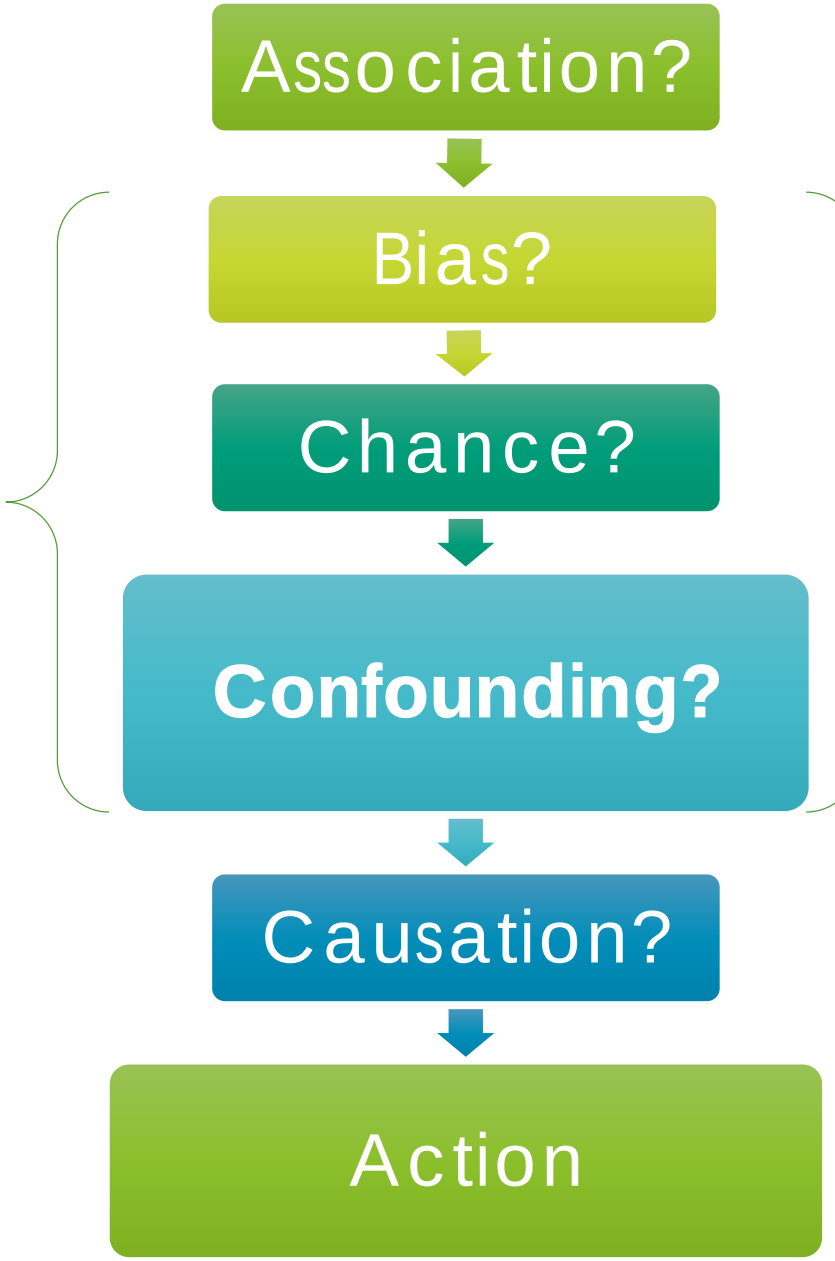
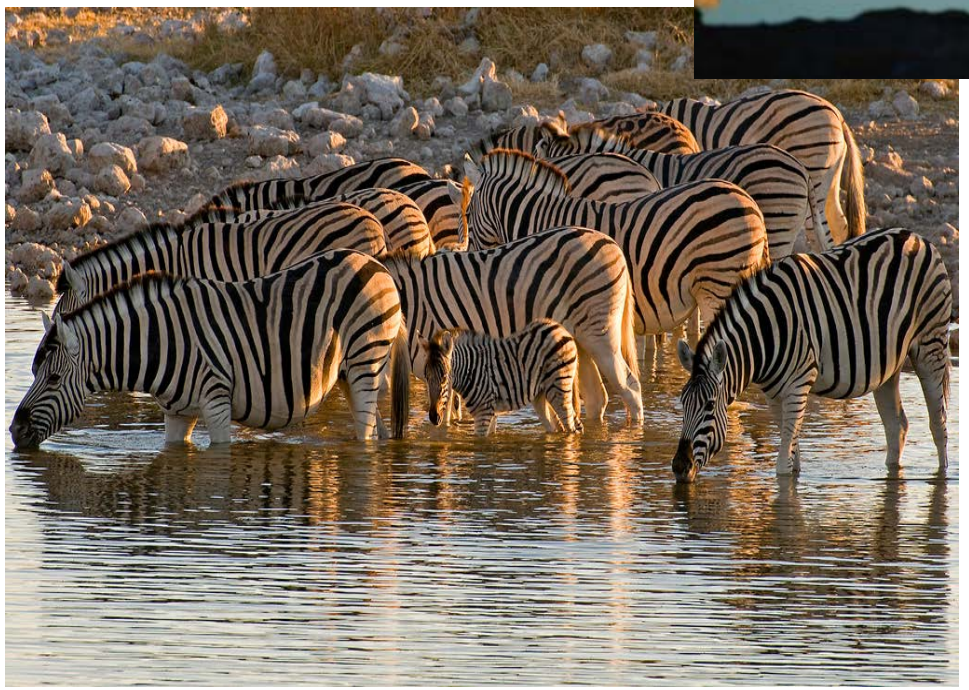
Class 12: Confounding

Health Sciences 2003
Faculty of Health Sciences
University of Lethbridge
Walker



Process of epidemiological research leading to justifiable public health action.


blirk.net

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Learning Objectives:

1. Understand the concept of confounding and criteria for confounders
2. Learning to recognize possible confounders
3. Learn how confounding can be controlled
4. Practice being an aware consumer of epidemiologic research (i.e. study critique)

Consider a study examining the association between coffee and pancreatic cancer?

