Introduction to Epidemiology

Disease Causation

By

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<table>
<thead>
<tr>
<th>Topic</th>
<th>Time</th>
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<tbody>
<tr>
<td>Epidemiology and causation</td>
<td>12:00 to 12:10</td>
</tr>
<tr>
<td>Cause, Risk, factor, confounder and effect</td>
<td>12:10 to 12:20</td>
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<tr>
<td>Necessary and sufficient cause</td>
<td>12:20 to 12:30</td>
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<tr>
<td>Application of guidelines/criteria to associations</td>
<td>12:30 to 12:40</td>
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We can **End Polio**!

- Polio cases worldwide:
  - **1988**: 350000
  - **2016**: 27

- Since 1988, we have reduced polio cases by **99.9%**.

**World Polio Day**

24 October 2016

27 children have been paralysed for life by polio in 2016 to date in Afghanistan, Pakistan and Nigeria.

We won't stop until that number is **ZERO**.

www.polioeradication.org

#EndPolio

#WorldPolioDay
Introduction to unit 4 Epidemiology

- Definition, History of Epidemiology
- Purpose/Use of Epidemiology
- Concepts in the infectious diseases
- **Disease Causation**
- Levels of prevention
- Measurements of Morbidity and Mortality
- Sources of Data and methods of data collection
- Epidemic Investigation and Management
- Epidemiological Surveillance
Epidemiology

• **Epi** = upon
• **Demos** = population
• **Logos** = study of

**Definition**

• The study of the **distribution and determinants of health related states or events in specified human populations** and its **application to the control of health problems**

• Last, 1988
Epidemiological Principles

• Diseases (or other health events) don’t occur at random

• Diseases (or other health events) have causal and preventive factors which can be identified

• Diseases and health have a distribution

• Epidemiology focuses on populations rather than individual persons, tissues or organs.
• « The art of epidemiological thinking is to draw **conclusions from imperfect data**”

• George W. Comstock

• Based on what ????????
Epidemiologic triad

- **Host**
  - Demographic characteristics
  - Biological characteristics
  - Socioeconomic characteristics

- **Agent**
  - Biological agents
  - Physical agents
  - Chemical agents
  - Nutrient agents
  - Mechanical agents
  - Social agents

- **Environment**
  - Physical environment
  - Biological environment
  - Social environment
• **Hazard** is something with the potential to cause harm, such as a substance, a piece of equipment, a form of energy, a way of working or a feature of the environment.

• **Harm** includes death and major injury and any form of physical or mental ill health.

• **Risk** it is a measure of the probability that the hazard (defined previously) will manifest some degree of harm.
Risk

• Risk is the **likelihood of an event occurring.** In health care events, we usually consider a negative consequence arising from exposure to a hazard.

• Types of risk
  – **Absolute**: incidence of disease in any population
  – **Relative**: ratio of the incidence rate in the group exposed to the hazard to the incidence rate in the non-exposed group
  – **Attributable**: *Difference in incidence rates between exposed and non-exposed groups.*
Cause and effect

• Cause and effect understanding is the highest form of achievement of scientific knowledge.
• Causal knowledge permits rational plans and actions to break the links between the factors causing disease, and disease itself.
• Causal knowledge can help predict the outcome of an intervention and help treat disease.
• Quote Hippocrates "To know the causes of a disease and to understand the use of the various methods by which the disease may be prevented amounts to the same thing as being able to cure the disease".
A cause?

- The first and difficult question is, what is a cause?
- A cause is *something which has an effect*.
- In epidemiology a cause can be considered to be *something that alters the frequency of disease, health status or associated factors in a population*.
- Pragmatic definition.
- Philosophers have grappled with the nature of causality for thousands of years.
Cause - Definition

• “It is an antecedent event, condition or characteristic that is necessary for the occurrence of the disease at the movement it occurs, given that the other conditions are fixed.”

• Alternatively the particular disease will not occur if those antecedent event, condition or characteristic are different in a specified way.
Association and Causation

• Association is defined as “Occurrence of two variables more frequently than expected”.

• Association *between suspected cause and effect does not always mean a causal association.*
Association may be grouped into following three types;

1. **Spurious Association**: When the observed association between suspected cause and effect may not be real. Example- Perinatal mortality being high in hospital deliveries than home deliveries implying hospital is unsafe.

2. **Indirect Association**: It is a statistical association between a factor of interest and a disease due to presence of another factor known as Confounding Factor. Example- Iodine deficiency and Altitude association with Endemic Goitre.

