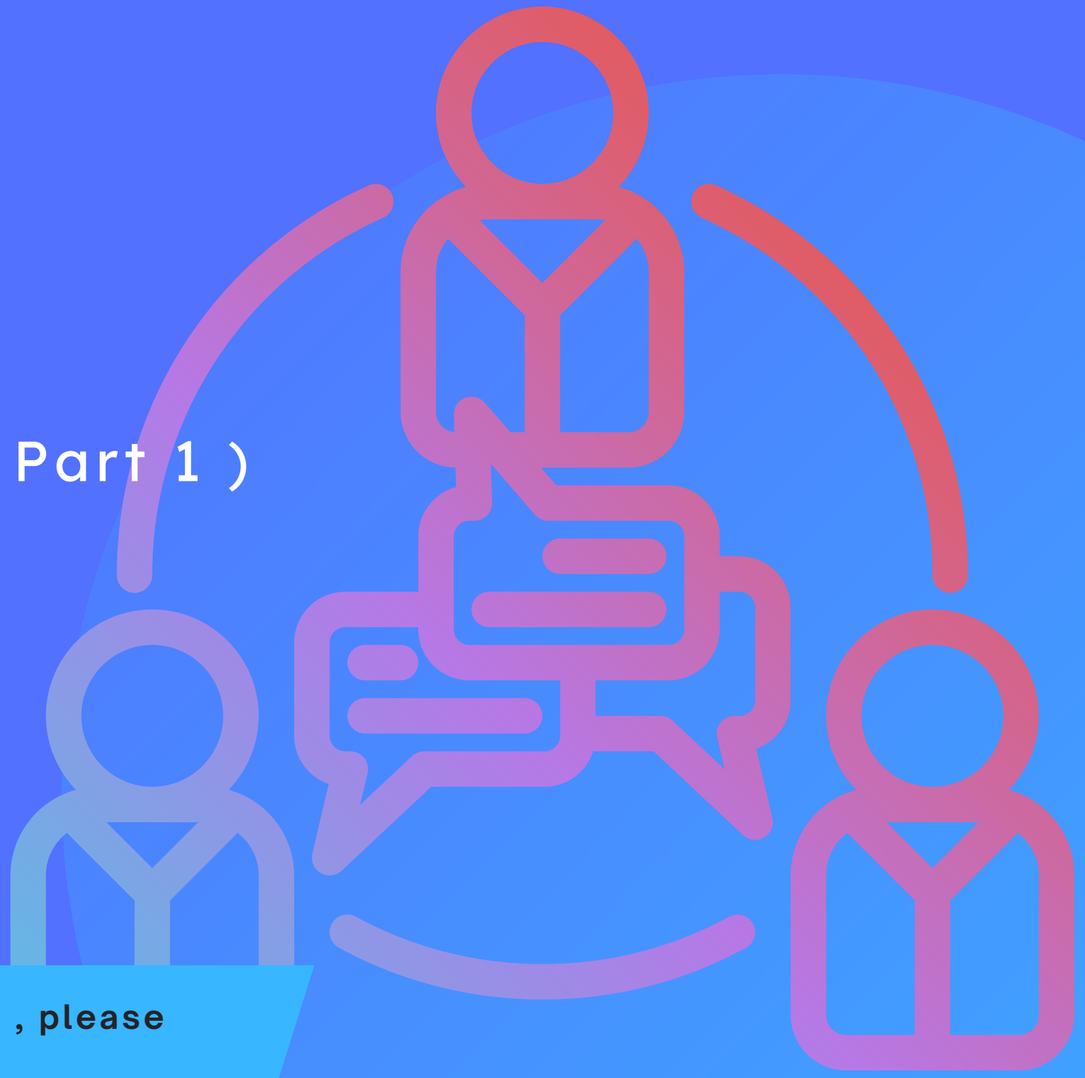
Yarmouk University

Community Medicine

Lec. 7 - Association VS Causation (Part 1)

Dr. Ola

Written By : Group B4



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Association Vs Causation

Lec. 7

MED 410

Dr. Ola Soudah

Cause and Effect

From record

- There is two type of variables dependent(response ,outcome) and independent(regressor).
- Independent effect on dependent but the relation is not straightforward bec. of in sometimes there is more than one independent variable .

