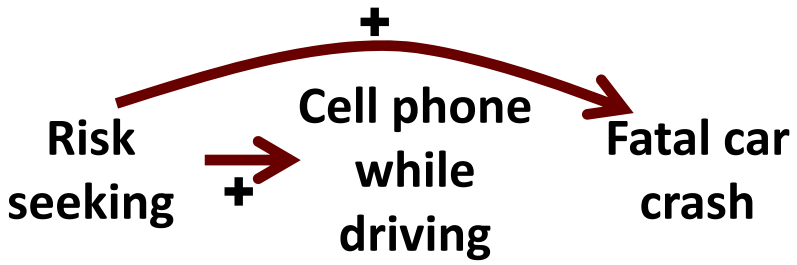
Magnitude of Confounding
Confounder and Outcome

- The extent to which a crude association can be attributed to a confounding variable is limited by the relative risk of the outcome from that confounding variable



Magnitude of Confounding
Confounder and Exposure

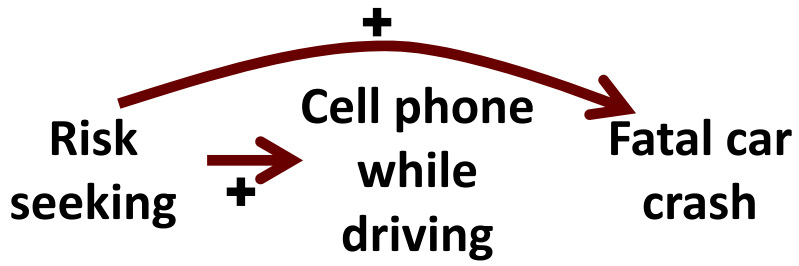
- Confounding is limited by the ratio of prevalence of the confounder in the exposed divided by the prevalence of the confounder among the unexposed



Magnitude of Confounding
Confounder Prevalence

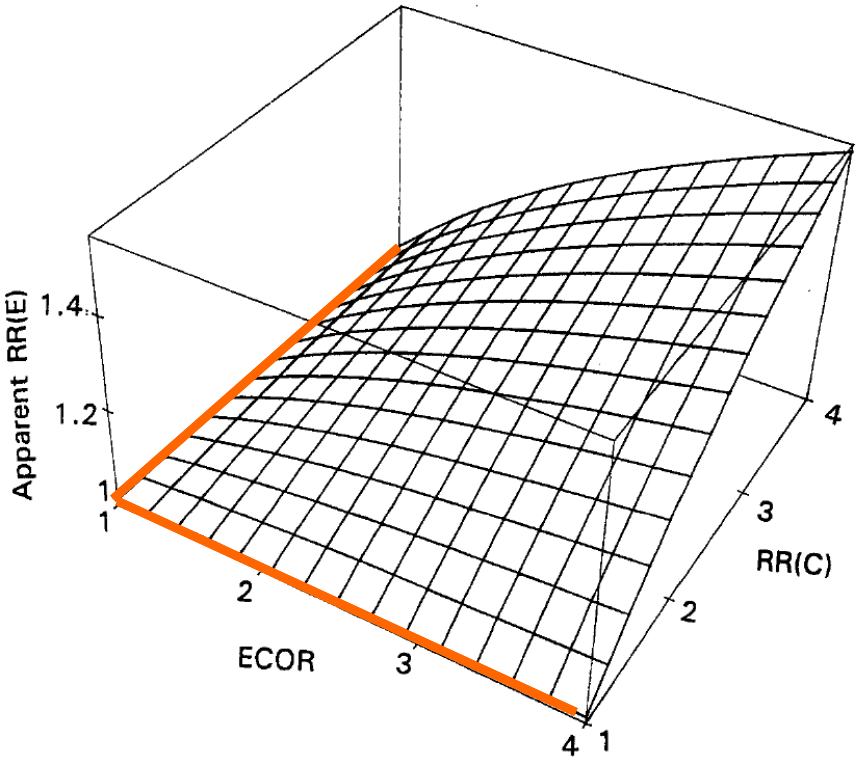
- The extent to which a crude relative risk is due to confounding is a function of the prevalence of the confounder