Adapted from study by MacMahon (1981)

What is the exposure? _____

What is the outcome? _____

What study design(s) might be useful here?_____

What potential sources of error might exist? _____

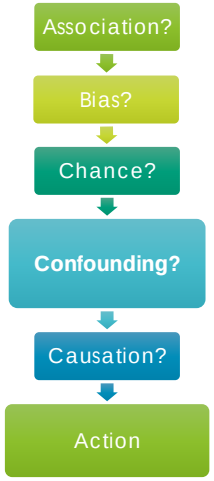
Imagine we calculate and Odds Ratio of 2.1 (CI 1.32-2.87)

How would this be interpreted? _____

Is this statistically significant? _____

Is this association real?

Does coffee cause pancreatic cancer? Or could it be due to some other factor?



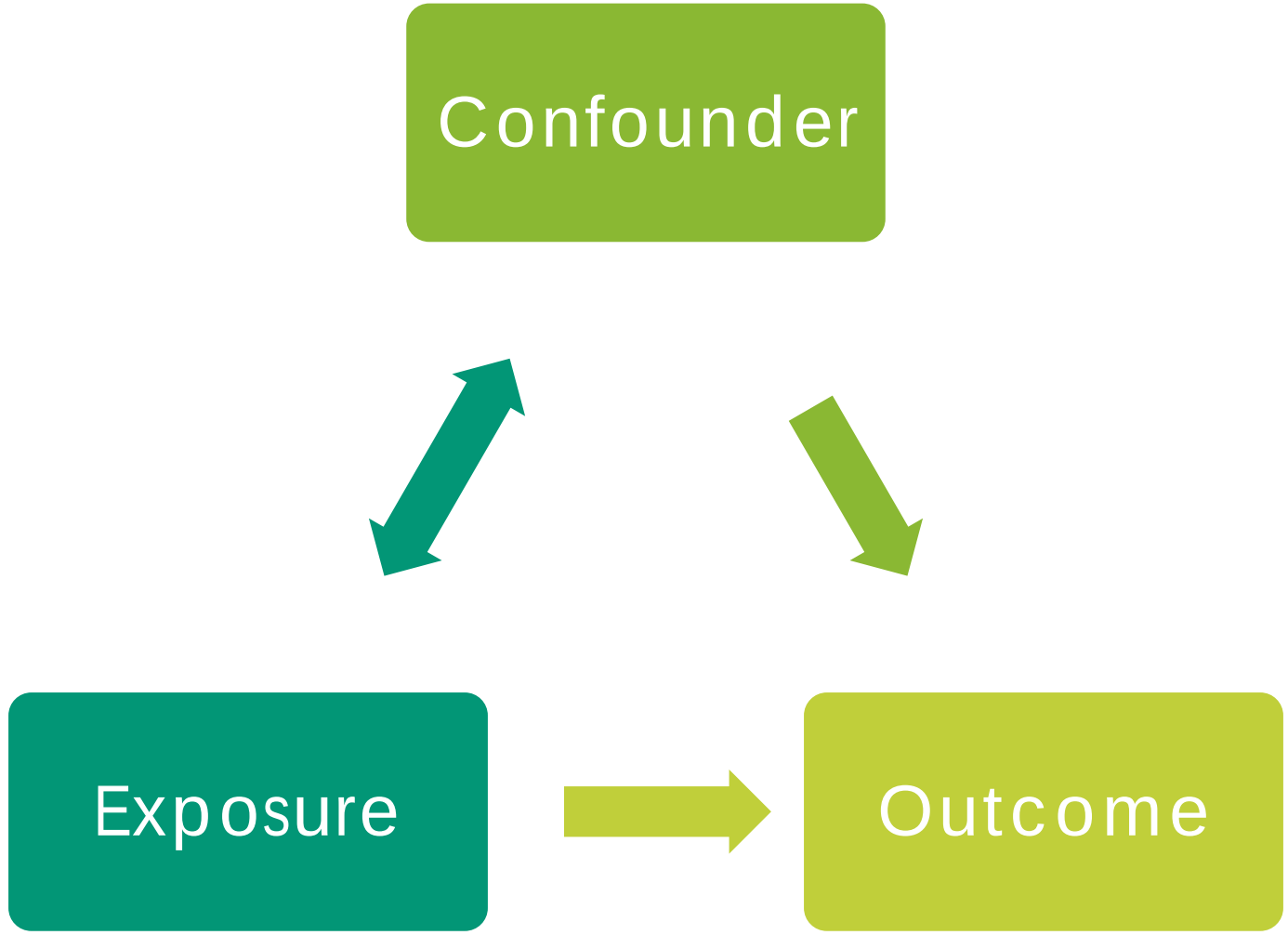
http://www.heartwiseministries.org/heartwise/wp-content/uploads/2013/09/Lady-Smoking-blackwhite.jpg

Confounding:

A distortion in the degree of association between an exposure and outcome due to the **mixing of effects** between the exposure and a third factor.

