

# Supercourse

## **Web of Causation; Exposure and Disease Outcomes**

<http://www.pitt.edu/~super1/lecture/lec19071/index.htm>

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University of Pittsburgh  
South Asian Cardiovascular  
Research Methodology Workshop

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THE AGA KHAN UNIVERSITY

Basic Epidemiology

# Web of Causation; Exposure and Disease Outcomes

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## Background

- Towards this purpose, epidemiology seeks to
  - describe the frequency of disease and it's distribution
    - consider person, place, time factors
  - assess determinants or possible causes of disease
    - consider host, agent, environment

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## Basic Question in Analytic Epidemiology

- Are exposure and disease linked?



Exposure → Disease

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### **Basic Questions in Analytic Epidemiology**

- Look to link exposure and disease
  - What is the exposure?
  - Who are the exposed?
  - What are the potential health effects?
  - What approach will you take to study the relationship between exposure and effect?

Wijngaarden

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### **A good epidemiologic exposure variable should....**

- Have an impact on health
- Be measurable
- Differentiate populations
- Generate testable hypotheses
- Help to prevent or control disease

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**What qualities should an exposure variable have to make it worthwhile to pursue?**

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### **A good epidemiologic exposure variable should....**

- Have an impact on health
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### **What qualities should a disease have to make it worthwhile to investigate?**


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### **Disease investigations should have some public health significance**

- The disease is important in terms of the number of individuals it affects
- The disease is important in terms of the types of populations it affects
- The disease is important in terms of its causal pathway or risk characteristics

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### Research Questions/Hypotheses



- Is there an association between Exposure (E) & Disease (D)?
- **Hypothesis:** Do persons with exposure have higher levels of disease than persons without exposure?
- Is the association “real,” i.e. causal?

Sever

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### Big Picture

- Look for links between exposure & disease
  - *to intervene and prevent disease*
- Look to identify what may cause disease
- Basic definition of “cause”
  - exposure that leads to new cases of disease
  - remove exposure and most cases do not occur

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### Big Picture

- On a population basis
  - *An increase in the level of a causal factor will be accompanied by an increase in the incidence of disease (all other things being equal).*
  - *If the causal factor is eliminated or reduced, the frequency of disease will decline*

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### Infectious Disease Epidemiology

- Investigations/studies are undertaken to demonstrate a link [relationship or association] between an agent (or a vector or vehicle carrying the agent) and disease

The diagram consists of a large yellow letter 'E' on the left and a large yellow letter 'D' on the right, connected by a pink arrow pointing from 'E' to 'D'. Below the 'E' is the word 'Exposure' in white, followed by '[ Agent ]' and '[ Vector/Vehicle ]' in red. Below the 'D' is the word 'Disease' in white.

Exposure  
[ Agent ]  
[ Vector/Vehicle ]

Disease

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### Injury Epidemiology

- Studies are undertaken to demonstrate a link [association] between an agent / condition and an injury outcome

The diagram consists of a large yellow letter 'E' on the left and a large yellow letter 'D' on the right, connected by a pink arrow pointing from 'E' to 'D'. Below the 'E' is the word 'Exposure' in white, followed by '[ Agent – Energy Transfer ]', '[ Vehicle carrying the agent – automobile ]', and '[ Condition – Risk taking behaviour ]' in red. Below the 'D' is the word 'Disease' in white.

Exposure  
[ Agent – Energy Transfer ]  
[ Vehicle carrying the agent – automobile ]  
[ Condition – Risk taking behaviour ]

Disease

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### Chronic Disease Epidemiology

- Studies are undertaken to demonstrate a link [relationship or association] between a condition/agent and disease

The diagram consists of a large yellow letter 'E' on the left and a large yellow letter 'D' on the right, connected by a pink arrow pointing from 'E' to 'D'. Below the 'E' is the word 'Exposure' in white, followed by '[ Condition – e.g. gene, environment ]' in red. Below the 'D' is the word 'Disease' in white.

