Causality in Epidemiology

Definition of causality

- Causality can be defined as cause effect relationship
- In epidemiology cause is the exposure and effect is disease or death
- Causal relation is a complex phenomenon
- The concept of cause itself continues to be debated as a philosophical matter in the scientific literature.

Cause and effect

How can we define “cause” and “effect”?

- First, we try to understand the term effect
- Standard dictionary defines effect as result, consequence or aftermath of a cause
- We can observe the effect or disease but not sure about the specific cause that resulted in the effect
- Effect of a particular cause can be best conceptualized by counterfactual model

Counterfactual Model

When we are interested to measure the effect of a particular cause, we measure the

- Observed amount of effect in a population who are exposed to that cause and
- Imagine the amount of the effect which would have been observed, if the same population would not have been exposed to that cause, all other conditions remaining identical.
- The difference of the two effect measures is the effect due the cause we are interested in.

Counterfactual Model

As the counterfactual effect is unobservable, we estimate a proxy/surrogate amount of effect from a population who are not exposed to the cause and otherwise they are comparable to study population to best of our knowledge and effort.

Cause

- We can easily observe an effect which is usually a disease or death
- But epidemiology is concerned about the cause (s) of the effect (death or disease)
- Is there any single cause that results in a disease or death inevitably?
- If yes, very few

Definition of cause

Dictionary defines cause as

a) The producer of an effect, result, or consequence.

b) The one, such as a person, an event or a condition, that is responsible for an action or a result.

Cause

- We know a factor does not always results in a disease and a disease may be caused in absence of a factor which is known to be a cause of the disease
- Smoking does not cause lung cancer to every smoker and many non-smoker develop lung cancer
- Is smoking a cause of lung cancer?

Causal Models

- Models are simplified representation of causal mechanism
- We would present two models

- Traditional model to explain infectious disease causation
- Sufficient component cause model for chronic disease causation

Epidemiologic triangle and triad

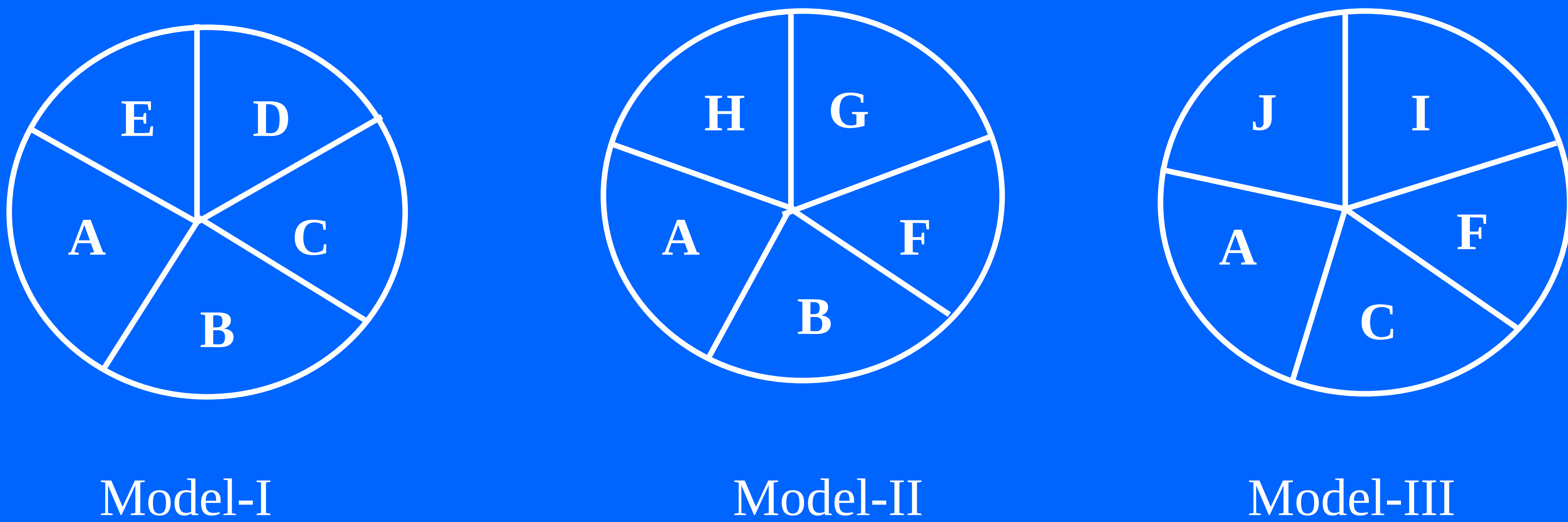
Model-I

Model-II

Infectious disease model

- Agent, host, and environmental factors interrelate in a variety of complex ways to produce disease in humans.
- Their balance and interactions are different for different diseases.
- When we search for causal relationships, we must look at all three components and analyze their interactions to find practical and effective prevention and control measures.