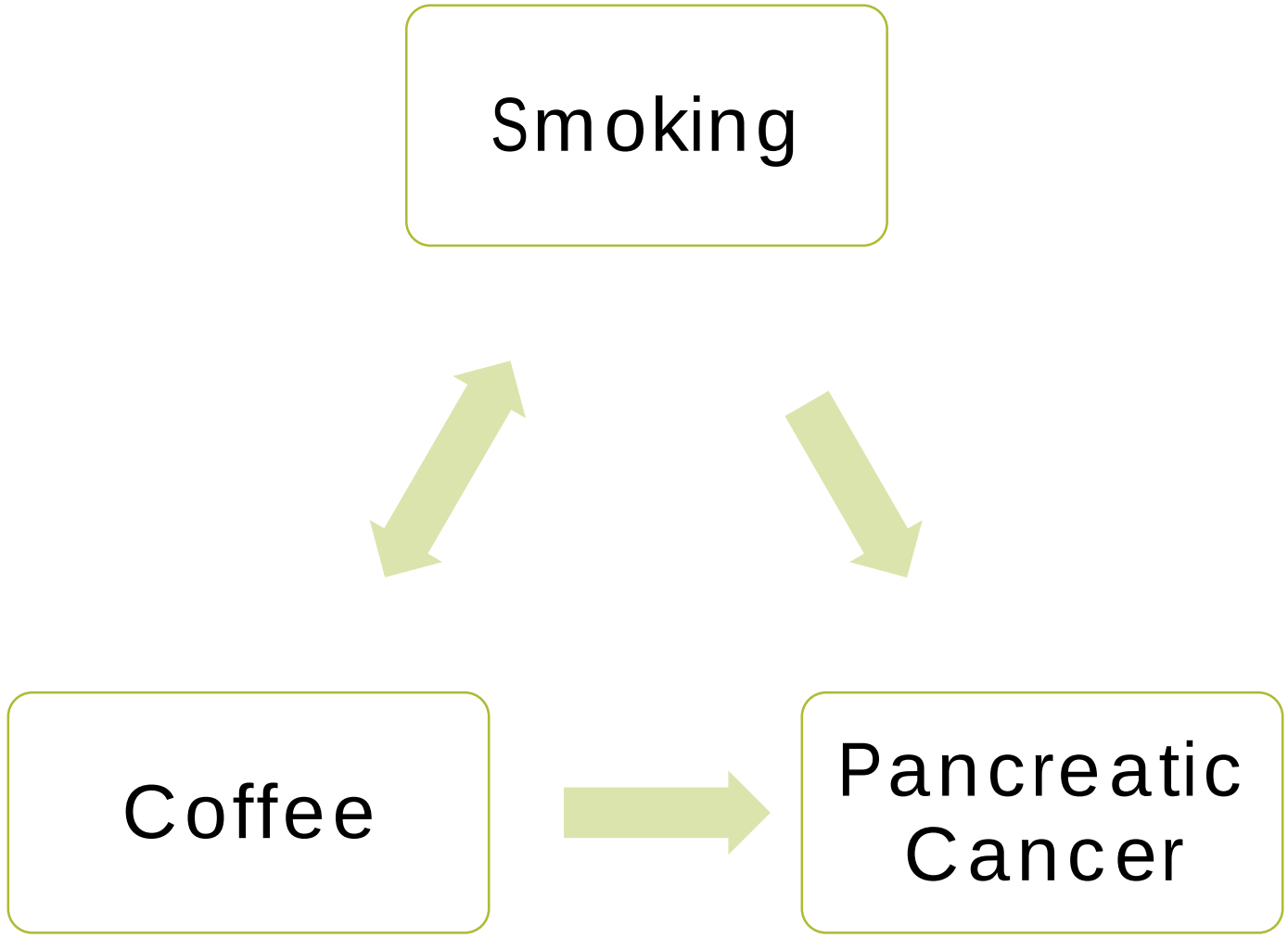
Criteria for confounders

1. It must be *associated with the exposure of interest*
2. It must be an *independent risk factor for the outcome*
3. It must *not lay on causal pathway* (i.e. be an intermediate) between the exposure and the outcome.


Confounder
Exposure
Outcome

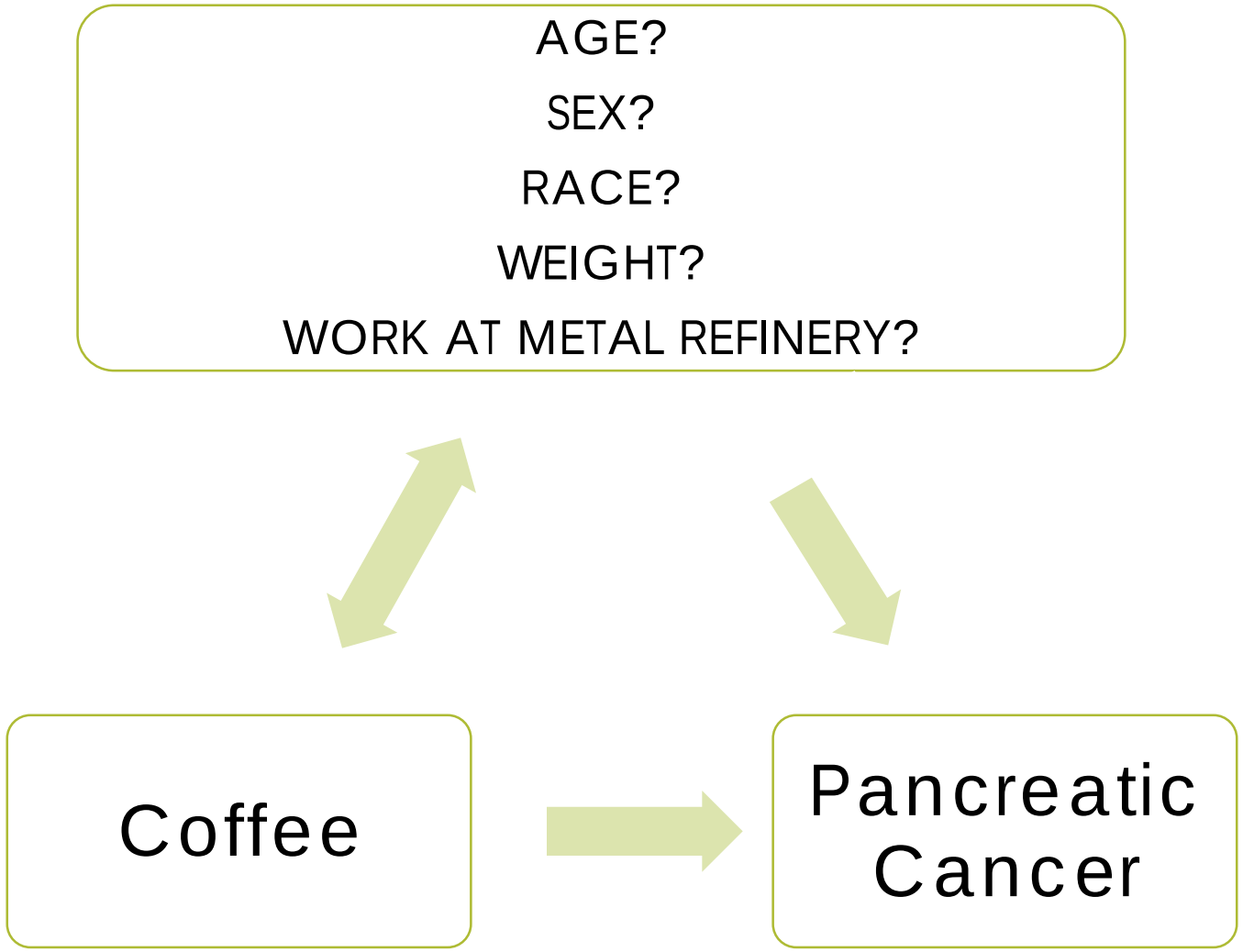
Are Criteria Met for Confounding?

