ASSOCIATION & CAUSATION

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Contents

INTRODUCTION

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- **Epidemiology** aims at Promotion of health by discovering the causes of diseases & the way in which they can be modified.

- **Identification of Causal relationships b/n disease and suspected factor.**

Environmental exposure

Disease or Other Outcome

Identify Disease in Community

Descriptive Study

Relate to Environment & Host Factor

Suggests an Aetiological hypothesis

Analytical & Experimental Studies

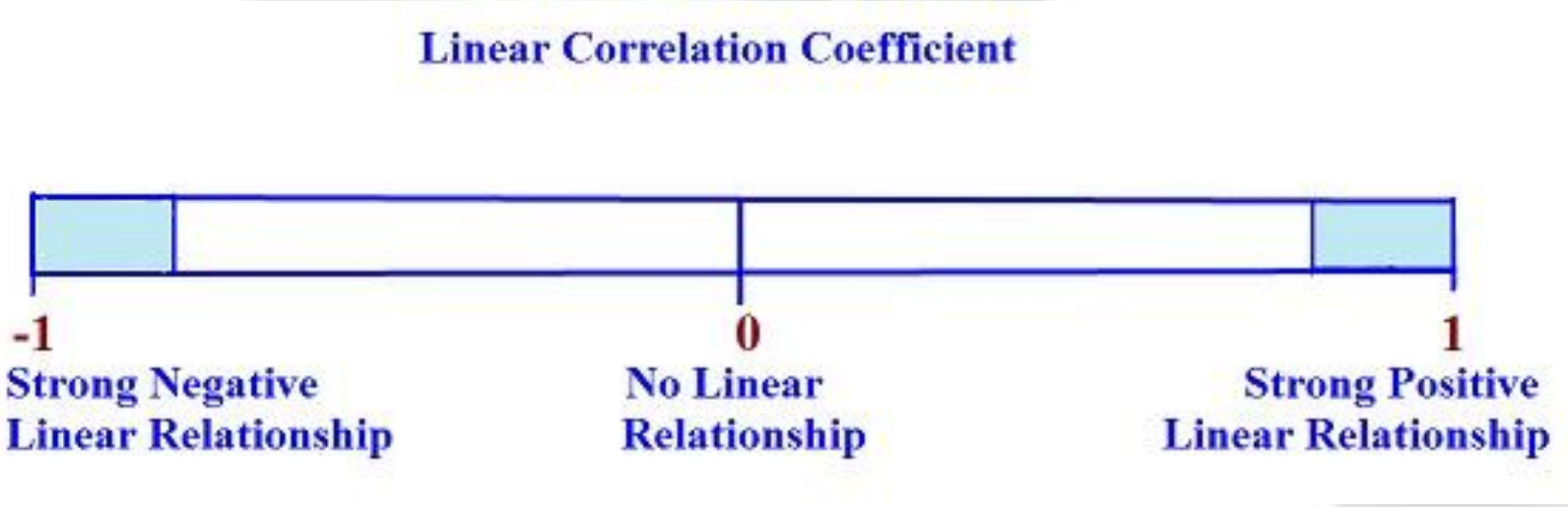
Test the Hypothesis

Which either confirms or refute the Observed Association. Causal or Not?

ASSOCIATION

- ✓ Concurrence of Two Variables more often, than would be expected by Chance.

- ✓ **CORRELATION indicates the Degree of Association.**



Association

- It is the relation between the two variables namely the suspected factor (smoking) and the disease (lung cancer).
- The relation is said to be ‘associated’ when the two variables occur concurrently more frequently.

CAUSATION

➢ **CAUSE -** an event, condition, characteristic (or a combination) which plays an important role / regular / predicable change in occurrence of the outcome (e.g. smoking and lung cancer)

Factors involved in Causation

Precipitating Factors	Exposure to agent, Imm. Co
Predisposing Factors	Age, Sex, Previous Illness
Enabling Factors	Low SEC, malnutrition
Reinforcing Factors	Repeated Exposure

Causation

- The association is said to causally associated when one event invariably gives rise to another event without exception.
- If the sales of the cigarettes is associated with increased incidence of lung cancer, their causality is proved.
- Their causality is also proved when the relation is stronger (i.e. when relative risk is increased).

- Similarly, the causal nature between maize consumption and development of pellagra is established, if on changing the diet of the patients from maize to wheat, they are cured of pellagra.

Similar examples of association with causal relation are

- Air pollution and Chronic Bronchitis,
- Tobacco chewing and Oral Cancer,
- Soft water and Cardiovascular Diseases,
- Alcoholism and Cirrhosis of liver,
- Maize eating and Pellagra,
- Saturated fats and Coronary Artery Disease, etc.

TYPES OF ASSOCIATION

1. SPURIOUS ASSOCIATION

2. INDIRECT ASSOCIATION

3. DIRECT ASSOCIATION

   A. One-to-One Causal Relationship

   B. Multi-Factorial Causation

SPURIOUS ASSOCIATION

- ✓ Some observed associations b/n a suspected factor and disease may not be real.
- ✓ This Fallacy of presumption arises when two variables are improperly compared (due to Bias).

