

# Causal Association : Cause To Effect

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# Measure of Association- Concepts

- If 'more' disease occurs in a group that smokes compared to the group that does not smoke, there is an 'association' between the disease and smoking
- If 'more' disease occurs in Hindus than in Muslims, there is an 'association' between the disease and race
- If 'more' lung cancer deaths occur in certain occupations than others, there is an 'association' between occupational exposure characteristics and lung cancer

# Why study association?

- Is the first step in establishing a hypothesized causal relationship
- Association by itself does not implicate causation

# From Association to Causation

- Does the association make biologic sense?
- An isolated study or, many studies in different populations find a similar association?
- Does the association support a **dose response**, i.e., more exposure is associated with more disease?

- All epidemiological hypotheses is based on the concept of association between exposure & disease
- Primary objective is to see whether an association is causal or not.
- Presence of an association in no way implies that the relationship is that of a cause & effect.
- The association means a statistical dependence between two variables i.e. when a change in one variable parallels or coincides with the change in other variable

a relationship between cause & effect  
may not be always a causal one, for  
the reason that

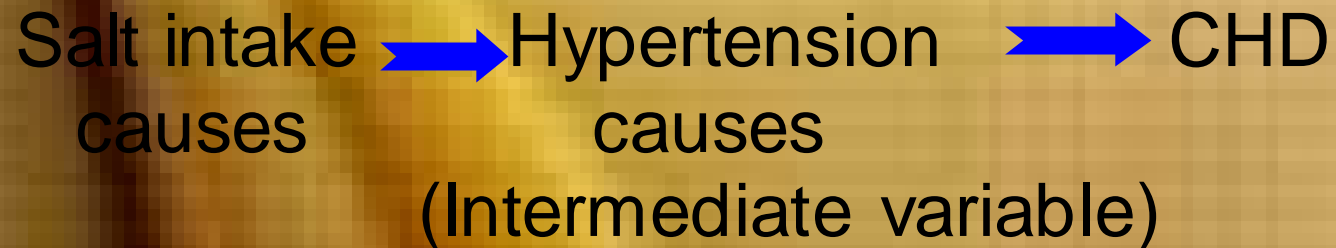
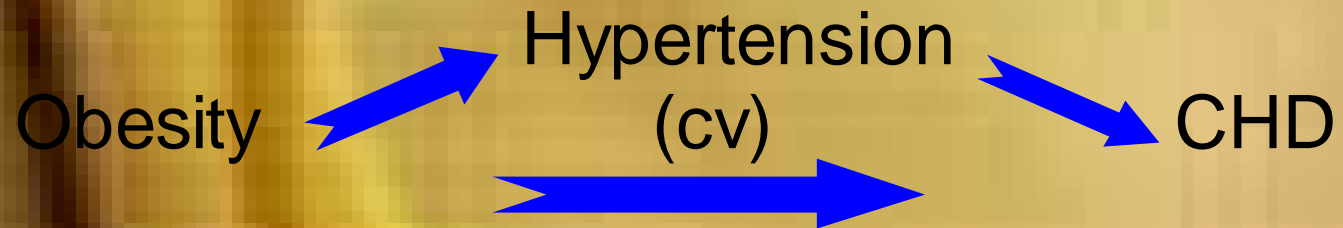
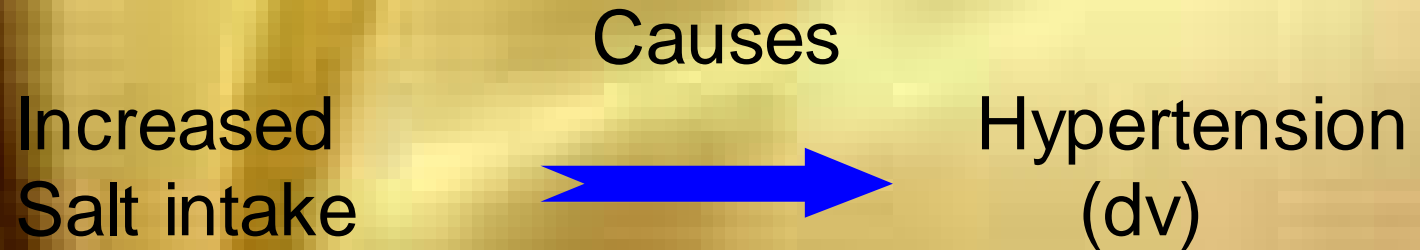
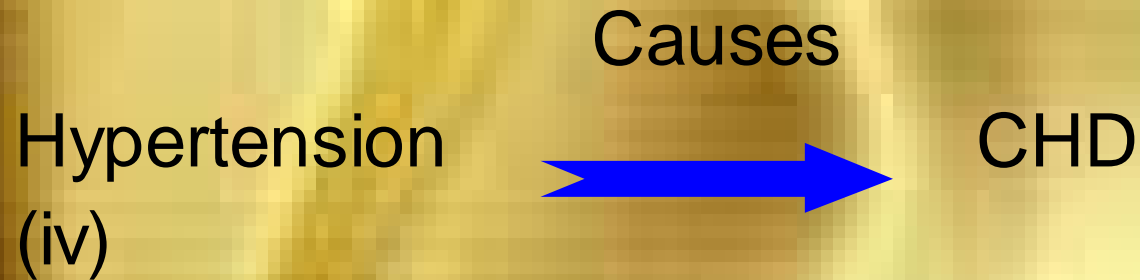
Bias,