1. MET - Smoking is related to coffee drinking
2. MET - Smoking is an independent risk factor for pancreatic cancer
3. MET - Smoking is not caused by coffee drinking (i.e. it is not the mechanism through which coffee would influence pancreatic cancer)

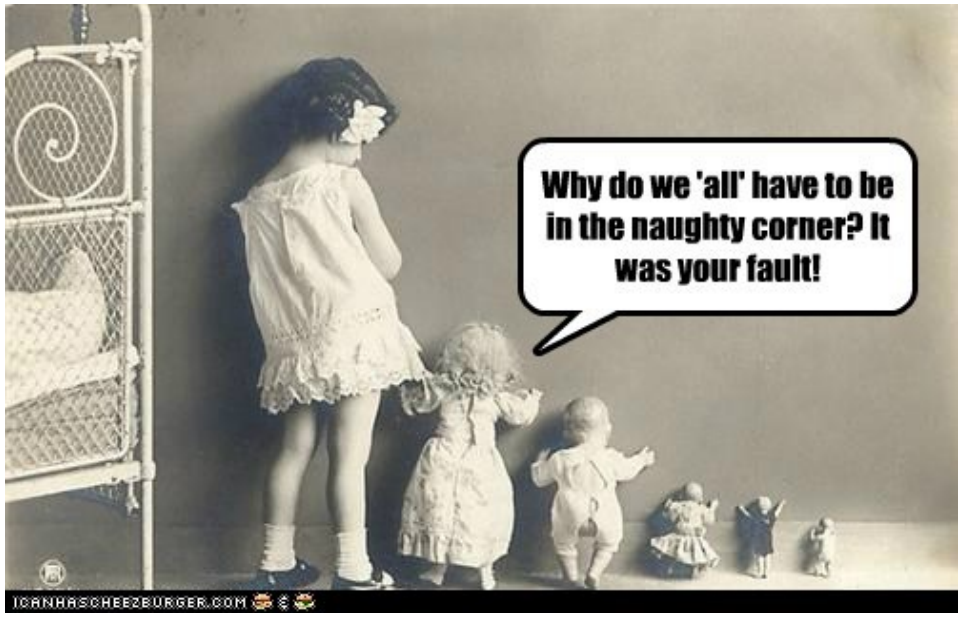


Are Criteria Met for Confounding?

1. Is it related to the exposure of interest? (should be yes)
2. Is it an independent risk factor for pancreatic cancer? (should be yes)
3. Does it lay on the causal pathway between coffee and cancer? (should be no)

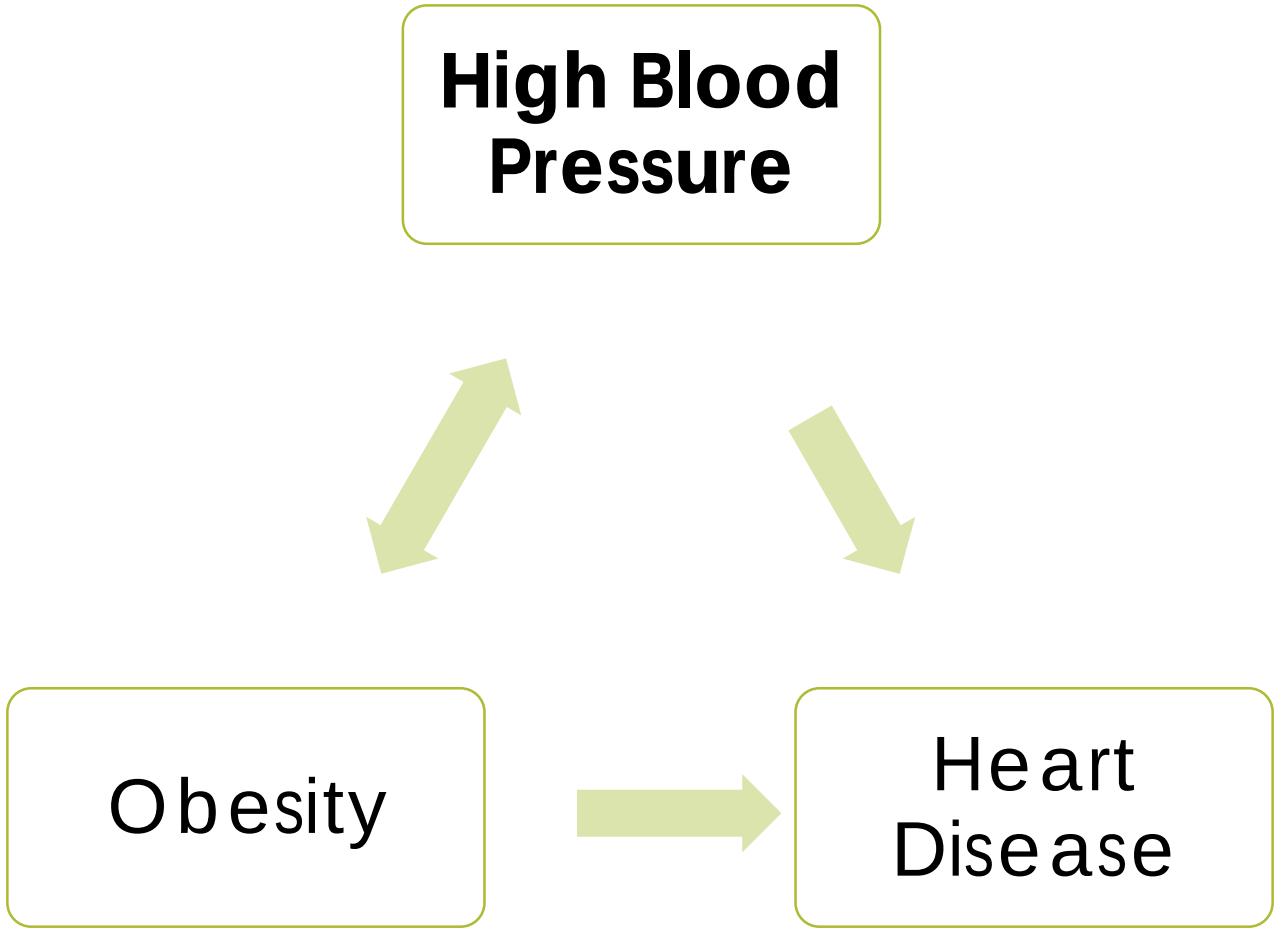


http://www.cancer.org/cancer/pancreaticcancer/detailedguide/pancreatic-cancer-risk-factors



Always suspect a confounder if the variable in question is a known (or suspected) independent risk factor to the outcome, and especially if it is known to be associated with the exposure of interest.