A. Spurious Association

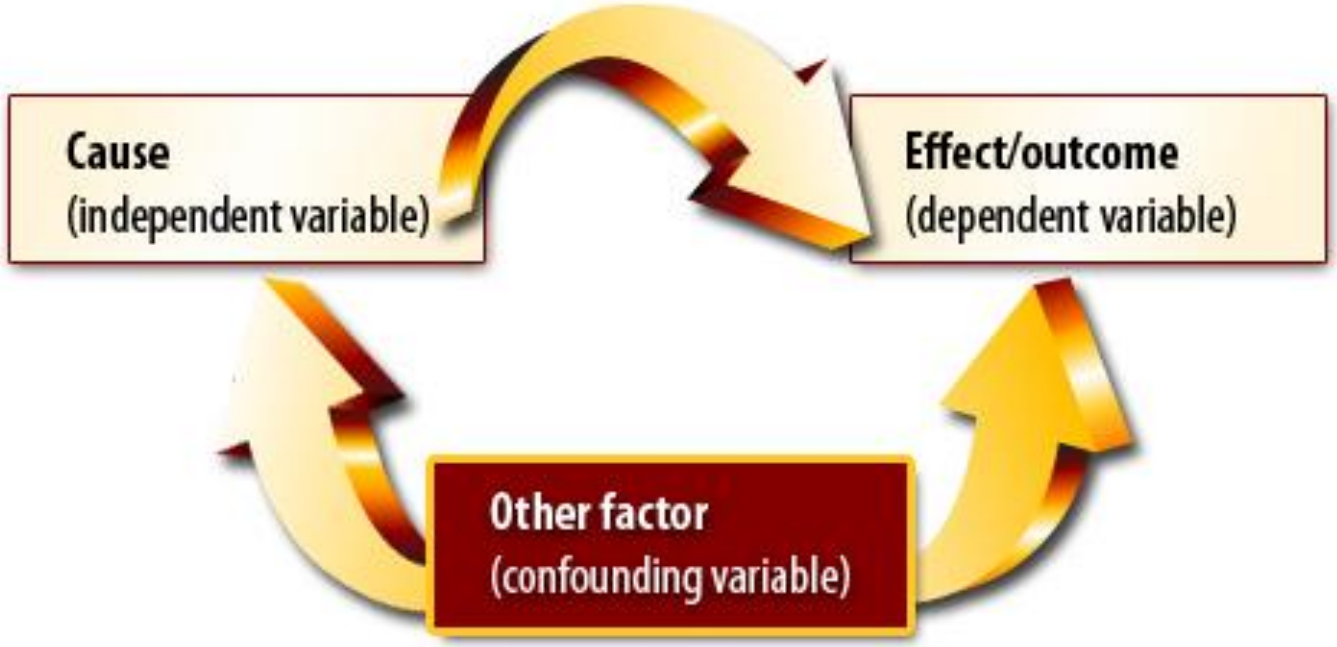
- For example, it was observed in a study done in UK that the peri-natal mortality was higher in hospital deliveries, than home deliveries,
- which is contradictory to the expected, leading to spurious association that home deliveries are better and safer places.

A. Spurious Association

- Such a conclusion is spurious because usually hospitals attract mothers of high-risk and therefore associated with high peri-natal mortality and not that the quality of care is poor.
- This spurious observation occurs if the selection of study group and control group is biased (i.e. selection bias).
- Since selection bias results in spurious observation, selection bias must be absent.

INDIRECT ASSOCIATION

- It is a statistical association between a characteristic of interest and a disease due to the presence of another factor i.e. common factor (*Confounding variable)*.

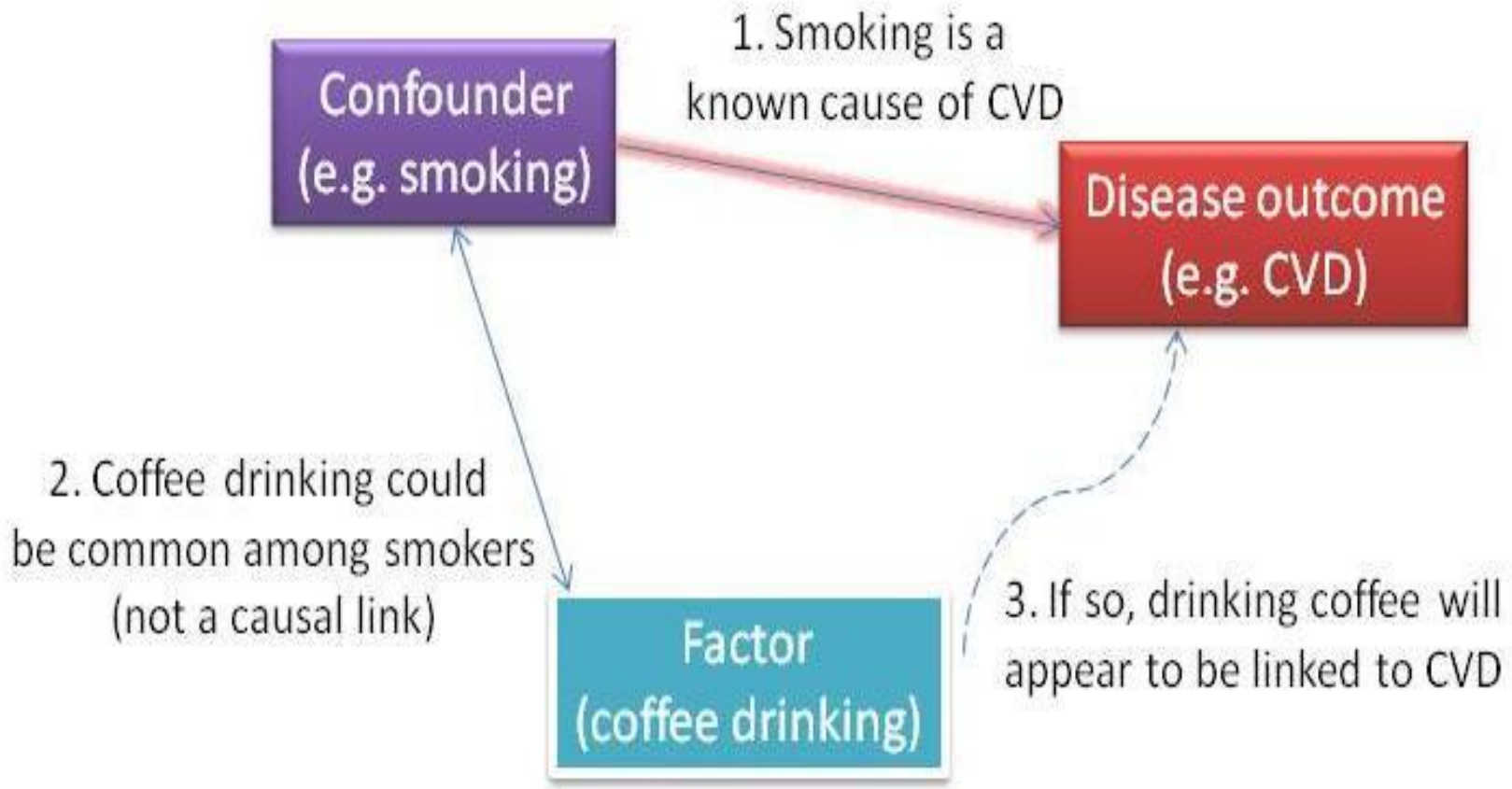


B. Indirect Association

- Confounding factor is the one which is related to both the variables and can independently results in a disease.

Confounding Factor

1.