Chance &

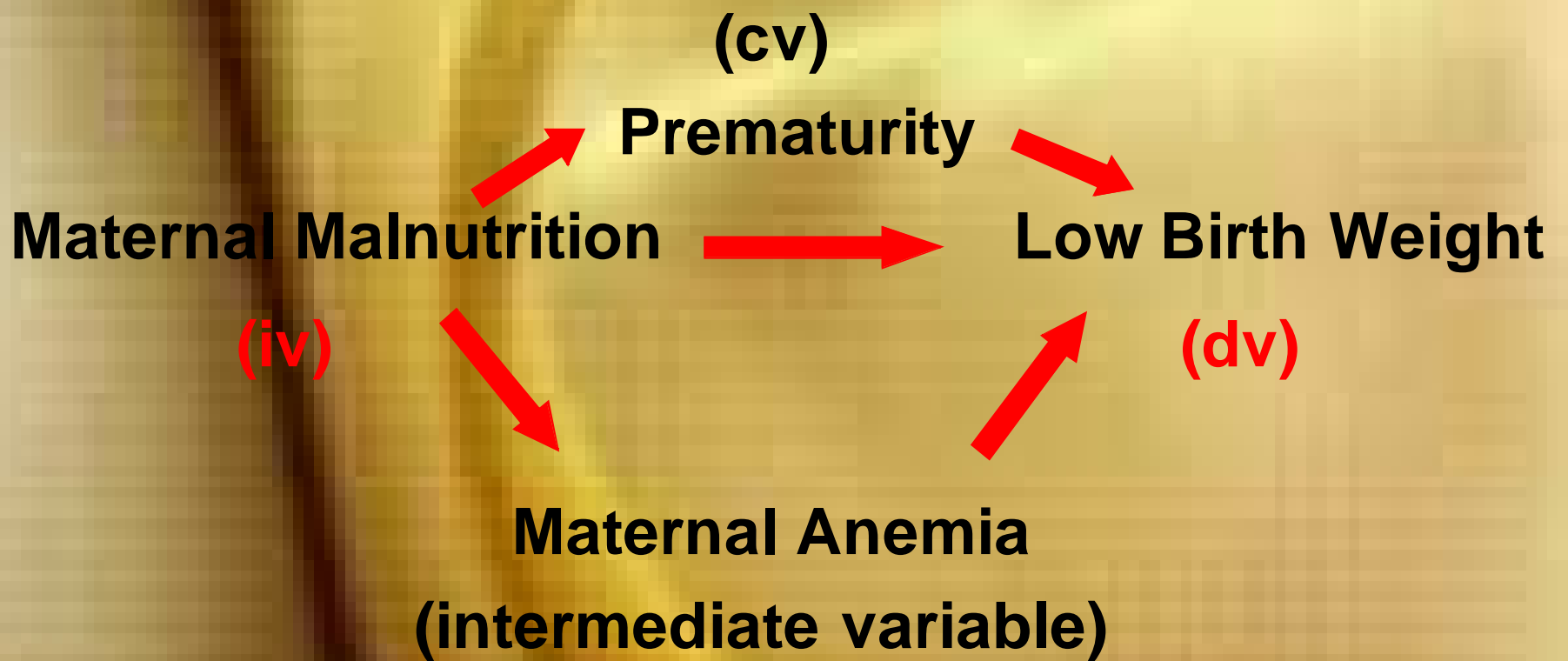
Confounding may under or over play  
the association