Confounder?



Common Confounders

- Age
- Sex
- Socioeconomic status
- Smoking

*many studies will control for these more common confounders, but others always need to be considered.

*for confounding to have effect on outcome in practice, it must also be prevalent in the population (rare confounders will not typically affect study results as most of the population are not exposed to the confounder)

Controlling for Confounding

- Almost always exist – but studies should acknowledge and try to control for confounding…HOW?

1. Prevention is key (in study design stage)
    1. Randomization
    2. Restriction
    3. Matching

2. Adjust for it in the analysis
    1. Stratification
    2. Statistical Modelling

*Increasing sample size will **not** fix confounders in observational studies…but may, however, in in RCTs

Randomization

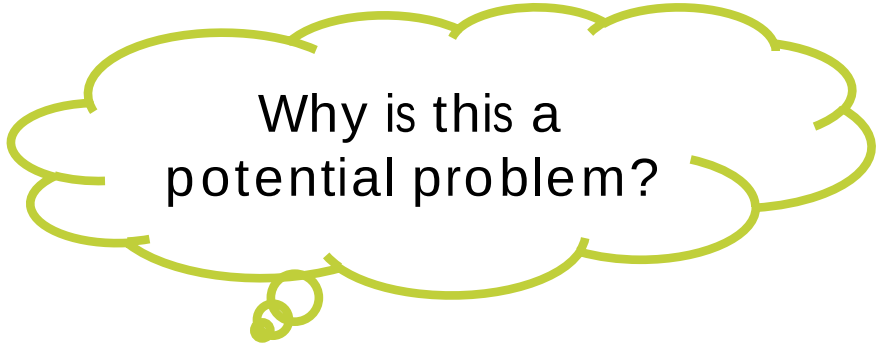
- Randomization is one of the greatest strengths of RCTs as randomization makes the study groups more comparable (i.e. less variability of factors – known and unknown - between the groups because of the equal probability of being assigned to the exposed and unexposed groups) and, as such, decreases the likelihood of bias or confounding.

Restriction

Why is this a potential problem?

- Limiting study subjects to those with certain characteristics

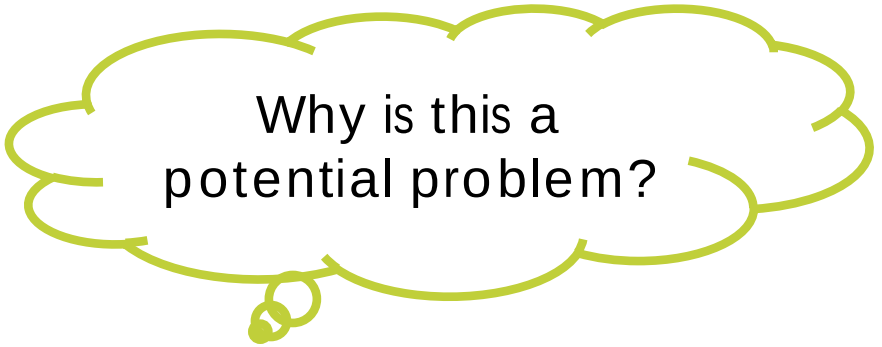
Matching



- Evenly distribute the potential confounders between the study groups by matching study participants based on the confounding characteristic

- Most common in case-control studies when we can select controls to match the cases

Stratification



- Study participants are divided into groups, or strata, based on the potential confounding factors and the measure of association is calculated in each group separately

- This is what is meant when outcomes are said to be “adjusted” by the confounder

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glucose Levels and Risk of Dementia

Paul K. Crane, M.D., M.P.H., Rod Walker, M.S., Rebecca A. Hubbard, Ph.D., Ge Li, M.D., Ph.D., David M. Nathan, M.D., Hui Zheng, Ph.D., Sebastien Haneuse, Ph.D., Suzanne Craft, Ph.D., Thomas J. Montine, M.D., Ph.D., Steven E. Kahn, M.B., Ch.B., Wayne McCormick, M.D., M.P.H., Susan M. McCurry, Ph.D., James D. Bowen, M.D., and Eric B. Larson, M.D., M.P.H.