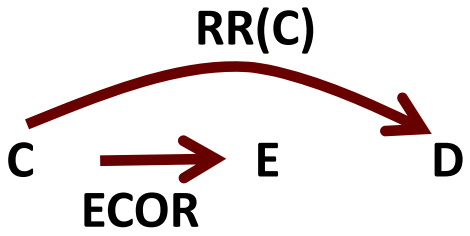
- The extent of confounding decreases as the confounder prevalence tends towards 0% or towards 100%, which in the limit produces restriction in the design



Walker's Bounds of Confounding (1)

P(E) = 0.2
P(C) = 0.2



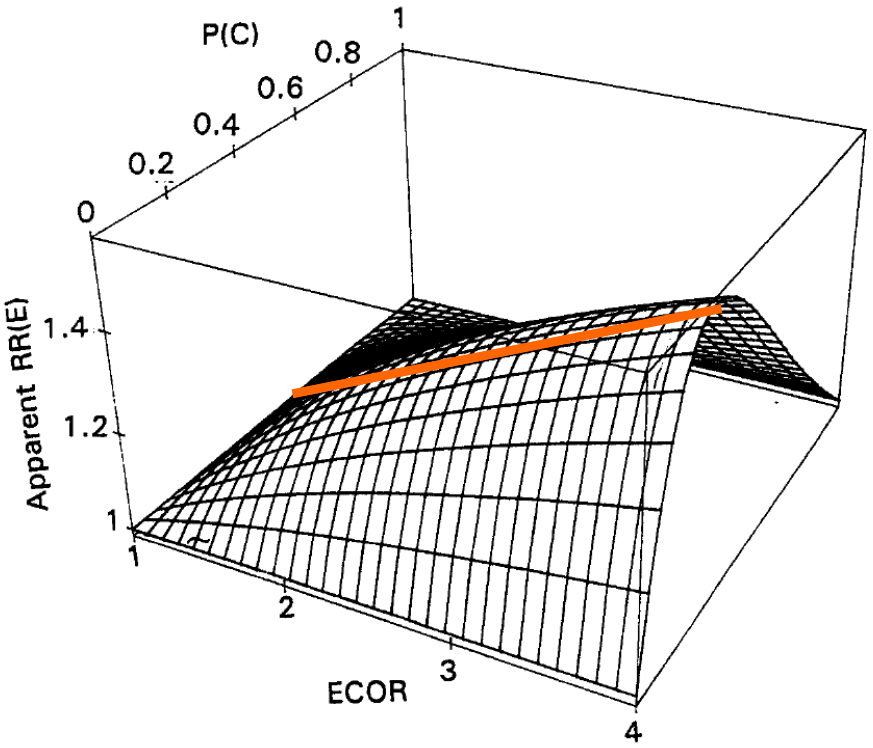


ECOR	Exposure-confounder OR
P(C)	Prevalence of confounder
RR(C)	Confounder-outcome RR
P(E)	Prevalence of exposure

Alexander Muir Walker. Observation and Inference: An Introduction to the Methods of Epidemiology. Epidemiology Resources, June 1991

Walker's Bounds of Confounding (2)