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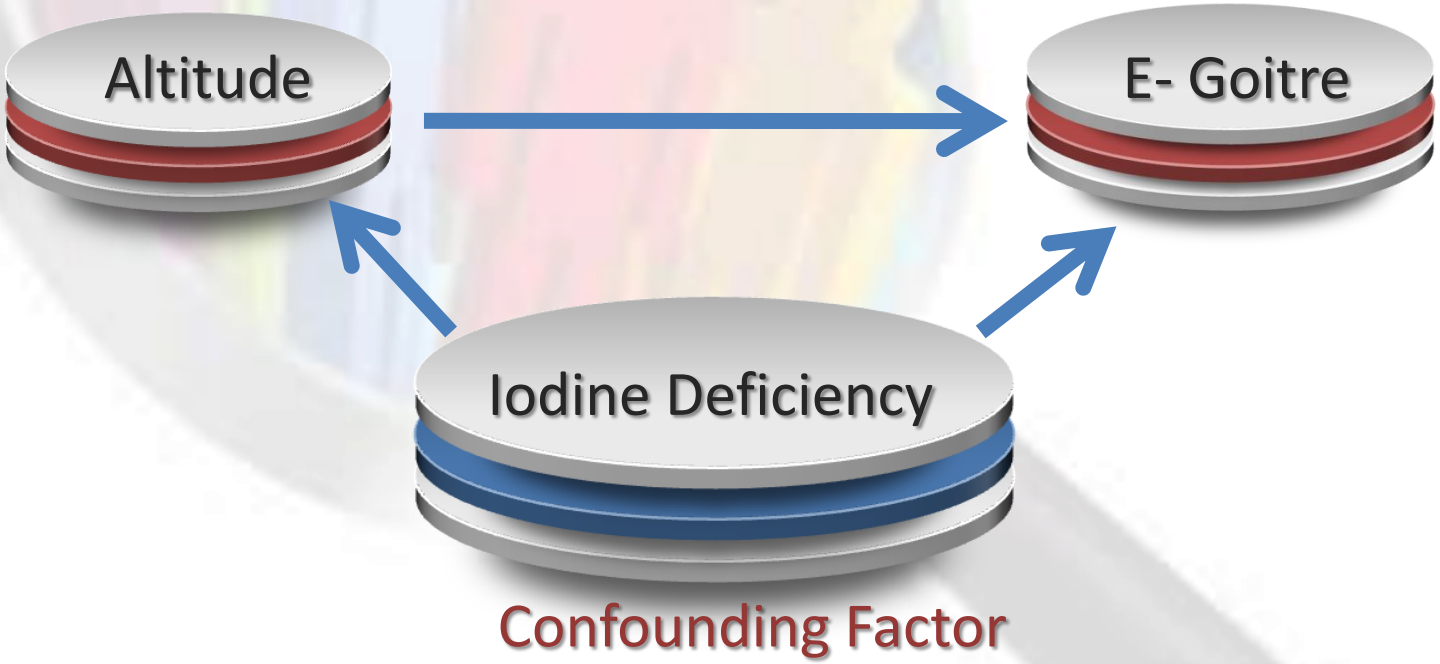

C. Direct (Causal) Association

This is of two types

1. **One-to-one causal relationship and**
2. **Multi factorial causation.**

DIRECT ASSOCIATION

A. One-to-One Causal Relationship

- This model suggests that two factors (A & B) exhibit one to one relationship, if – *Change in A is followed by Change in B*.

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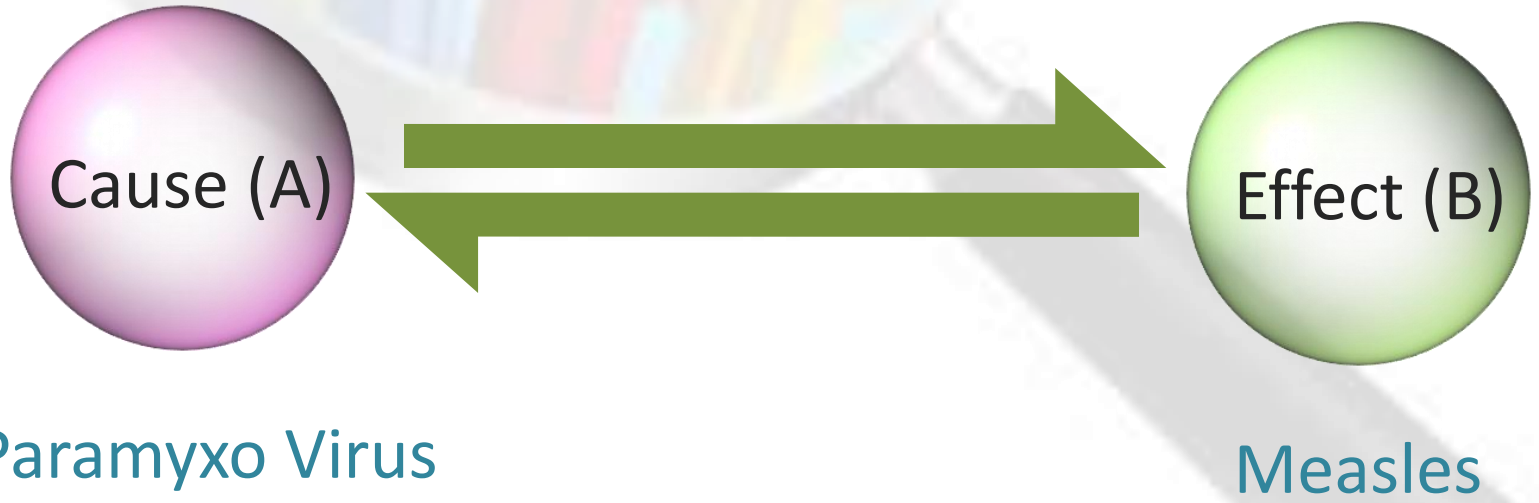
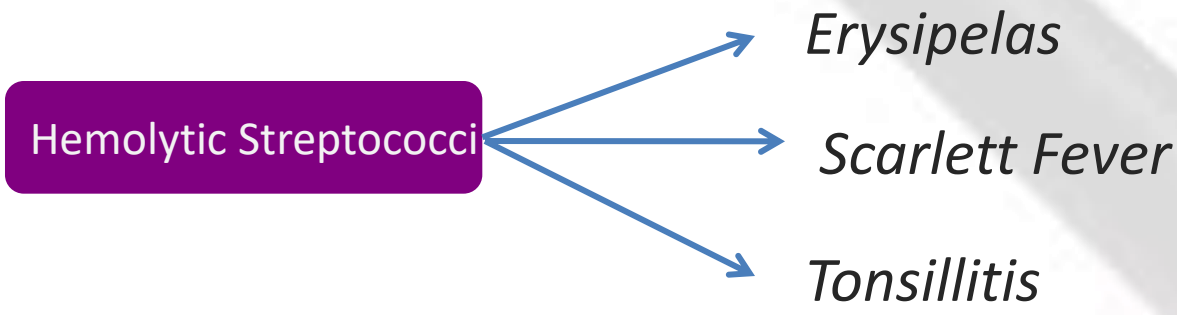


KOCH'S POSTULATES (Germ Theory of Disease)

1. Necessary, and
2. Sufficient.

- But this model does not fit well for many diseases, like in *Tuberculosis,* tubercle bacilli is clearly a necessary factor, but its presence may or may not be sufficient to produce the d/s.

