

causal thinking in epidemiology

Why is Jason in the hospital?

Because he has a bad infection in his leg.

But why does he have an infection?

Because he has a cut on his leg and it got infected.

But why does he have a cut on his leg?

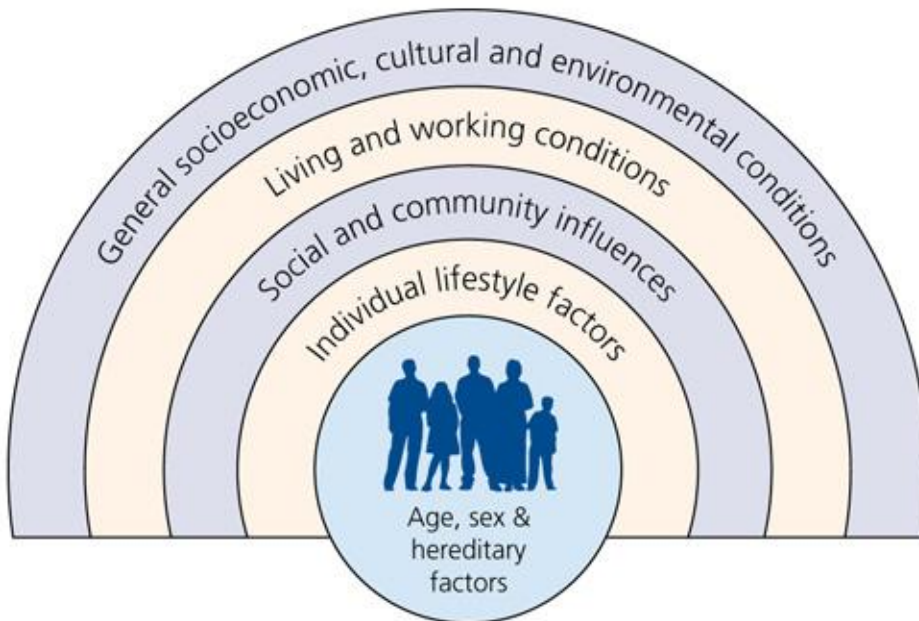
Because he was playing in the junk yard next to his apartment building and there was some sharp, jagged steel there that he fell on.

But why was he playing in a junk yard?

Because his neighbourhood is kind of run down. A lot of kids play there and there is no one to supervise them.

But why does he live in that neighbourhood?
Because his parents can't afford a nicer place to live.
But why can't his parents afford a nicer place to live?
Because his Dad is unemployed and his Mom is sick.
But why is his Dad unemployed?
Because he doesn't have much education and he can't find a job.
But why ...?"

- from **Toward a Healthy Future: Second Report on the Health of Canadians**





Determinants of Variations in Morbidity and Mortality

- ◆ **Proximate determinants:** Factors that directly influence the risk of disease and the outcomes of disease processes in individuals.
- ◆ **Distal (underlying) determinants:** Social, economic, and cultural factors that influence the health status of a population by operating through one or more of the proximate causes.

Proximate Determinants Of Morbidity and Mortality

Personal behaviors: Diet, hygiene, alcohol and tobacco use, sexual behavior, etc.

Environmental exposures: Exposure to infectious or chemical or physical agents, occupational hazards, etc.

Nutrition: Under nutrition, micronutrient deficiency, over nutrition/obesity etc.

Injuries: Intentional or accidental injuries.

Personal illness control: Specific preventive and sickness care actions.

Underlying Determinants Of Morbidity and Mortality

Socio-economic factors: Household wealth, community development, women's education and employment, etc.

Institutional factors: Health systems, health regulations, technological developments, information programs, environmental interventions, etc.

Cultural factors: Traditional beliefs about health and disease, religious values, role and status of women etc.

Broader context: Ecological setting, political economy, transportation and communication systems, agricultural development, markets, urbanization, etc.