ABSTRACT

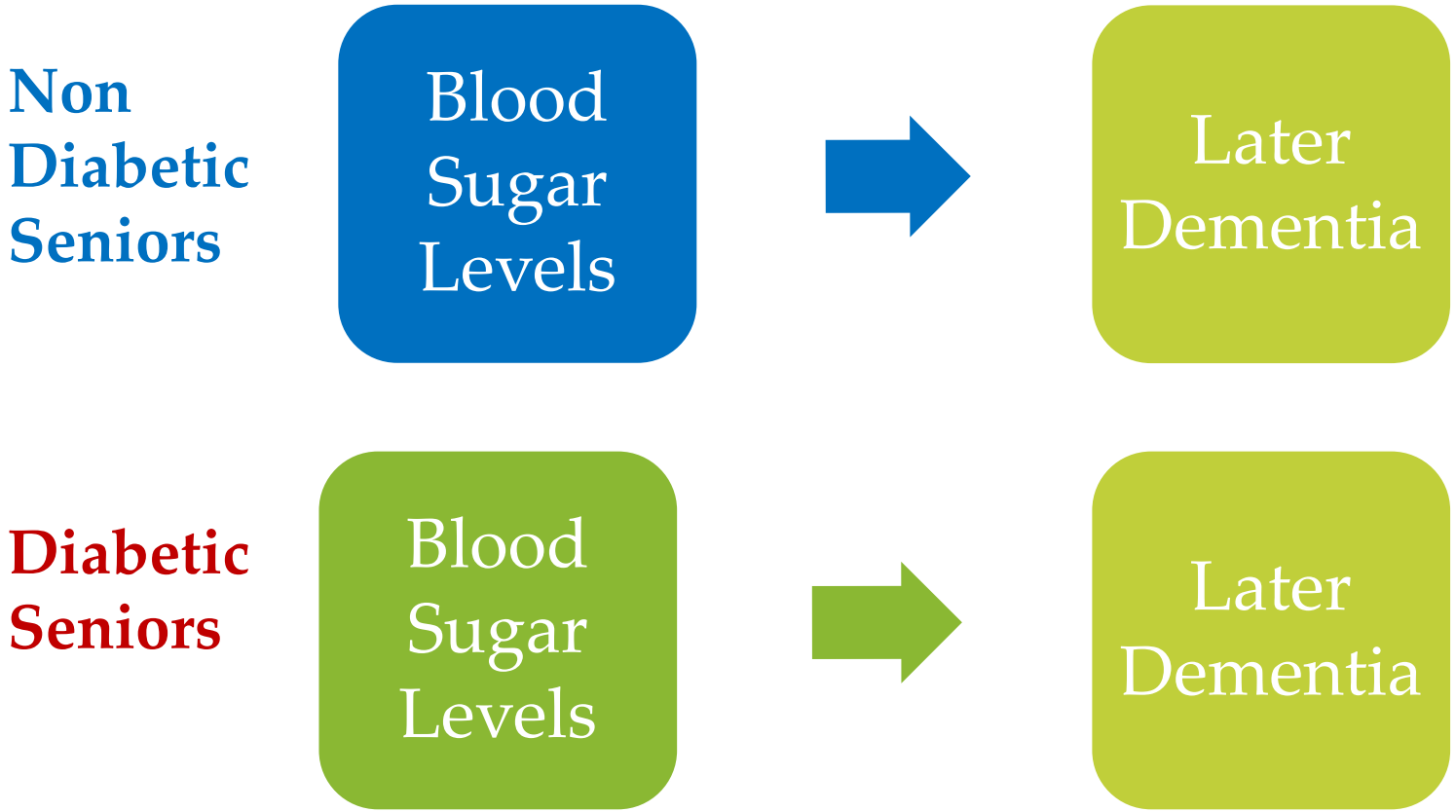
BACKGROUND

Diabetes is a risk factor for dementia. It is unknown whether higher glucose levels increase the risk of dementia in people without diabetes.

METHODS

We used 35,264 clinical measurements of glucose levels and 10,208 measurements of glycated hemoglobin levels from 2067 participants without dementia to examine the relationship between glucose levels and the risk of dementia. Participants were from the Adult Changes in Thought study and included 839 men and 1228 women whose mean age at baseline was 76 years; 232 participants had diabetes, and 1835 did not. We fit Cox regression models, stratified according to diabetes status and adjusted for age, sex, study cohort, educational level, level of exercise, blood pressure, and status with respect to coronary and cerebrovascular diseases, atrial fibrillation, smoking, and treatment for hypertension.

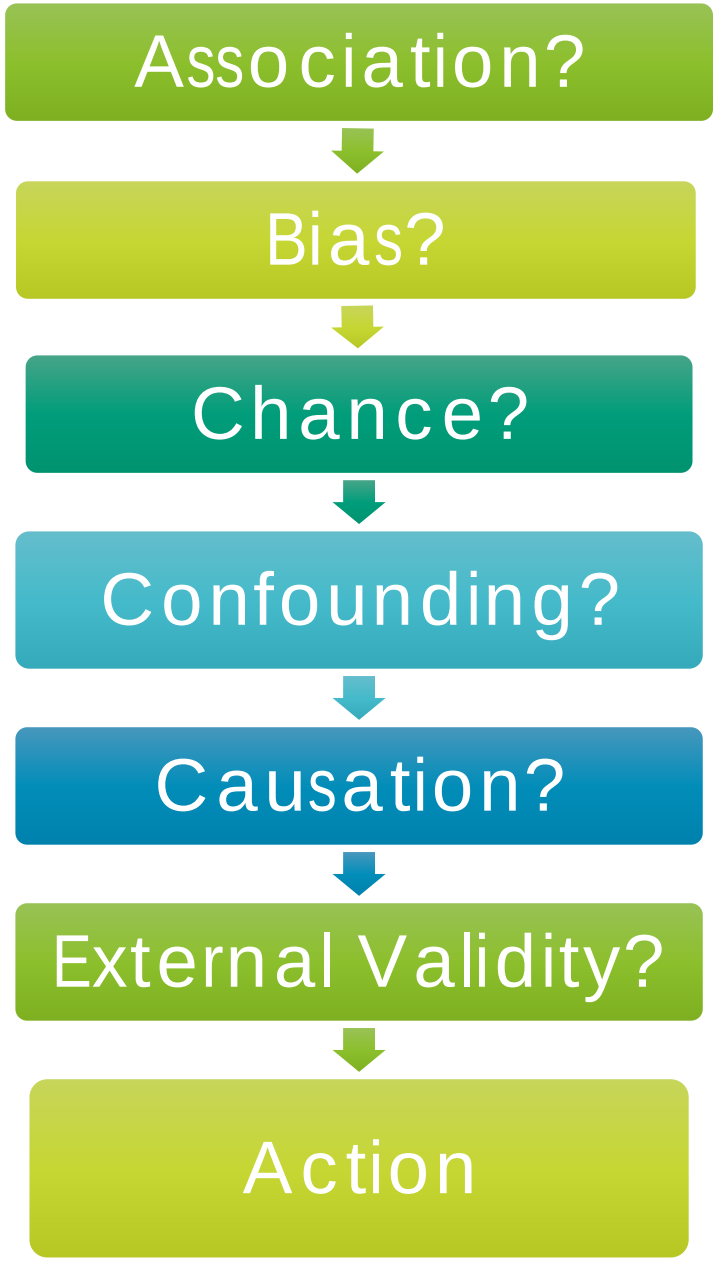
Dealing with Confounding in the Analysis via **Stratification**