- A Single Factor may produce several Outcomes.

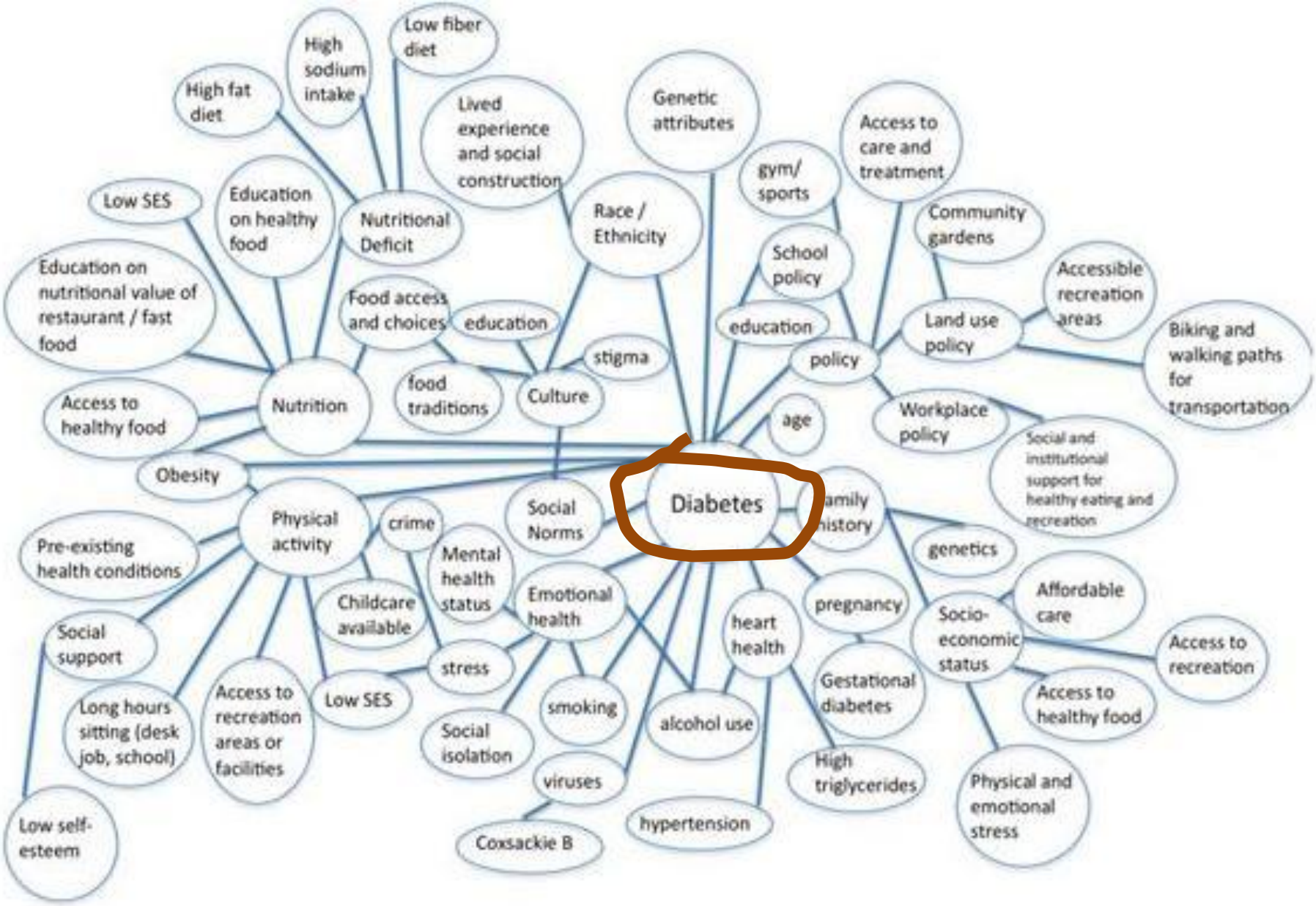


B. Multifactorial Causation

- In Several Modern Diseases, more than one factor is implicated in the Web of Causation.

Eg: Both *Asbestos exposure* and *Smoking* cause Lung Cancer independently.

- As our Knowledge on disease increases, we may discover a common biochemical event, which can be altered by each of these factors



Web of Causation of Diabetes Mellitus

Multi factorial Causation

- This is often found in non communicable diseases such as cancer, obesity, coronary artery disease, protein energy malnutrition, etc.
- Wherein multiple factors are involved, which may act independently or synergistically.
- This concept of multi factorial causation was put forward by Pettenkofer.