"Cause"

"that which produces an
effect or result"
- Webster's



"Cause"

"an event, condition, or
characteristic that preceded the
disease event and without which the
disease event either would not have
occurred at all or would have not
have occurred until some time later"
- Rothman & Greenland

presence of association

≠

causal relationship



Why not?

- **Bias?**

Why not?

- **Confounding?**

Why not?

**Risk Marker?
Or
Risk Factor?**



Why not?

- Random error (chance)?

**Statistical significance
(p-value, confidence interval)**

A cause of a disease is an event, condition, characteristic or a combination of these factors which plays an important role in producing the disease. Logically, a cause must precede a disease.

A cause is termed sufficient when it inevitably produces or initiates a disease and is termed necessary if a disease cannot develop in its absence.

A sufficient cause is not usually a single factor, but often comprises several components. In general, it is not necessary to identify all the components of a sufficient cause before effective prevention can take place, since the removal of one component may interfere with the action of the others and thus prevent the disease.

17

For example, cigarette smoking is one component of the sufficient cause of lung cancer.

Smoking is not sufficient in itself to produce the disease. the cessation of smoking reduces the number of cases of lung cancer in a population.

18

- Each sufficient cause has a necessary cause as a component. For example, in a study of an outbreak of food borne infection it may be found that chicken salad and creamy dessert were both sufficient causes of salmonella diarrhea. The occurrence of salmonellae is a necessary cause of this disease.
- A causal factor on its own is often neither necessary nor sufficient, e.g., smoking as a factor in causing stroke.

19

Factors in causation:

Four types of factor play a part in the causation of disease. All may be necessary but they are rarely sufficient to cause a particular disease or state:-

- Predisposing factors, such as age, sex and previous illness, may create a state of susceptibility to a disease agent.

20

Factors in causation:

- Enabling factors such as low income, poor nutrition, bad housing, and inadequate medical care may favour the development of disease. Conversely, circumstances that assist in recovery from illness or in the maintenance of good health could also be called enabling factors.

Factors in causation:

- Precipitating factors such as exposure to a specific disease agent or noxious agent may be associated with the onset of a disease or state.
- Reinforcing factors such as repeated exposure and unduly hard work may aggravate an established disease or state.

- The term “risk factor” is commonly used to describe factors that are positively associated with the risk of development of a disease but that are not sufficient to cause the disease.

Interaction:

The effect of two or more causes acting together is often greater than would be expected on the basis of summing the individual effects. This phenomenon, called interaction, is illustrated by the particularly high risk of lung cancer in people who both smoke and are exposed to asbestos dust; the risk of lung cancer in this group is much higher than would be indicated by a simple addition of the risks from smoking and exposure to asbestos dust.

Establishing the cause of a disease:

Causal inference is the term used for the process of determining whether observed associations are likely to be causal; the use of guidelines and the making of judgments are involved.

Before an association is assessed for the possibility that it is causal, other explanations, such as chance, bias and confounding have to be excluded.

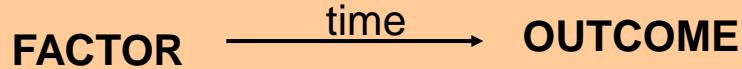
25

Temporal relation	Does the cause precede the effect? (essential)	CAUSATION
Plausibility	Is the association consistent with other knowledge? : mechanism of action, evidence from experimental animals	
Consistency	Have similar results been shown in other studies?	
Strength	What is the strength of the association between the cause and the effect? (relative risk)	
Dose-response relationship	Is increased exposure to the possible cause associated with increased effect?	
Reversibility	Dose the removal of a possible cause lead to reduction of disease risk?	
Study design	Is the evidence based on a strong study design?	
Judging the evidence	How many lines of evidence lead to the conclusion?	

26

Temporal Relationship (time order)

- Exposure must always precede the outcome
- This is the only necessary condition



Temporal Relationship

- Difficulties may arise in Case-Control and Cross-Sectional Studies
- Repeated measurement of the exposure at more than one point in time and in different locations may strengthen the evidence

Plausibility:

- An association is plausible, and thus more likely to be causal, if consistent with other knowledge. For instance, laboratory experiments may have shown how exposure to the particular factor could lead to changes associated with the effect measured.