Sufficient component cause model

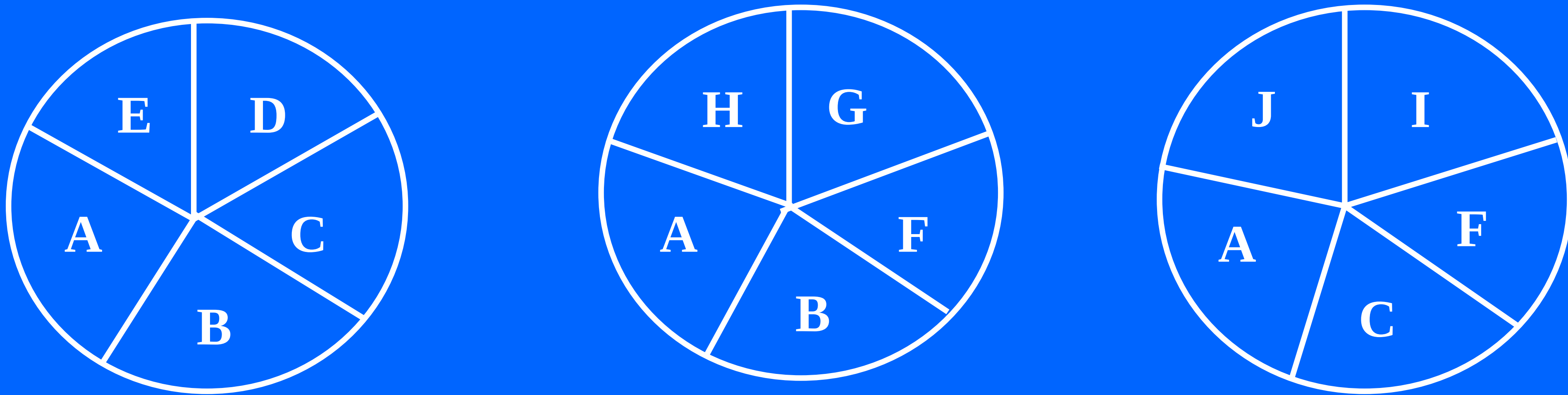


Rothman pie

- **Cause:** A cause of a disease is an event, condition, or characteristics that plays an essential role in producing an occurrence of the disease.
- Rothman points out that the cause of any effect must consist of a constellation of components that act in concert.
- **Sufficient cause:** A set of minimal conditions and events that inevitably produce disease.

- **Component cause:** An individual event, condition, or characteristic required by a given sufficient cause.
- **Necessary cause:** A component cause present in every sufficient cause.
- Often there are many sufficient causes, which may produce a given effect.
- A given component cause may play a role in any number of sufficient causes (i.e. different sufficient causes may share some component causes

Sufficient component cause model



Model-I

Model-II

Model-III

Rothman pie

How to establish causal inference

For infectious disease → Koch’s postulate

For Chronic disease → Hill’s criteria

Henle-Koch postulate (1884)

1. The parasite (the original term) must be present in all who have the disease.
2. The parasite can never occur in healthy persons.
3. The parasite can be isolated, cultured and capable of passing the disease to healthy experimental animal.
4. The organism must be reisolated from the experimentally infected animal.

*Not suitable for all microbial diseases

Limitations of Koch postulate

1. Disease production may require co-factors.
2. Viruses cannot be cultured like bacteria because viruses need living cells in which to grow.
3. Pathogenic viruses can be present without clinical disease (sub-clinical infections, carrier states).

Hill’s Criteria of causal association

Bradford Hill proposed the following criteria for a association to be causal:

Hill’s criteria:

1. Strength of association
2. Consistency
3. Specificity
4. Temporality

Hill’s Criteria of causal association

5. Biological gradient
6. Plausibility
7. Coherence
8. Experiment
9. Analogy

Strength of Association

- The stronger an association, the more likely to be causal in absence of known biases (selection, information, and confounding).
- May be misleading for unknown confounding.