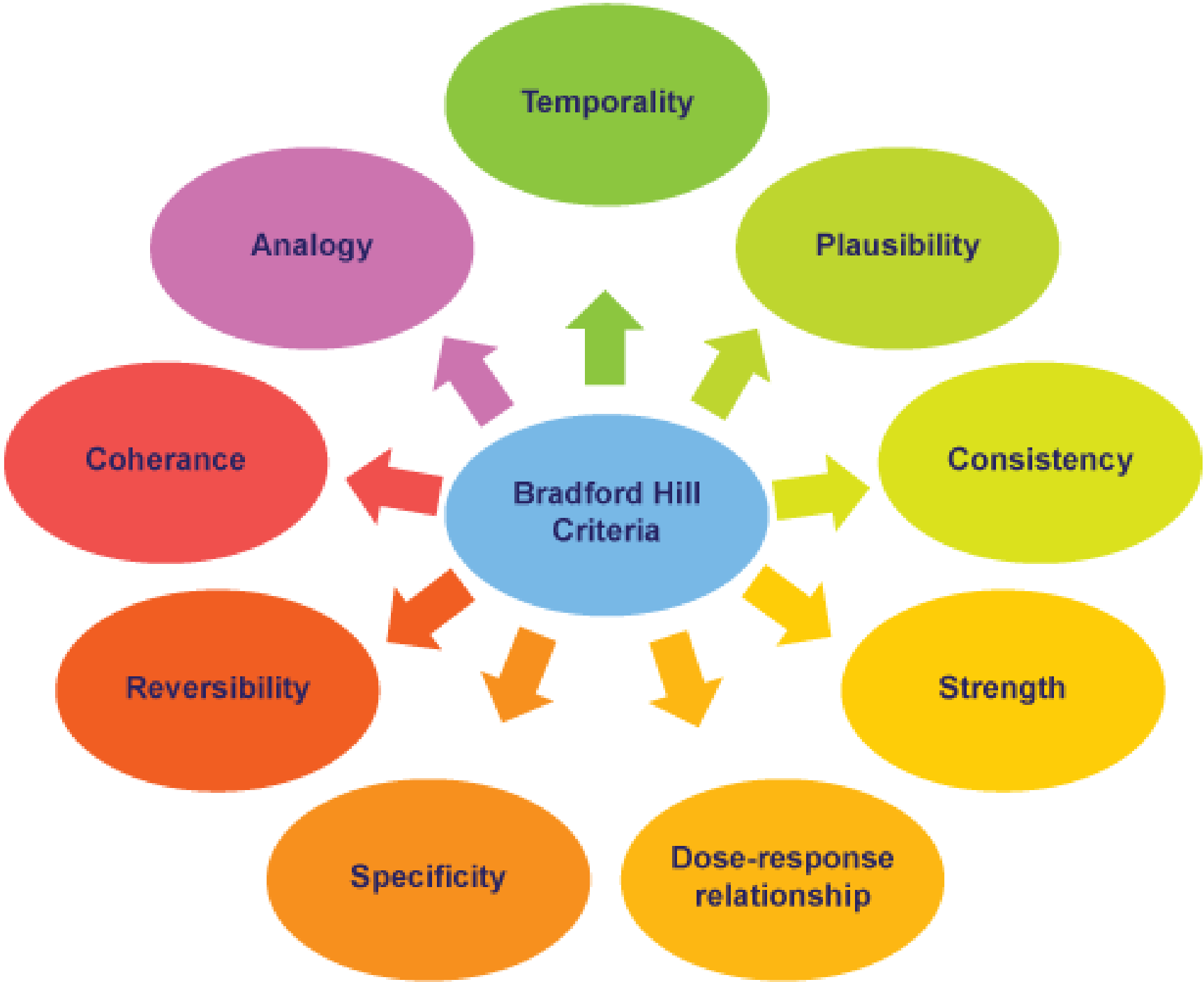
Guidelines for Judging Causality

- Without any Experimental aid, the evidence to justify Causation was lacking in our methods. So, certain additional Criteria was added by *U.S. Surgeon general (1964)*, which is further strengthened by *BRADFORD HILL (1965)* Criteria.

Austin Bradford Hill

It first appeared in "Smoking and Health" Report by advisory Committee


Temporality
Plausibility
Consistency
Strength
Specificity
Coherance
Surgeon General's Criteria

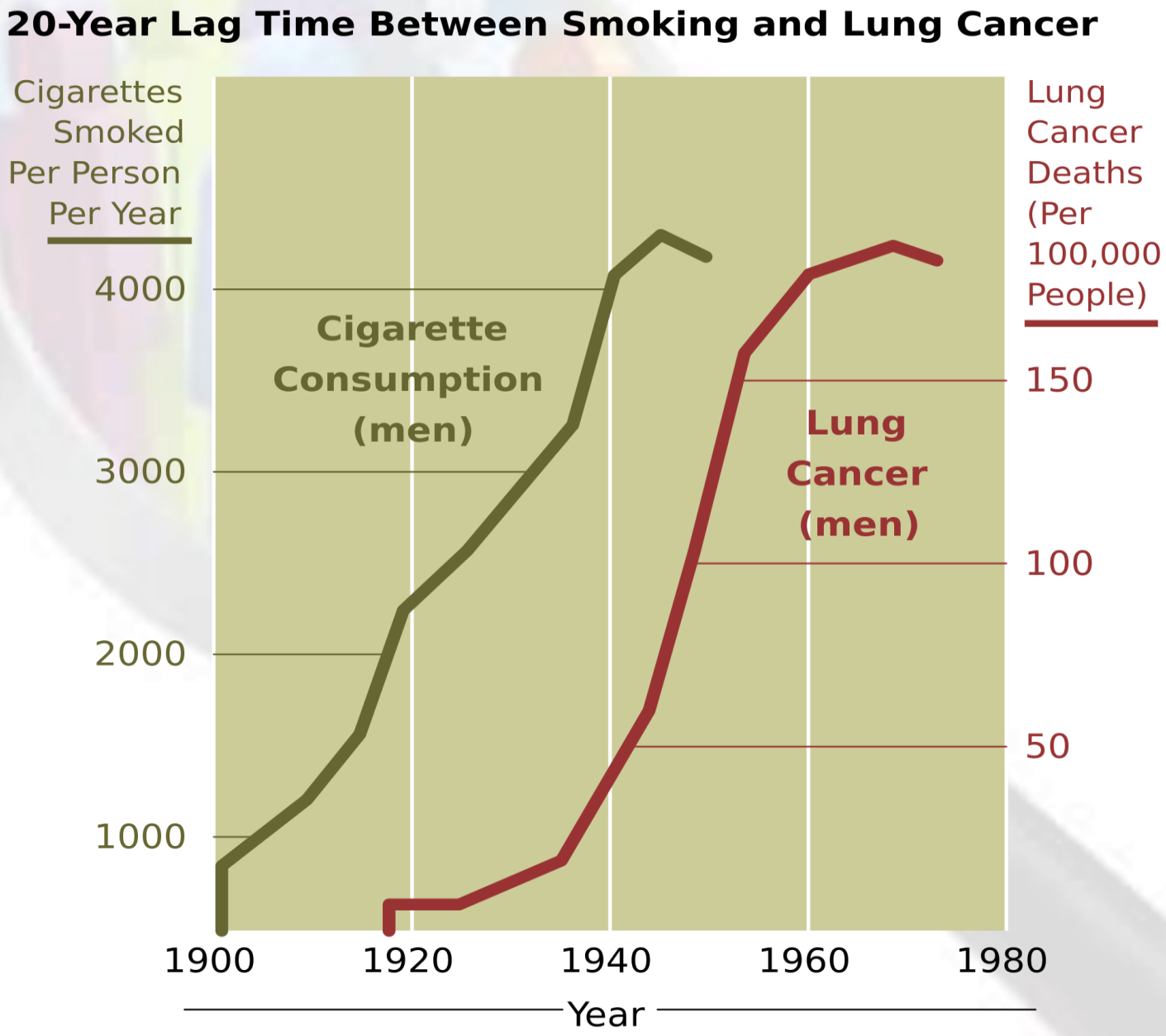

Temporality
Plausibility
Consistency
Strength
Dose-response relationship
Specificity
Reversibility
Coherance
Analogy
Bradford Hill Criteria

1. Temporal Relationship

- The causal attribute must precede the disease or unfavorable outcome. (*Exposure before Disease*)

- Length of interval between exposure and disease very important. (*Asbestos exposure takes 20 yrs to cause d/s*)

They are swinging in Temporal Sequence. Its not bullying, its Science.