# The variable in an association are-

- Dependent (dv)
- Independent (iv)
- Confounding (cv)
- Intermediate (im.v)







# Factors governing association

- A. Magnitude of association or strength of association
- B. Biological likelihood
- C. Consistency with other findings
- D. Time sequence &
- E. Dose-response relationship

# Approaches in establishing a causal association-

Basic questions are -

- Is there an association actually existing
- Is the association likely to be causal

An association should satisfy **confirmatory criteria for causality**, like

- Strength
- Biological gradient (dose- response relationship)
- Temporality ( time sequence)
- Biological plausibility
- Specificity
- Consistency &
- Experimental proof

# Types of Association

- **Causal**
  - **Direct** causal (iodine deficiency-goiter)
  - **Indirect** causal (iodine deficiency-goiter-thyroid adenoma)
- **Non-causal**
  - Chance,
  - Numerator analysis alone
  - Bias

E → D (Direct causality)

E → D (Indirect causality)

C

E1 → D (Independently causal)

E2 → D

E1 + E2 → D (conditionally causal)

E2

(E1 and E2 need to be present simultaneously)

**E= Exposure**

**D= Disease**

**C=Confounding**

# Two ways to get at the 'Association'

- Start with a group of 'exposed' and a group of 'unexposed'. Determine how many (what proportion) in each group have or develop the disease in question.
- Start with a group of people with the disease and a group free of the disease. Determine how many (what proportion) in each group has the exposure in question

➤ Prospective approach;

- Comparison of the proportion of those developing disease in the exposed and the unexposed group constitutes a measure of association (relative risk) between the disease and the exposure.

➤ Retrospective approach.

- Comparison of odds (related to proportion) of having exposure in the disease and the disease-free group constitutes a measure of association (odds ratio) between the disease and the exposure.



# Measures of Association

- Standardized Morbidity Ratio (SMR)
- Standardized Mortality Ratio (SMR)
- Relative Risk (RR)
- Odds Ratio (OR)
- Attributable Risk (AR)

# Standardized Morbidity (Mortality) Ratio

- SMR= Ratio of an 'observed' to an 'expected'
- If 'observed' and 'expected' are equal, that is, if  $SMR=1$ , there is no association
- If SMR is different than 1, there is association
- Remember, association does not implicate causation

# Examples of SMR

- Observed= number of cases of lung cancer deaths actually observed in an occupational group.

Expected= number of lung cancer deaths expected in this group based on general population rates.

- If observed and expected are equal, there is no reason to suspect that the particular occupation carries higher risk of lung cancer.
- If, on the other hand, observed is different than the expected, one can infer an 'association' between the particular occupation and lung cancer.