3. **Direct Causal Association**: One to one and multifactorial
Direct (Causal) Association

1. One to one causal Association:

   • Two variables /factors are considered to be causally related if any change in one is followed by a change in the other.
   • The initial criteria used by Henle and Koch to distinguish causal association from indirect and spurious ones were applied to infective disease and included:
     1. The causative agent must be recovered from all diseased individuals.
     2. The agent recovered from diseased individuals must be grown in pure culture.
     3. The organism grown in culture must replicate the disease when introduced in susceptible animals.
2. Multifactorial Causation:

- Single causation theory does not explain causation of Non-Communicable diseases where multiple factors are involved in causation of disease viz; CHD and Ca-Lung.

- Two models presented below may explain multifactorial causation mechanism;

1. Factor –A
   Factor- B
   Factor -C
   Cellular reaction
   Disease

2. Factor –A
   Factor- B
   Factor-C
   Disease
Recent Concepts of Causation

- **Sufficient Cause**: Sufficient cause imply a complete causal mechanism, a minimal set of conditions and events that are sufficient are sufficient to cause disease or outcome to occur.

- **Component Cause & Necessary Cause**

ABCD
Unknown
Koch's Postulates

• 1. The specific organism should be shown to be present in all cases of animals suffering from a specific disease but should not be found in healthy animals.

• 2. The specific microorganism should be isolated from the diseased animal and grown in pure culture on artificial laboratory media.

• 3. This freshly isolated microorganism, when inoculated into a healthy laboratory animal, should cause the same disease seen in the original animal.

• 4. The microorganism should be reisolated in pure culture from the experimental infection.
Hill’s criteria

- Strength of association
- Temporal relationship
- Distribution of the disease
- Gradient
- Consistency
- Specificity
- Biological plausability
- Experimental models
- Preventive trials
Temporal Association

• Exposure to causative factor must occur before the onset of disease.
• This criteria is basic to the causal association.
• Establishment of temporal association is easy in acute communicable diseases
• It is difficult to establish temporal sequence in chronic insidious non communicable diseases as to which came first.
• The consumption of cigarette smoking preceded by 30 years to the increase in the death rates due to lung cancer. Theses observations are compatible with the long latent period pathogenesis of carcinogenesis.
Strength of Association

• The larger the Relative Risk the more likely the association is causal.
• Likelihood of causal association is strengthened if there is dose and duration response relationship.
• In the absence of experimental evidence in humans, the causal association between cigarette smoking and lung cancer has been based on following;
  – Relative Risk
  – Dose response relationship
  – Decrease in risk on cessation of smoking
Dose Response Relationship

- **Dose Response** Relationship:
  - More intense and longer exposure should result into more frequent and severe disease.
  - This has been clearly established in the relationship of smoking and lung cancer.

- **Dose and Duration Response** Relationship
  - The cumulative effect of dose and duration has also been well established in relationship of smoking and lung cancer.
Specificity of Association

• The concept of specificity implies a “one to one” relationship between the cause and effect.
• The causal factor should produce one specific disease or effect.
• In recent past, the controversy over cigarette smoking and lung cancer relationship has centered around specificity of the association.
• Cigarette smoking is linked with lung cancer and several other conditions such as CHD, Chronic Respiratory conditions and Ca-Cervix etc.
• Lack of specificity can be explained by the fact that tobacco smoke contains several harmful substances such as nicotine, carbon monoxide, benzpyrene, tar and other particulate matters with possible additive and synergistic actions.
Consistency of Association

• The result from single study is seldom sufficient to establish causal association.
• An association has to be replicated and confirmed by different investigators, in different populations using different design in order to be established as causal association.
• More than fifty retrospective studies and at least nine prospective studies in different countries have shown a consistent association between cigarette smoking and subsequent development of lung cancer has lent support to a causal association.
Biological Plausibility

• Causal association is substantiated if biological plausibility is present.
• The notion that food intake and cancer is interrelated is an old concept.
• The positive association of intestine, colon and rectum with food intake is biologically plausible.
• The cigarette smoking and lung cancer is also biologically plausible as it is well established that tobacco contains carcinogen which cause Ca-lung
Causal Inference in Epidemiology

Bridging the gap between our ideas and our observations.

Criteria:

- Strength of association
- Consistency of findings
- Specificity of association
- Temporality (lack of ambiguity)
- Biologic gradient (dose-response effect)
- Biologic plausibility of the hypothesis
- Coherence of evidence
- Experimental evidence
Confounding: A Fundamental Problem of Causal Inference

- Confounding is **bias** due to inherent (unobservable) differences in risk between exposed and unexposed populations, i.e., a **lack of comparability**.