Smoking(Cause) Precedes Cancer (Effect)

2. Strength of the association

- With increasing level of exposure to the risk factor an increase in incidence of the disease is found.

- This can be calculated either by ODDS ratio or Relative Risk.

2. Strength of the Association

- The two variables are said to be causally associated strongly when the relative risk or Odd's ratio is high.
- Higher the relative risk and Odd's ratio, greater is the strength of the association.
- For example, smokers are relatively at a greater risk than non smokers, establishes strong association between smoking and lung cancer.

Relative Risk

$$\text{Relative Risk} = \frac{\text{Incidence among Exposed}}{\text{Incidence among Non Exposed}}$$

- ✓ It is direct measure of the strength of association.

RR = 1	No association
RR > 1	Positive association (possibly causal)
RR < 1	Negative association (possibly protective)

Odds Ratio

	Cases(with disease)	Controls (without disease)
H/O of exposure	a	b
No H/O exposure	c	d

$$OR = ad/bc$$

$$\text{Odds Ratio} = \frac{\text{Odds of disease in exposed group}}{\text{Odds of disease in Non-exposed group}}$$

3. Dose-Response Relationship

- As the dose of exposure increases, the risk of disease also increases.

Presence of D-R relationship strengthens Causality, whereas its absence doesn't rule out Causal relationship.

- In some cases in which a threshold may exist, no disease may develop up to a certain level of exposure (a threshold); above this level, disease may develop.

4. Cessation of exposure

- If a factor is a cause of a disease, we would expect the risk of the disease to decline when exposure to the factor is reduced or eliminated.

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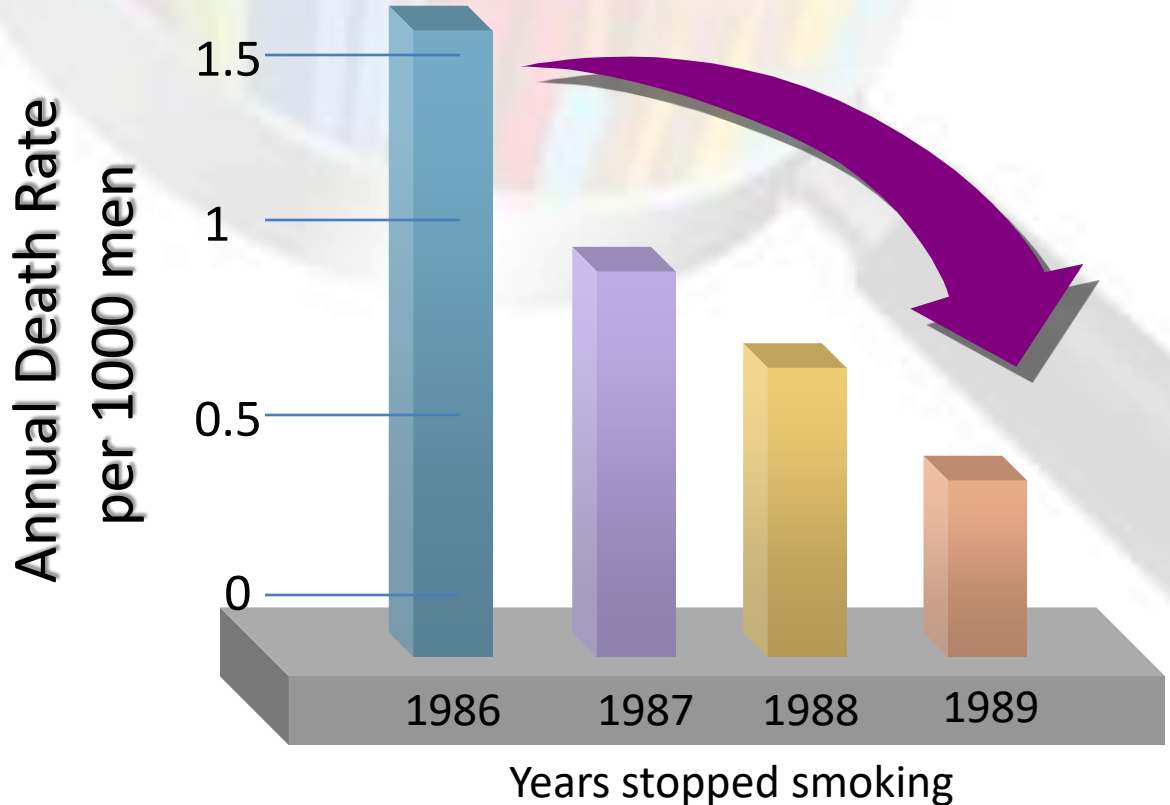


5. Specificity Of The Association

- Specificity implies a one to one relationship between the cause and effect (Weakest Criteria).

- Not everyone who smokes develop Lung Cancer,
- Not everyone who develops cancer has smoked.

- Lack of specificity does not negate causation.

3. Specificity of the Association

- The two variables are said to be specifically associated, when the attributable risk is high.
- Higher the attributable risk, greater is the specificity of the association between the two variables. This establishes **'one-to-one'** relationship.
- For example,

  Smoking is **'the'** cause of lung cancer. **But it is difficult to establish the specificity because not all smokers develop lung cancer nor all cases of lung cancer had smoked**.