Consistency

- is demonstrated by several studies giving the same results.
- associations more likely to be causal if observed repeatedly “by different persons, in different places, circumstances and times... There will be occasions when repetition is absent or impossible and yet we should not hesitate to draw conclusions”
 - Hill

Strength

- in association between possible cause and effect, is measured by the size of the risk ratio: $RR = \text{Relative Risk}$.
When the RR is greater than 2, the causation can be considered **STRONG**

Strength of Association



weak associations suggest non-causal explanations;
Strong associations suggest causality

- The higher the odds ratio, risk ratio, or correlation, the easier it is to make a case the cause is necessary and sufficient
- a PAR of 100% means that the cause is necessary - all cases would be prevented if the cause were removed



Weak associations may be causal but it is harder to rule out **bias** and **confounding**.

Strength of Association

"We must not be too ready to dismiss a cause-effect hypothesis merely on the grounds that the observed association appears to be slight. There are many occasions in medicine when this in truth so"
- Hill

- **In epidemiology, most causes have weak to moderate associations with health outcomes**

Dose- response relationship:

A dose-response relationship occurs when changes in the level of a possible cause are associated with changes in the prevalence or incidence of the effect: illustrated in the dose-response relationship between noise and hearing loss; as the prevalence of hearing loss increases with noise level and exposure time.

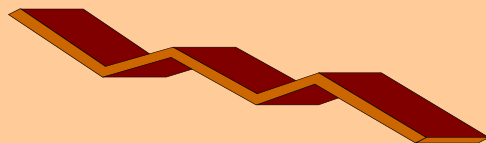
37

Reversibility:

When the removal of a possible cause results in a reduced disease risk, the likelihood of the association being causal is strengthened.

Does removal of the putative cause lead to a reduction in risk?

Not always!



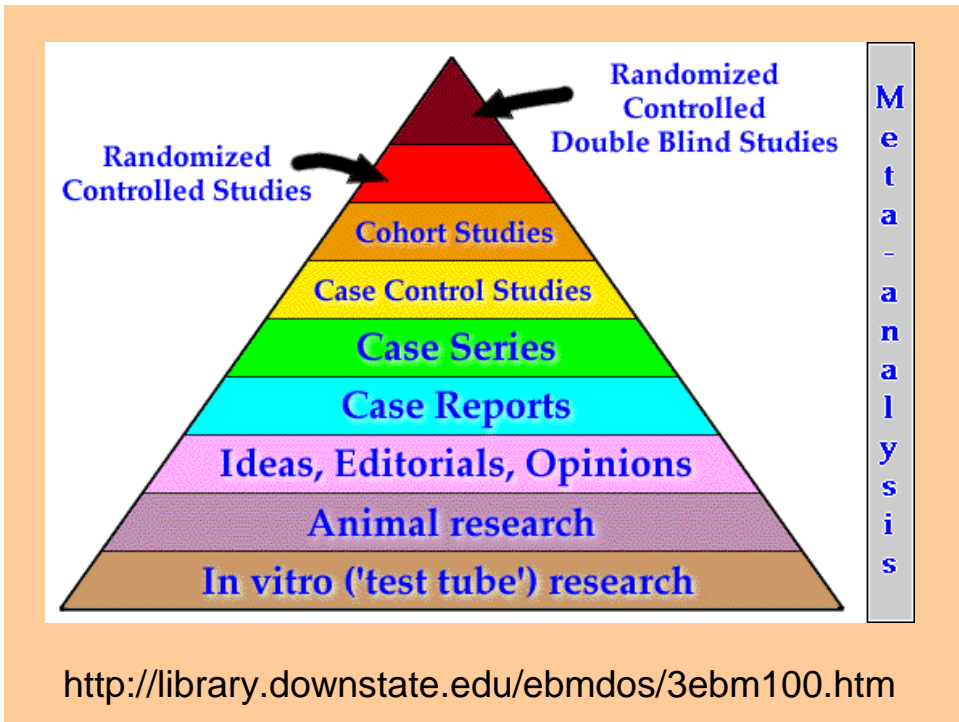
Study design:

The ability of study design to prove causation is most important consideration. The best evidence comes from well-designed, competently conducted randomized controlled trials. Other experimental studies, such as field and community trials, are seldom used to study causation.