Approaches to etiology in human populations

- Story
- Tobacco was introduced to Europe as a new world crop in the early 1600s.
- The mass production and consumption of tobacco through cigarette smoking did not begin until the development of the cigarette rolling machine by James Duke in the 1880s.
- Men were the first mass consumers of cigarettes.
- During World War I, cigarettes were widely distributed free of charge to U.S. soldiers.

- Cigarette smoking first became popular among women in the 1920s.

- By the 1950s, over 50% of adult males and approximately 25% of adult females were regular cigarette smokers.

- Epidemiologists observed that lung cancer deaths were increasing in frequency in the 1930s and 1940s.

Lung cancer especially among men

- In the 1950s, the number of lung cancer deaths in females also began to increase, and by the 1960s, the disease had become the most common cause of cancer-related deaths in males and was still rising among women association mean relationship but not necessarily to be causation

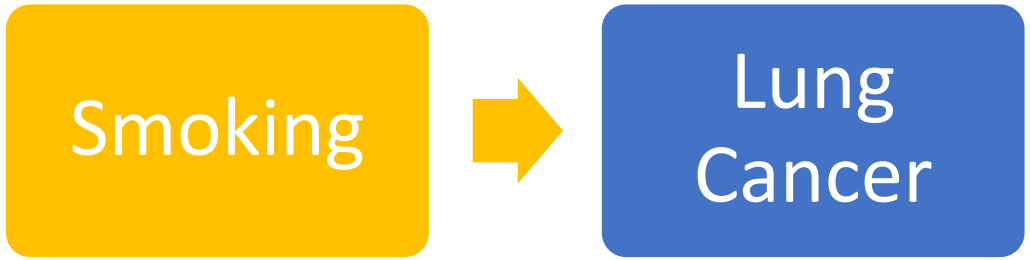
Causation: (x) present (y) will be present

1. Directed: there is arrow
2. Cyclic: arrow head
3. Graph: by pic.

Directed a cyclic graph (DAG)

- **Directed acyclic graphs (DAGs)** are visual representations of causal assumptions that are increasingly used in modern epidemiology.
- A graph is called directed if all variables in the graph are connected by arrows.
- A cause is a factor that produces an effect on another factor.
- An arrow reflects a causal pathway: one factor causes the other and not the other way around.

In this story they suggest there is possible causation btw. Smoking and lung cancer