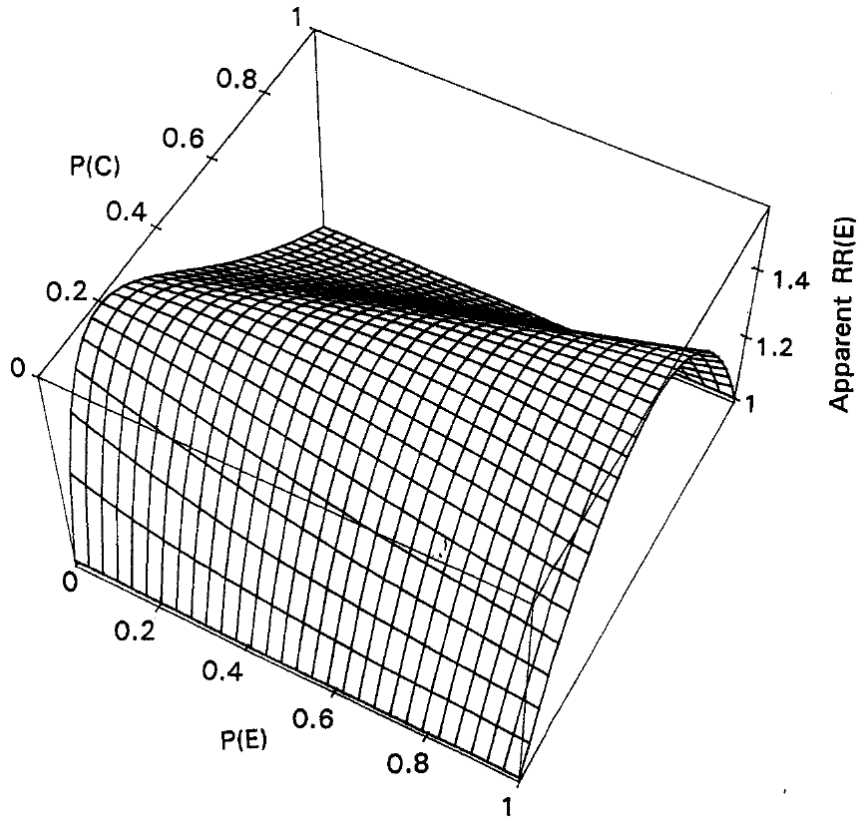
P(E) = 0.2
RR(C) = 4



Alexander Muir Walker. Observation and Inference: An Introduction to the Methods of Epidemiology. Epidemiology Resources, June 1991

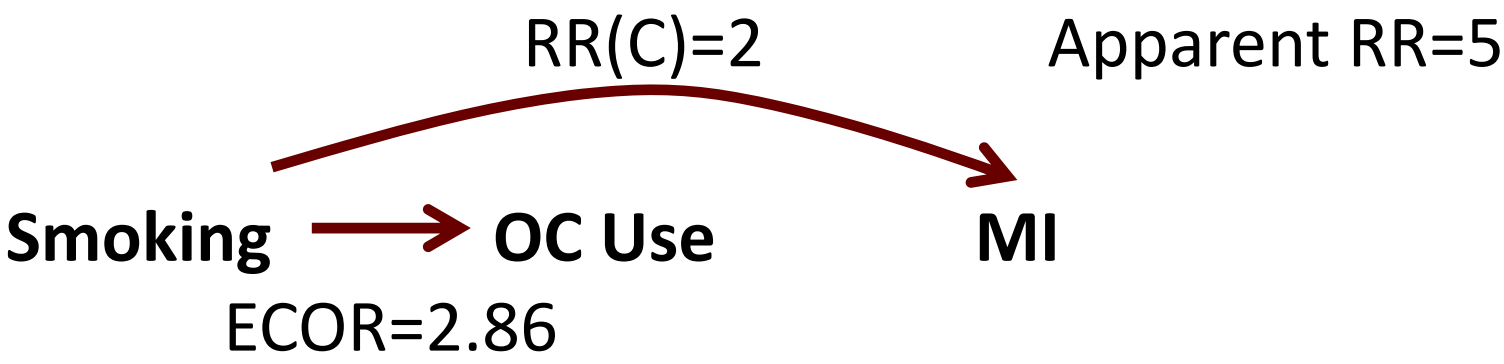
Walker's Bounds of Confounding (3)

ECOR = 4
RR(C) = 4



Alexander Muir Walker. Observation and Inference: An Introduction to the Methods of Epidemiology. Epidemiology Resources, June 1991

Maximum RR Due to Confounding
Example



- What is the maximum relative risk that could be attributed to smoking?
- If there are no other confounders of the observed association, then some of the observed elevation in relative risk from OC use must represent the real effect of OC use on MI incidence, regardless of the prevalence of the confounder.

BREAK

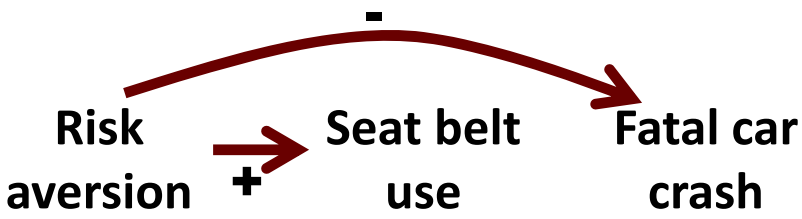
Week 4: Magnitude of Bias due to Confounding

Video 4: E-Values

EPI202 – Epidemiologic Methods II
Murray A. Mittleman, MD, DrPH
Department of Epidemiology, Harvard TH Chan School of Public Health