- Confounding is usually not a major source of bias in randomized trials (assuming sample size is large enough) because randomization tends to equalize inherent risks between treatment groups (treated group = exposed, untreated = unexposed).
Confounding

- May lead to observation of association when none exists
- May obscure an association that exists
- Information on potential confounders should be collected in the study and used in analysis, otherwise they cannot be excluded as alternate explanations for findings
- Confounding factors must be considered during study design
Confounding

- Mixing of the effect of the exposure on disease with the effect of another factor that is associated with the exposure

- Bias in estimating the effect of exposure (E) on disease (D) occurrence, due to the lack of comparability between exposed and unexposed populations

- Risk among exposed ≠ Risk among exposed if they had been unexposed
Properties of Confounders

3 Criteria for a variable to be a confounder (C):

- C must be a risk factor for the disease (D) in the unexposed population

- C must be associated with exposure (E) in the population from which the cases arose

- The association between C and E must not be due entirely to the effect of E on C (meaning C cannot be an intermediate step between E and D)
Confounding or Intermediate Effect?

Physical Activity → Colorectal Cancer

Body Mass Index

Obesity

?
Is the disease predominantly genetic or environmental?

Clues
- Stable in incidence
- Clusters in families

Clues
- Incidence varies rapidly over time or between genetically similar populations
Figure 5.3

- Down’s syndrome
  - Phenylketonuria
  - Sickle cell disease
  - Diabetes

- Asthma
- Coronary heart disease
- Stroke
- Lung cancer
- Road traffic accidents
### Example of judging causality: lung cancer

<table>
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<tr>
<th>Question</th>
<th>Answer</th>
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<tr>
<td>Does the supposed cause precede the disease (effect) (temporality)</td>
<td>Yes, clearly so</td>
</tr>
<tr>
<td>By how much does exposure to the cause raise the incidence of disease?</td>
<td>Greatly and as much as 20 to 30 fold in smokers of 20 or more cigarettes per day</td>
</tr>
<tr>
<td>Does varying exposure lead to varying disease? (does-response)</td>
<td>Yes, there is clear relationship and more smoking causes more disease</td>
</tr>
<tr>
<td>Does the cause lead to a rise in a few relevant diseases? (specificity)</td>
<td>No. Numerous diseases show an association with smoking</td>
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# Causality: Lung Cancer

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<tr>
<td>Is the association consistent across different studies and between groups?</td>
<td>Yes. The association is demonstrable in men and women, and across social groups.</td>
</tr>
<tr>
<td>Is the way that the cause exerts its effect on disease understood?</td>
<td>Only partly. The tar in cigarettes contains important carcinogens.</td>
</tr>
<tr>
<td>(biological plausibility)</td>
<td></td>
</tr>
<tr>
<td>Does manipulating the level of exposure to the cause change disease experience?</td>
<td>Yes. Reducing consumption of cigarettes reduces risk. Persuading people to smoke more would be unethical. Tobacco is carcinogenic to animals</td>
</tr>
<tr>
<td>(experimental confirmation)</td>
<td></td>
</tr>
<tr>
<td>Overall judgement</td>
<td>Originally, bitterly contested, now accepted as causal</td>
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Figure 5.13  The pyramid of associations

1 Causal and mechanisms understood
2 Causal
3 Non-causal
4 Confounded
5 Spurious / artefact
6 Chance
Summary

• Cause and effect understanding is the highest form of scientific knowledge.
• Epidemiological and other forms of causal thinking shows similarity.
• An association between disease and the postulated causal factors lies at the core of epidemiology.
• Demonstrating causality is difficult because of the complexity and long natural history of many human diseases and because of ethical restraints on human experimentation.
Summary

• All judgements of cause and effect are tentative.
• Be alert for error, the play of chance and bias.
• Causal models broaden causal perspectives.
• Apply criteria for causality as an aid to thinking.
• Look for corroboration of causality from other scientific frameworks.
**Necessary Condition**

- Must be there for the effect, the charge, to be true
- *If absent, cannot occur.*
- No oxygen, no combustion.
- No seeds, no plants to grow
- Car runs only if gas in tank.
Sufficient Condition

• **Whenever A is present, B will follow**- decapitation is sufficient for death.

• **Getting a B in the course is sufficient for passing.**

• **Necessary cause**: must always PRECEDE the effect. This effect need not be the sole result of the one cause.

• **Sufficient cause**: inevitably initiates or produces an effect.
Necessary & Sufficient

• **Something can serve as both necessary and sufficient**- “You will get Malaria if and only if you are bitten by a mosquito carrying the germ. Malaria ≈ Mosquito (germ)

• **If you have Malaria you must have been bitten by the mosquito with the germ.**