3. *Specificity of the Association*

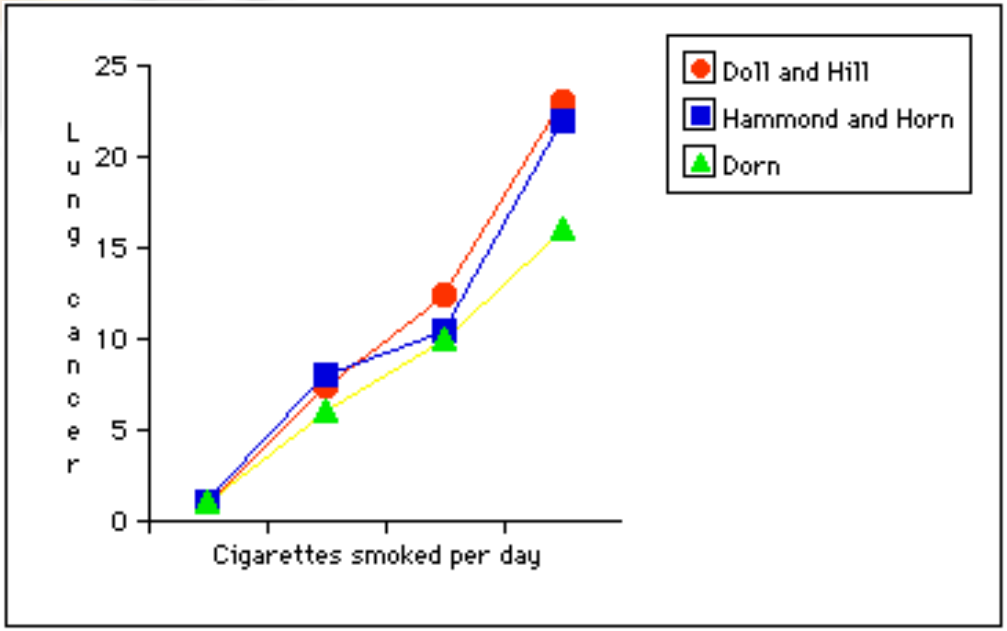
- Moreover lung cancer can occur due to multiple factors other than smoking such as air pollution, occupational exposure to asbestos dust, thus deviating from ‘one-to-one’ relationship.
- So Specificity supports causal relationship and lack of specificity does not rule out specificity.
- Therefore, ‘attributable risk’ is taken into consideration.
- If attributable risk is 80 percent, that means among 80 percent of lung cancer cases, smoking is attributed as the (specific) cause.

6. Consistency Of The Association

✓ If the relationship is causal, we would expect to find it consistently in different studies and in different populations.

Causal Association b/n Smoking and Lung cancer is found consistently in:

- *50 retrospective studies*
- *9 prospective studies*.



Consistency of the Association

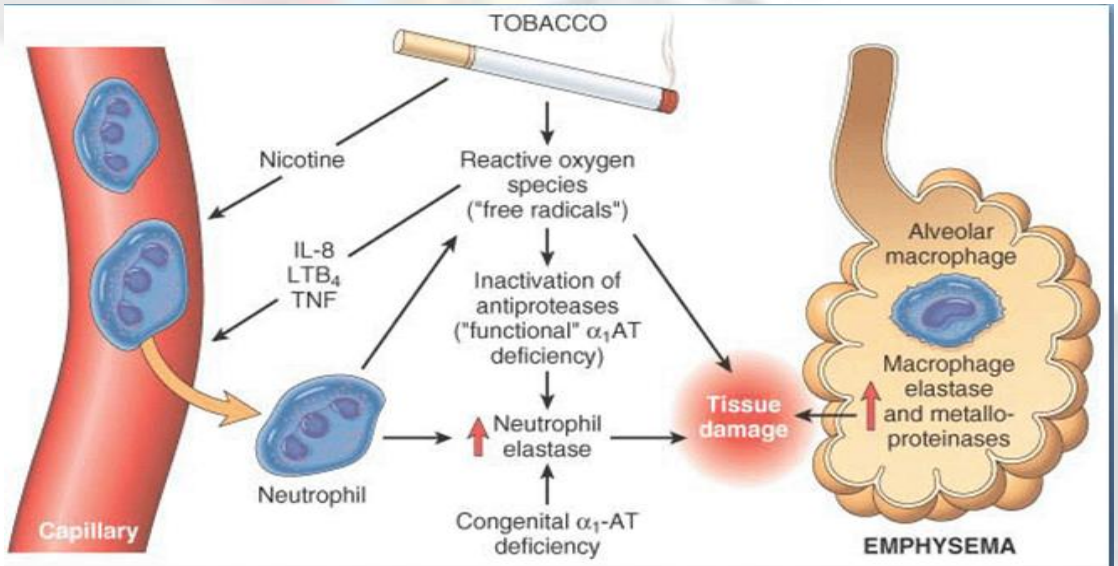
Similar consistent association has been shown between

- smoking and coronary artery disease,
- smoking and chronic bronchitis,
- smoking and peptic ulcer
- smoking and lung cancer.

7. Biological Plausibility

- The association must be consistent with the current knowledge of disease. (viz mechanism of action, evidence from animal experiments etc).

- Sometimes the lack of plausibility may simply be due to the lack of sufficient knowledge about the pathogenesis of a disease.