HARVARD T.H. CHAN
SCHOOL OF PUBLIC HEALTH

E-Value



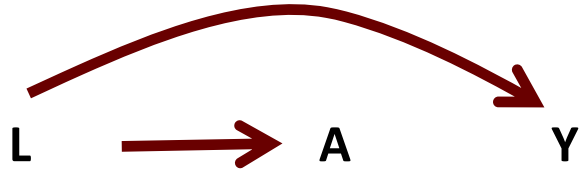
- The E-value is the smallest value for the association between an unmeasured confounder and both exposure and outcome that could fully explain the observed association.

$$\text{E}-\text{value} = RR + \sqrt{RR(RR-1)}$$

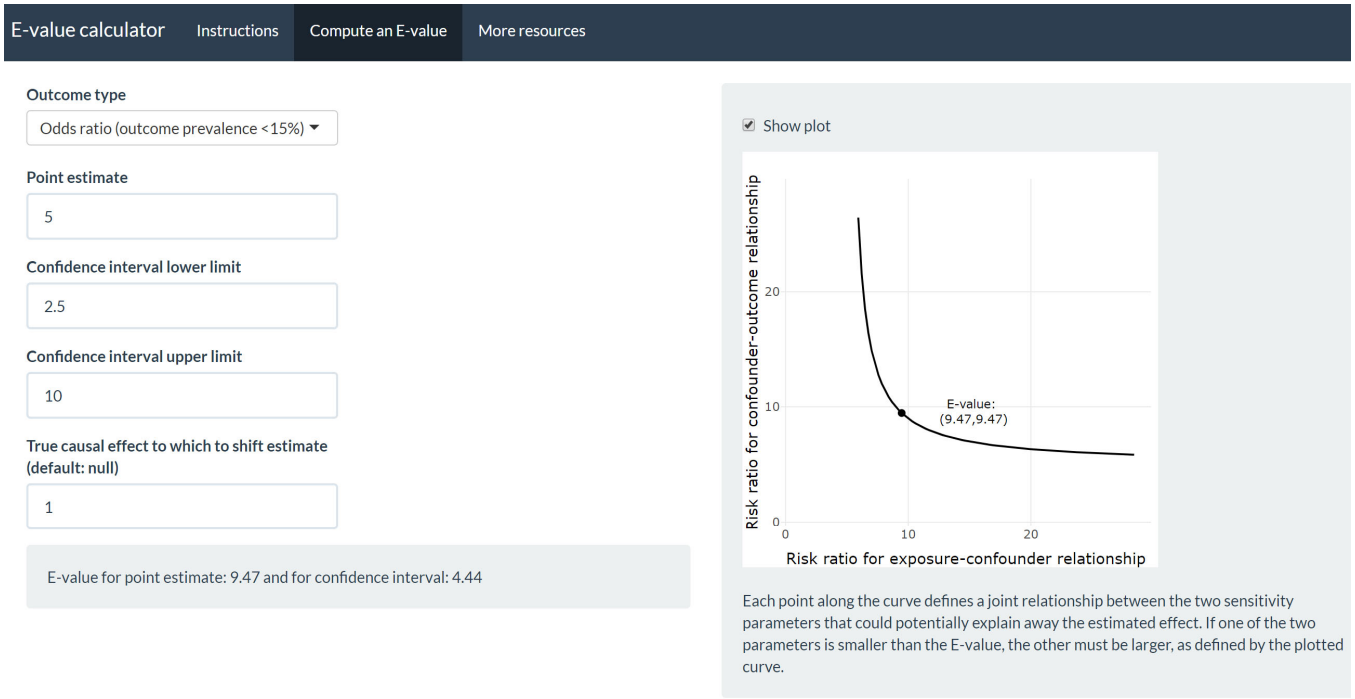
- If RR < 1, take the reciprocal before computing the E-value

VanderWeele TJ, & Ding P. (2017). Sensitivity analysis in observational research: introducing the E-value. Annals of Internal Medicine, 167(4), 268-274.

E-Value Web Calculator



OR= 5.0, 95% CI (2.5,10.0)



https://www.evalue-calculator.com/

Mathur MB, Ding P, Riddell CA, VanderWeele TJ. (2018). Website and R package for computing E-values. Epidemiology, 29(5), e45-e47.

BREAK