Exposure  
[ Condition – e.g. gene, environment ]

Disease

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### Issues to consider

- Etiology (cause) of chronic disease is often difficult to determine
- Many exposures cause more than one outcome
- Outcomes may be due to a multiple exposures or continual exposure over time
- Causes may differ by individual

-- Whereas a physician tries to determine presence of disease and causes in individuals, epidemiologists focus on populations

-- Unlike microorganisms (like a bacteria) which can be linked to a given disease (disease is defined as exposure to that microorganism) - few chemical/physical factors have a unique effect on health - for example exposure to asbestos - causes lung cancer, but other things may also cause lung cancer

-- Also, outcomes may be due to a combination of factors - e.g., genetics + environmental exposure = disease, so env. exposure is a component cause

-- Different individuals within population with the disease may have gotten it through different causal pathways - one person through env. exposure another through personal factor, etc.

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### Causation and Association

- Epidemiology does not determine the *cause* of a disease in a given individual
- Instead, it determines the *relationship or association* between a given exposure and frequency of disease in populations
- We infer causation based upon the association and several other factors

-- Therefore, an epidemiologic study cannot predict the exact cause of the disease in every individual

-- It looks at a population and tries to determine whether exposure is significantly associated to the disease *on average* - uses statistical techniques to make conclusions about the strength of these relationships

-- Often these relationships are more strongly supported/concluded when a plausible biological mechanism exists for the effect

-- In general, epidemiologic studies are not experimental - can't expose humans deliberately

to something that may affect their health, instead often look at populations that were inadvertently exposure to an agent due to job or where they live (clinical trials is exception)

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### Association vs. Causation

- Association - an identifiable relationship between an exposure and disease
  - implies that exposure might cause disease
  - exposures associated with a difference in disease risk are often called "risk factors"
- Most often, we design interventions based upon associations



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## Association vs. Causation

- **Causation** - implies that there is a true mechanism that leads from exposure to disease
- Finding an association does not make it causal

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## General Models of Causation

- **Cause:** event or condition that plays a role in producing occurrence of a disease

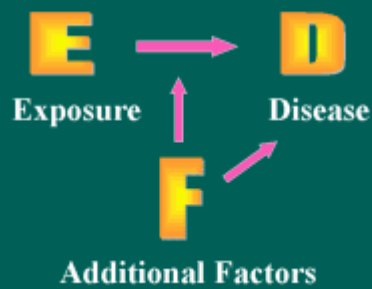
**How do we establish cause in situations that involve multiple factors/conditions?**

For example, there is the view that most diseases are caused by the interplay of genetic and Environmental factors.

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## General Models of Causation

**How do we establish cause?**





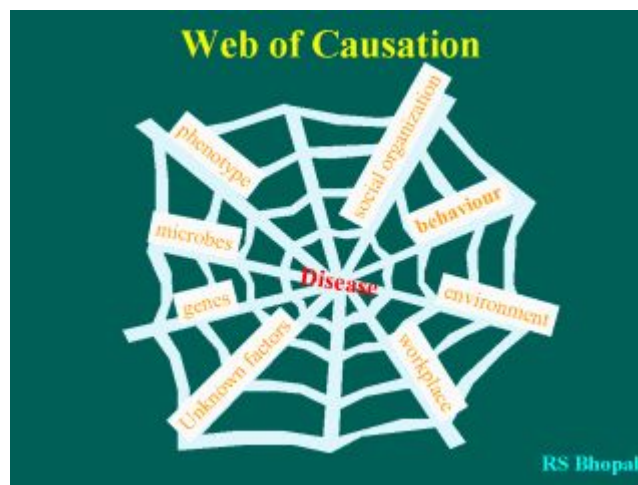
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### Web of Causation

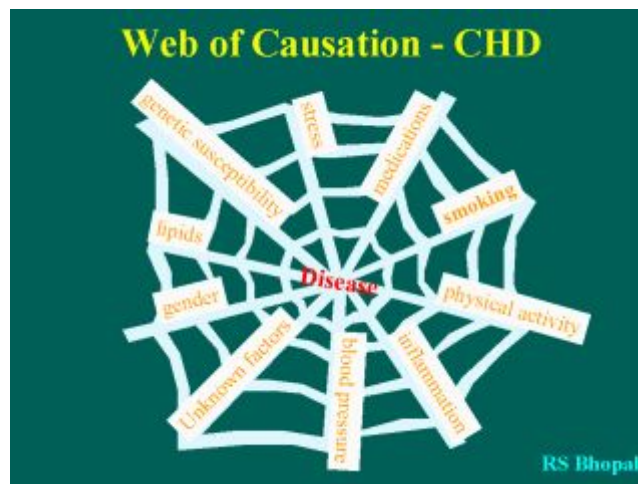
- There is no single cause
- Causes of disease are interacting
- Illustrates the interconnectedness of possible causes