Pathogenesis of emphysema

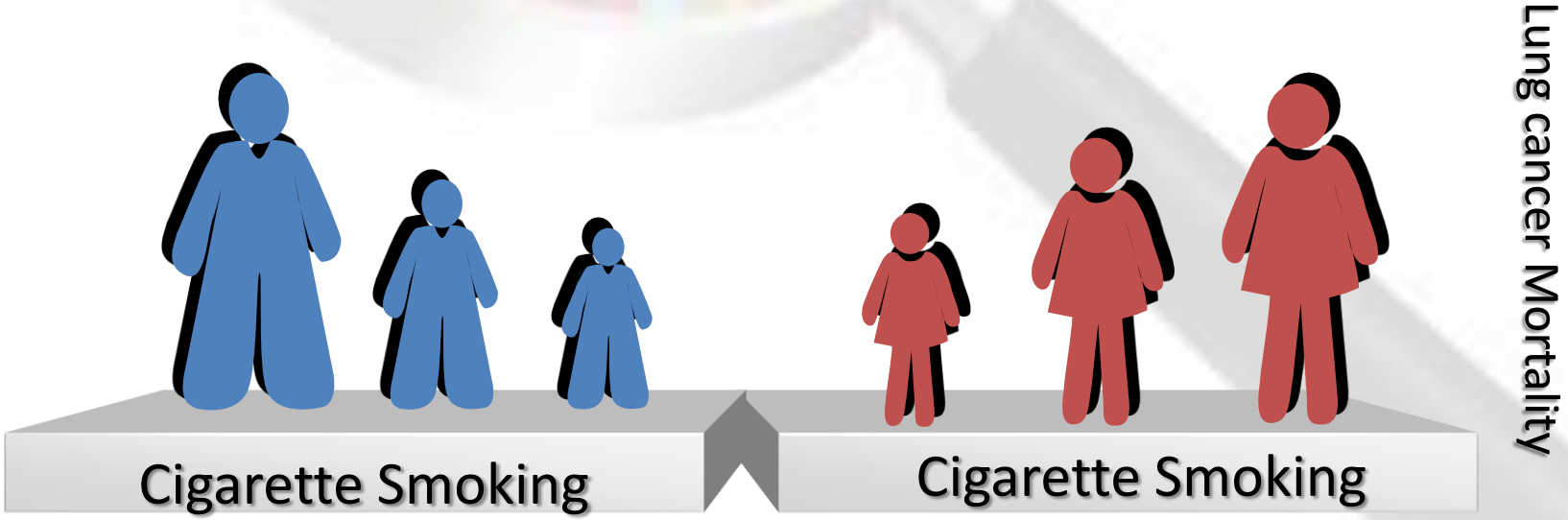
Biological Plausibility

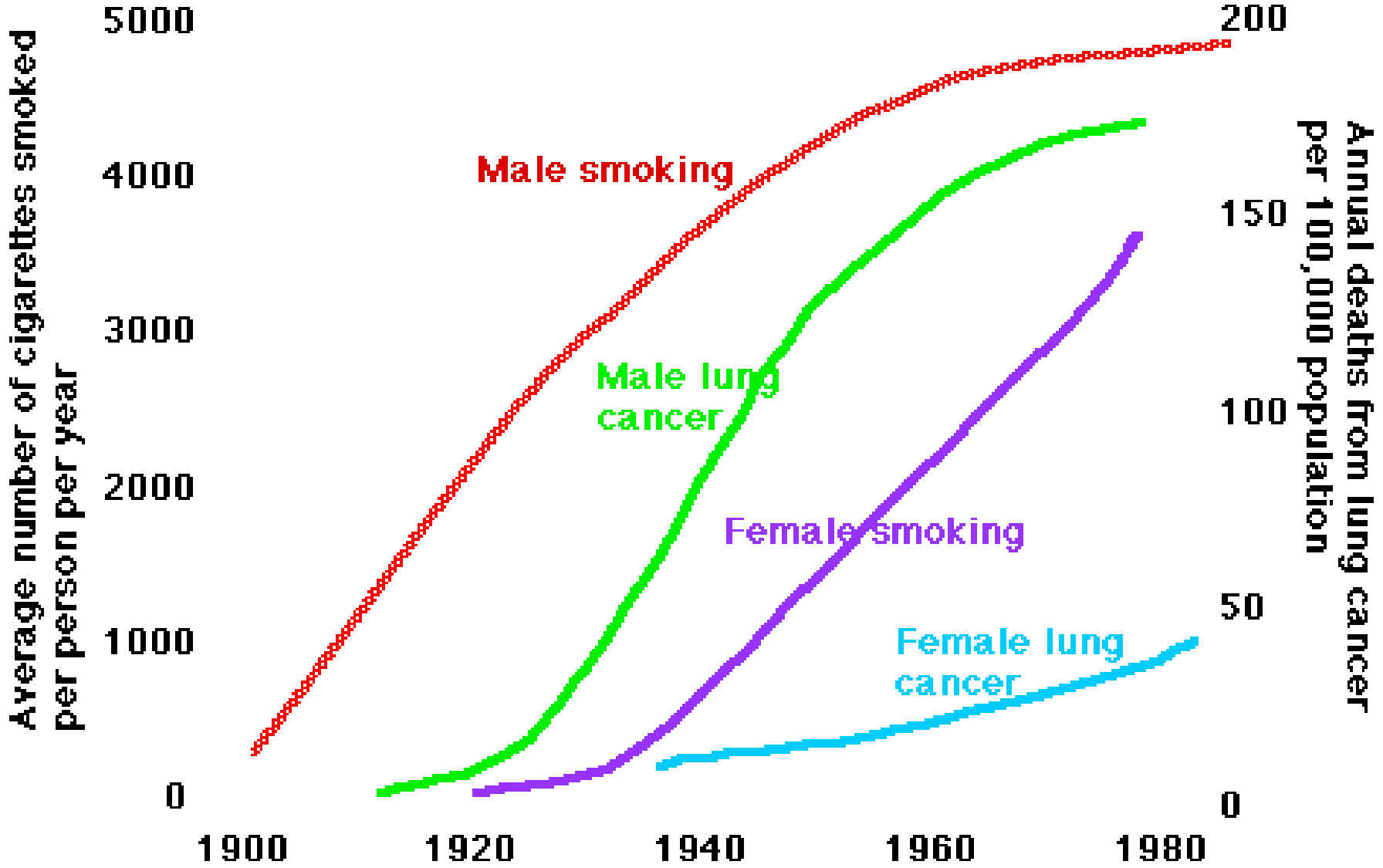
- The causal association between the two variables (cause and the effect), i.e. smoking and lung cancer, is said to be biologically plausible, if there is a biological mechanism involved in the body.
- For example, deposition of carcinogen of the smoke in the lungs, over a period of time, builds up to a threshold level and then induces neo plastic changes in the lung tissue.
- That means there is a biological response of the cells, tissues, organs or system to the stimulus.

8. Coherence of the Association

✓ The association must be coherent with the known facts of relevant origins.

Male and Female differences in trends of lung cancer Deaths is coherent with recent adoption of Cigarette smoking by women.





Coherence of the Association

6. Coherence of the Association

- The causal association between the two variables is said to be coherently associated when there is historical evidence since ancient times.
- For example, the historical evidence of rising consumption of tobacco smoking and rising incidence of lung cancer are coherent.
- Similarly, male and female differences in trends of lung cancer death rates are also coherent with the more recent adoption of cigarette smoking by women.

OBSERVED ASSOCIATION

Could it be due to BIAS?

No

Could it be CONFOUNDING?

No

Could it be result of CHANCE?

No

Could it be CAUSAL RELATION?

Yes

Apply Guidelines and
Make Judgement.

CONCLUSION

- The Causal inferences resulted from the Epidemiological Studies are very important to Public health and provide inputs for Political and Judicial decisions.

Eg: The Causal association b/n Smoking and Lung Cancer has resulted in labeling of Cigarette packets and Increased campaign ads.

- Correlation does not Imply Causation.

- Apart from outbreak investigations, no single study is capable of establishing a causal relation or fully informing either individual or policy decisions.

- It is thus important for public health and policy makers to understand the fundamentals of causal inference.

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THANK YOU