Statistical (multivariable) Modelling

Think about that tomorrow…in advanced Epi or Biostatistics

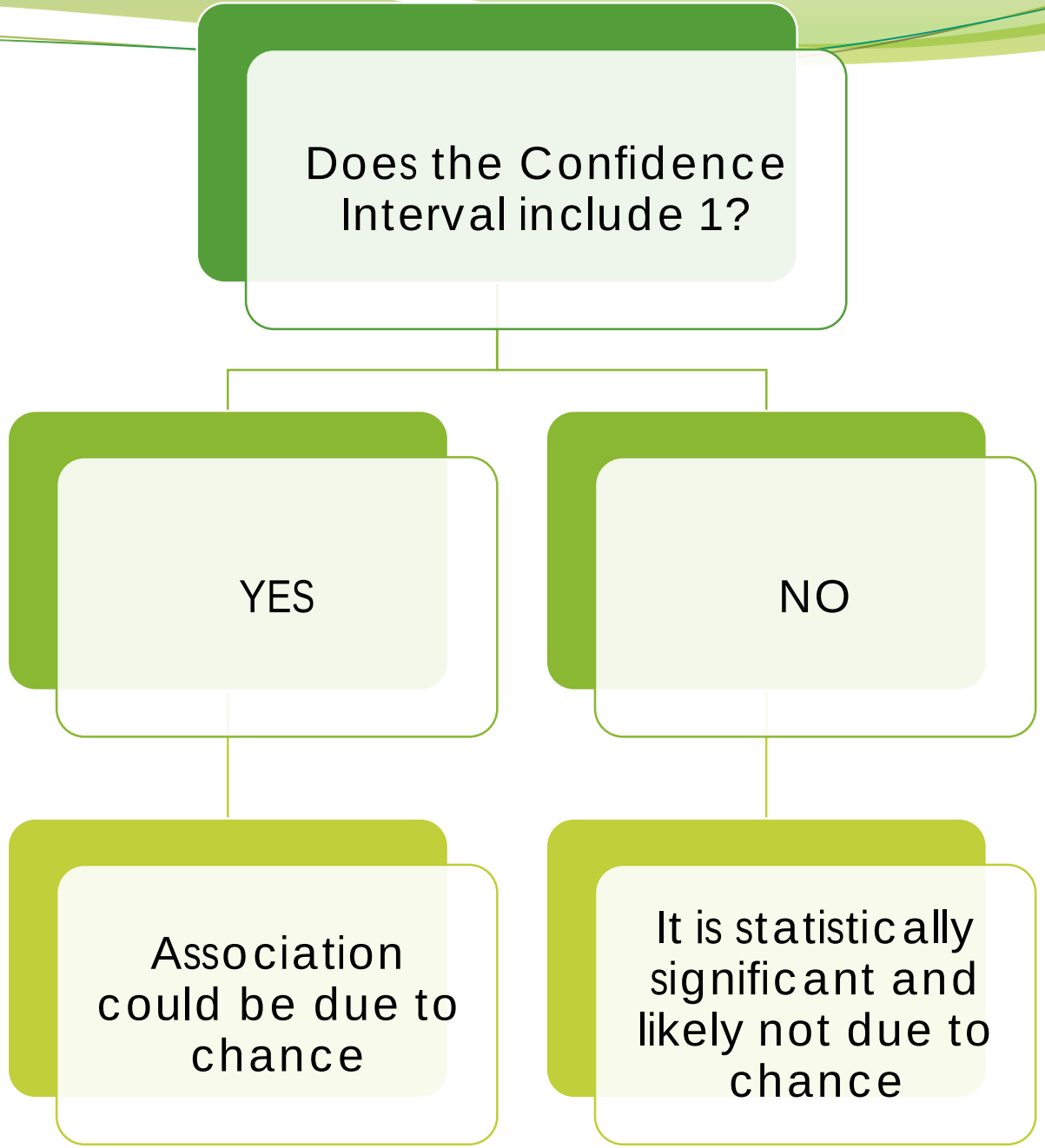
Process of epidemiological research leading to justifiable public health action.



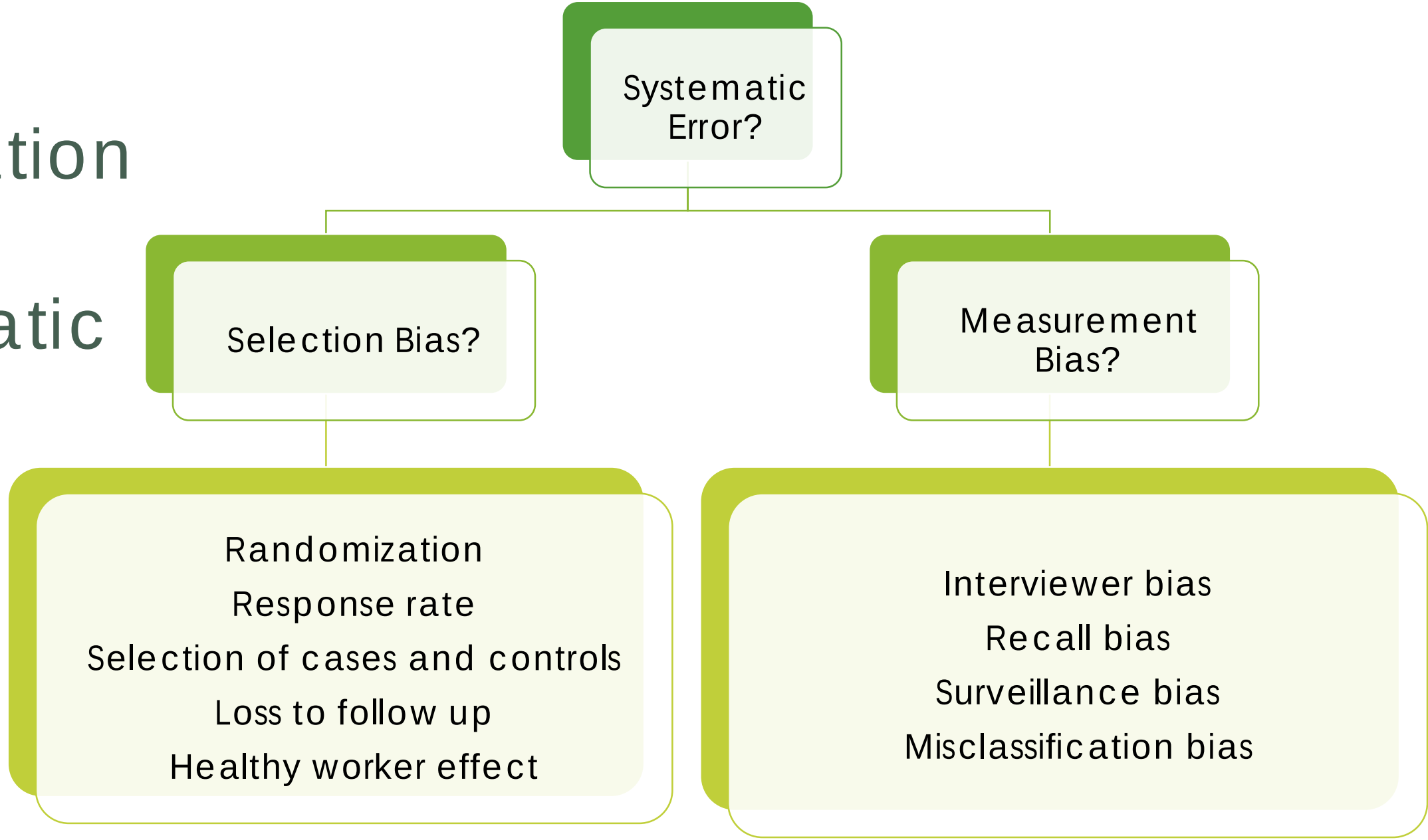
So, you see gold flecks...(i.e. an association between exposure and outcome)...are you sure the mines are not salted?!