Strength of Association

- How strong is strong (rule of thumb)

Relative risk	"Meaning"
1.1-1.3	Weak
1.4-1.7	Modest
1.8-3.0	Moderate
3-8	Strong
8-16	Very strong
16-40	Dramatic
40+	Overwhelming

Consistency

- Replication of the findings by different investigators, at different times, in different places, with different methods and the ability to convincingly explain different results.

Specificity

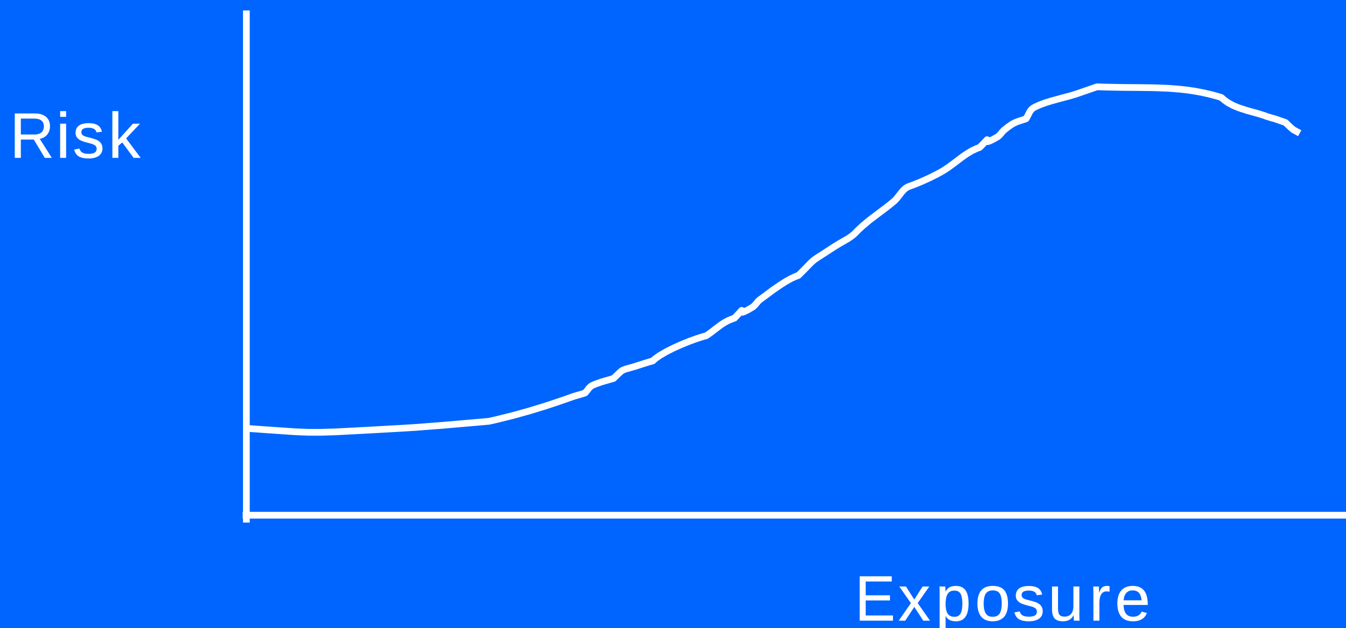
- This means a cause lead to a single effect, not multiple effect
- However, a single cause often leads to multiple effect. Smoking is a perfect example

Temporality

- It refers that the putative cause in fact precede in time the presumed effect.
- First exposure, then disease.
- This is essential to establish a causal relation

Biologic Gradient / Dose Response

- incremental change in disease rates in conjunction with corresponding changes in exposure.



Need to consider threshold and saturation effects, characteristics of the exposure.

Plausibility

- Does the association make sense biologically.

Coherence

- Does a causal interpretation fit with known facts of the natural history and biology of the disease
- Very similar to plausibility

Experimental Evidence

- The demonstration that under controlled conditions changing the exposure causes a change in the outcome is of great value, some would say indispensable, for inferring causality.

Analogy

- We are readier to accept arguments that resemble others we accept
- Have there been similar situations in the past?

Hill's criteria for causal inference

- Except for temporality, none of the Hill's criteria is absolute for establishing a causal relation
- Hill himself recognized that and stated clearly
- He argued that none of his criteria is essential
- However, temporality is absolutely essential to establish a causal relation

Implication of casual inference

- Presence of a cause leads to excess amount of disease compared to absence of the cause
- An increase in the amount of cause leads to an increase in disease.
- Reduction in the amount of cause leads to a reduction in disease
- Challenge is to identify the most important component cause for public health intervention

Thank you