# SMR Example

- In a city, observed number of deaths by various causes are available by occupation  
Expected number of deaths for each occupation are calculated by applying the citywide rates to each occupation.
- If number of observed and actual deaths are equal for each occupation, one would not suspect a relationship between occupational characteristics and risk of death for a certain cause.
- If, on the other hand, for a specific cause of death, some occupations exhibit excess while others exhibit a deficit, an association between occupational characteristics and the specific cause of death would be inferred.

# Prospective Approach: Relative Risk

	Disease Present	Disease Absent	Total
Exposed	30	70	100
Un-exposed	10	90	100

$$\text{Relative Risk} = (30 / 100) / (10 / 100) = 3.0$$

# Relative Risk (RR)

- Consider incidence rate of lung cancer in heavy smokers and non-smokers
- If the incidence rate is the same for heavy smokers and non-smokers, no association can be inferred between smoking and lung cancer
- If the incidence rate is higher among heavy smokers **RELATIVE** to non-smokers, an association would be suggested.
- Incidence rate can be taken as a measure of risk, and the ratio of the two incidence rates would then be the Relative Risk (RR)

## Relative Risk (RR) cont...

- Relative Risk (RR)= Ratio of the risk of disease in 'exposed' and 'unexposed'
- $RR=1 \Rightarrow$  No association between the exposure and the disease.
- $RR>1 \Rightarrow$  There is an association (risk factor)
- $RR<1 \Rightarrow$  There is an association (protective factor)
- Farther from the null value the RR is, stronger is the association
- No matter how strong the association, it can not in and by itself implicate causation

# Retrospective Approach: Odds Ratio

	Disease Present	Disease Absent	Total
Exposed	30	70	100
Un- exposed	10	90	100

$$\text{Odds Ratio} = (30 / 10) / (70 / 90) = 3.85$$

If the disease is rare, the odds ratio provides a good approximation of relative risk.

However, in the literature, odds ratio and relative risks are (erroneously) considered synonymous.



# Attributable Risk (Risk Difference)

Incidence in exposed – incidence in unexposed

AR is an expression of existence of a cause-effect relationship.

An AR value of 0 (Zero) means no association between cause and effect.

AR is basically a Ratio

- *Ratios* are appropriate measures for examining the importance of a given risk factor in the etiology of the disease. This is because the ratio provides an indication of how many times is the risk of the disease to a person with the exposure to the factor compared to one who is not so exposed.

But suppose we are interested in finding out to what extent a disease can be prevented in a population if a particular risk factor was eliminated?

Or suppose we are interested in finding out to what extent is the particular risk factor responsible for the disease in an exposed individual?

The first question pertains to what is known as the **population attributable risk (AR )**

The second question pertains to what is known as the **exposure attributable risk (AR% )**.

Exposure	Disease		Total
	Hypertension		
Smokers	a (120)	b (280)	a + b =400
Non-smokers	c (30)	d (570)	c + d =600
Total	a + c (150)	b + d (850)	1000

$$RR = \frac{a/a+b}{c/c+d}$$

$$RR - 1$$

$$AR = \frac{RR - 1}{RR} \times 100$$

$$OR = \frac{ad}{bc}$$

Incidence in Total pop. – Incidence in exposed

$$AR_p \% = \frac{\text{Incidence in Total pop.} - \text{Incidence in exposed}}{\text{Incidence in total Pop.}} \times 100$$

Incidence in total Pop.

$$AR_p \% = \frac{AR}{le} \times 100 = \frac{le - lo}{le} \times 100$$

$$RR = \frac{a / a + b}{c / c + d} = \frac{120 / 400}{30 / 600} = 6.0$$

$$AR = \frac{RR - 1}{RR} = \frac{6 - 1}{6} = 0.83$$

$$AR\ p\ \% = \frac{0.83}{120 / 400} = \frac{0.83}{0.25} = 3.32$$

$$O.R. = \frac{a\ d}{b\ c} = \frac{120 \times 570}{280 \times 30} = 8.14$$