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### **Hill's Criteria for Causal Inference**

- Consistency of findings
- Strength of association
- Biological gradient (dose-response)
- Temporal sequence
- Biological plausibility
- Coherence with established facts
- Specificity of association

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### **Consistency of Findings of Effect**

- Relationships that are demonstrated in multiple studies are more likely to be causal
- Look for consistent findings
  - across different populations
  - in differing circumstances
  - with different study designs

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### **Strength of Association**

- Strong associations are less likely to be caused by chance or bias
- A strong association is one in which the relative risk is
  - very high, or
  - very low

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### Biological Gradient

- There is evidence of a dose-response relationship
- Changes in exposure are related to a trend in relative risk

Dose (cigs/day)	Standardized Mortality Ratios (Lung Ca)		
	Study 1	Study 2	Study 3
<10	1.3	1.8	1.4
10-20	2.8	2.3	2.4
>40	4.7	3.7	6.3

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### Temporal Sequence

- Exposure must precede disease
- In diseases with latency periods, exposures must precede the latent period
- In chronic diseases, often need long-term exposure for disease induction

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### Plausibility and Coherence

- The proposed causal mechanism should be biologically plausible
- Causal mechanism must not contradict what is known about the natural history and biology of the disease, but
  - the relationship may be indirect
  - data may not be available to directly support the proposed mechanism
  - must be prepared to reinterpret existing understanding of disease in the face of new findings

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### **Specificity of the Association**

- **An exposure leads to a single or characteristic effect, or affects people with a specific susceptibility**
  - easier to support causation when associations are specific, but
  - this may not always be the case
    - many exposures cause multiple diseases

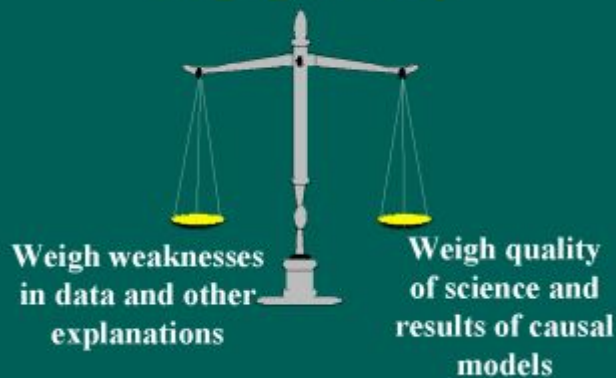
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### **Causal Inference: Realities**

- **No single study is sufficient for causal inference**
- **Causal inference is not a simple process**
  - consider weight of evidence
  - requires judgment and interpretation
- **No way to prove causal associations for most chronic diseases and conditions**

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### **Judging Causality**



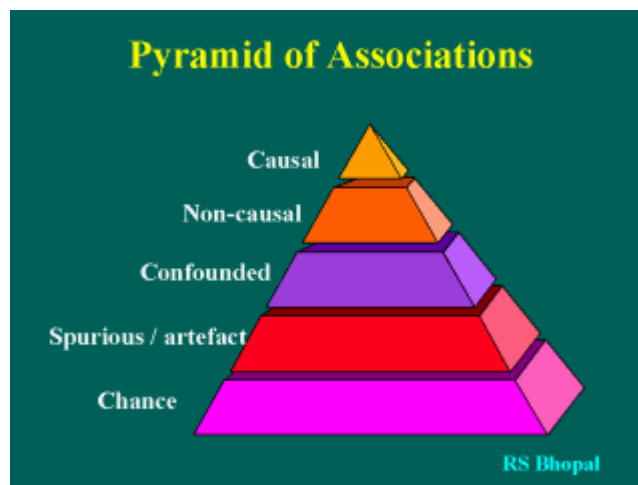
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### Prevailing Wisdom in Epidemiology

- Most judgments of cause and effect are tentative, and are open to change with new evidence

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Review

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