1. Is it due to random error – chance?
2. Is it due to systematic error?
3. Is it due to confounding?
4. Is it causal?
5. Is it externally valid (is it generalizable)?

Is the association due to chance?

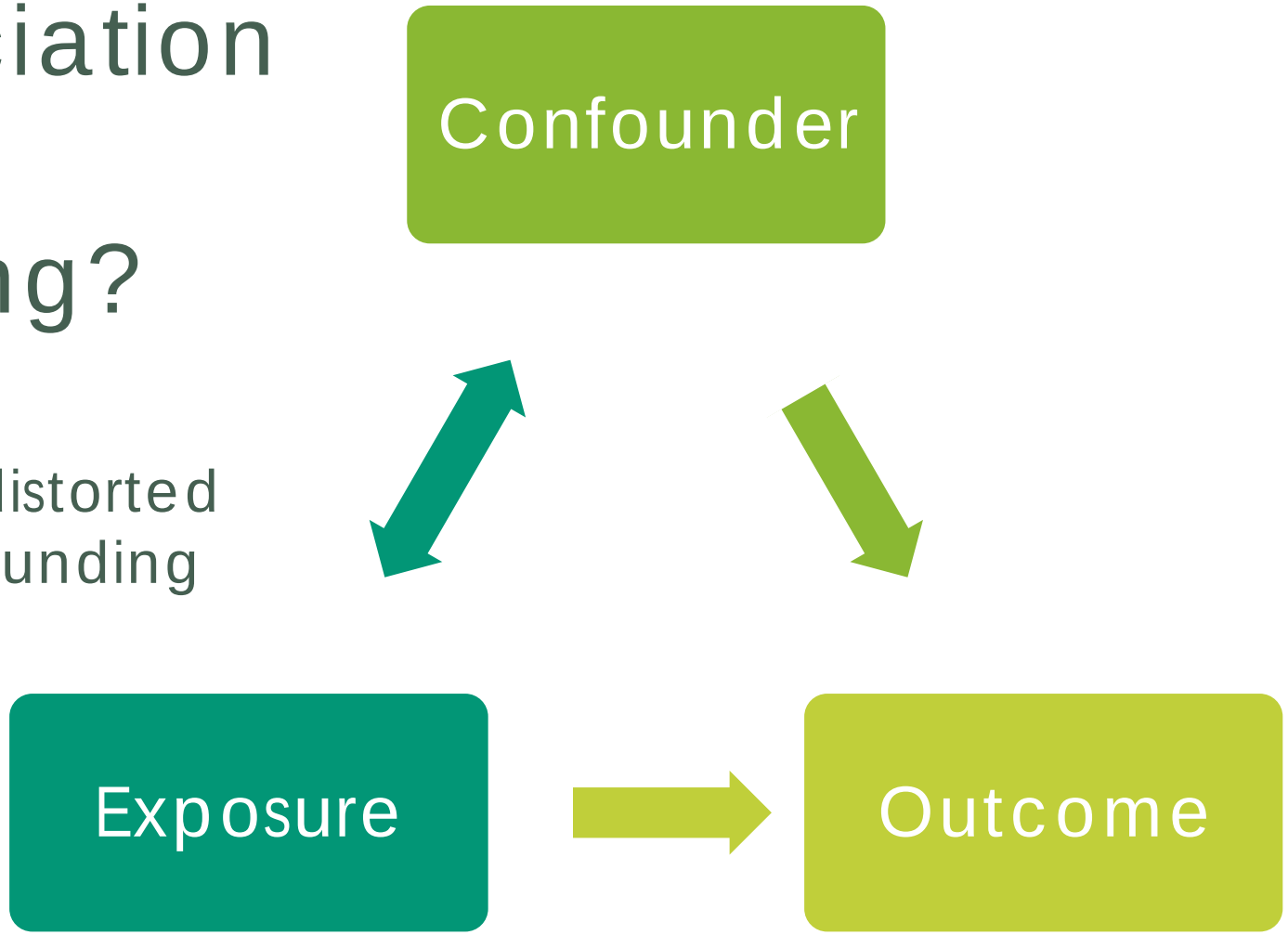


Is the association due to systematic error?



Is the association due to confounding?

Is the association distorted by potential confounding variables?



Is it a cause-and-effect relationship?

HILL's Postulates

1. Strength of association
2. Temporal sequence
3. Dose-Response relationship
4. Biological Plausibility
5. Repetition
6. Experimental evidence

Is it generalizable (external validity)?

- It is true for the sample, but would it be true for the entire population or other populations?
- Is the sample population representative of the larger population?
- No hard rule on this, but based on biological relevance

In-Class Assignment #4