Evidence comes most often from observational studies; almost all the evidence on the health consequences of smoking comes from observational studies.

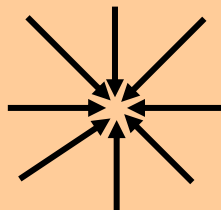
Strength of Study Design

Is the evidence based on a "strong" study design (e.g., RCT or cohort)?



Judging the Evidence

The more lines of evidence leading to the conclusion, the stronger the case for causality



GENERAL MODEL OF CAUSATION (CAUSAL PIES) BY KJ ROTHMAN



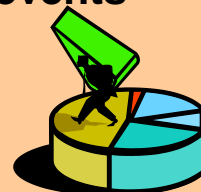
Sufficient cause:

- A set of conditions without any one of which the disease would not have occurred (this is one whole pie)
- Completion of a sufficient cause is synonymous with occurrence of disease

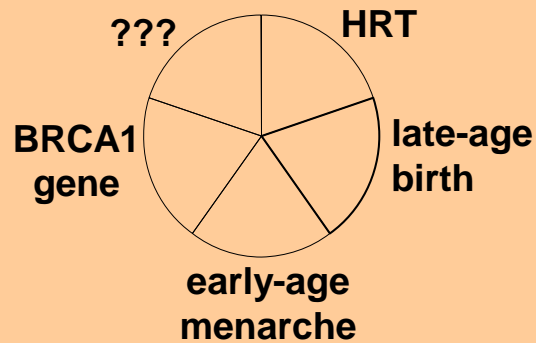
GENERAL MODEL OF CAUSATION (CAUSAL PIES)

Component cause:

- Any one of the set of conditions which are necessary for the completion of a sufficient cause (this is a piece of the pie)
- Blocking the action of any component cause prevents the completion of the sufficient cause and therefore prevents the disease by that pathway



one possible causal component of breast cancer



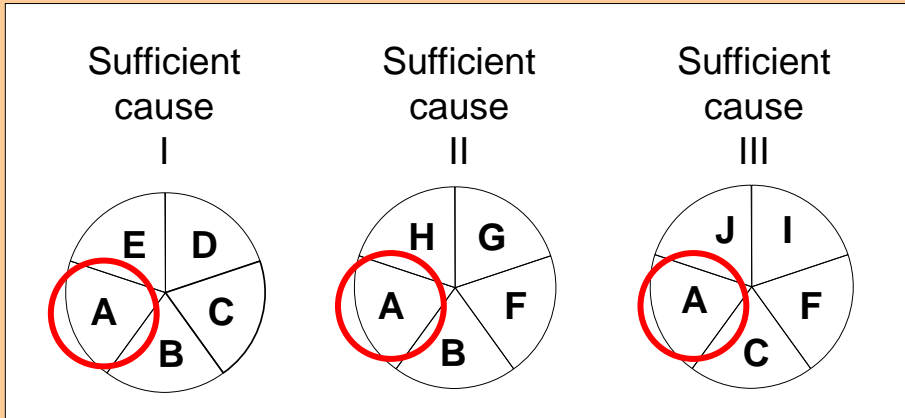
Some component causes are distal and some proximate, action of these components span a woman's entire lifetime

GENERAL MODEL OF CAUSATION (CAUSAL PIES) BY KJ ROTHMAN

Necessary cause:

- A component cause that is a member of every sufficient cause

CAUSAL PIES



from Rothman, AJE, 1976