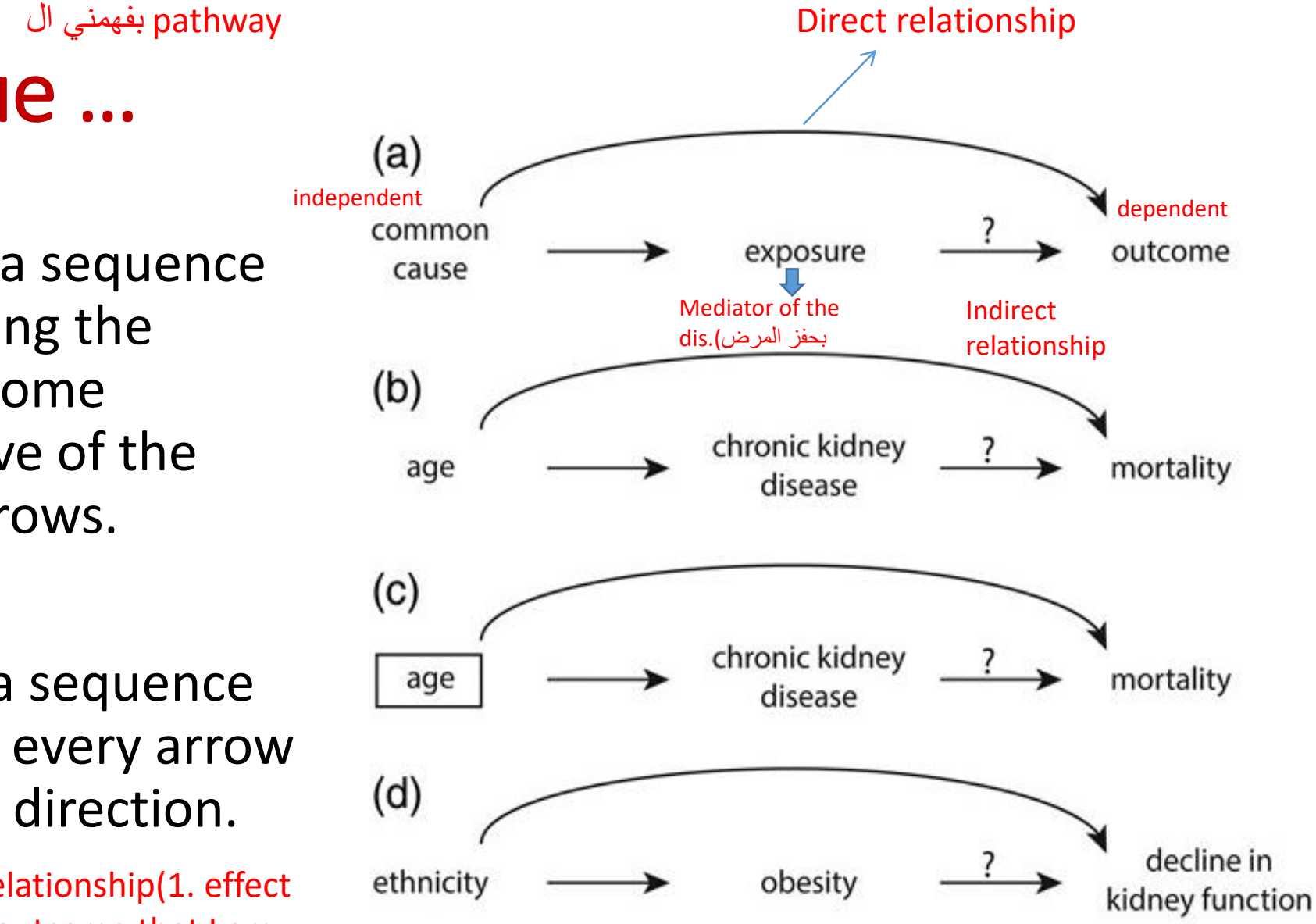


If there is multiple arrows ,DAG بفهمني ال pathway

DAG. Continue …

- A *path* in a DAG is a sequence of arrows connecting the exposure and outcome studied, irrespective of the direction of the arrows.

- A *directed path* is a sequence of arrows in which every arrow points in the same direction.



From DAG I can determine factor of relationship(1. effect which is independent variable and 2. outcome that I am as researcher interested to see the effect on it and 3.confounders that help me to see the story clearly)

- Conceptually, a two-step process is followed in carrying out studies and evaluating evidence:

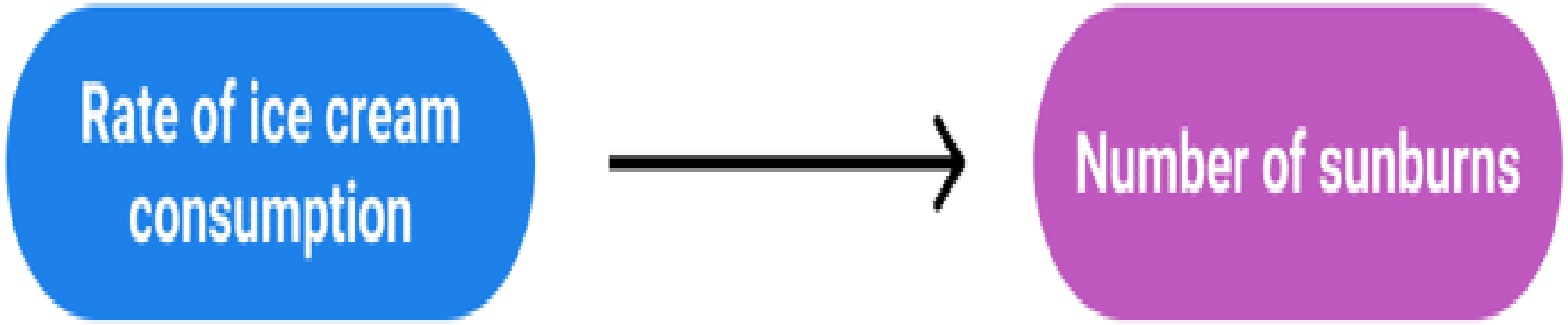
1. We determine whether there is an association or correlation between an exposure or characteristic and the risk of a disease. To do so, we use:
    1. Studies of group characteristics: ecologic studies
    2. Studies of individual characteristics: cohort, case-control, and other types of studies

2. If an association is demonstrated, we determine whether the observed association is likely to be a causal one.

We suspect causal effect relationship btw. Variable :
Firstly there should be association btw. Two variable and these association determined by etiological, cohort or case control studies

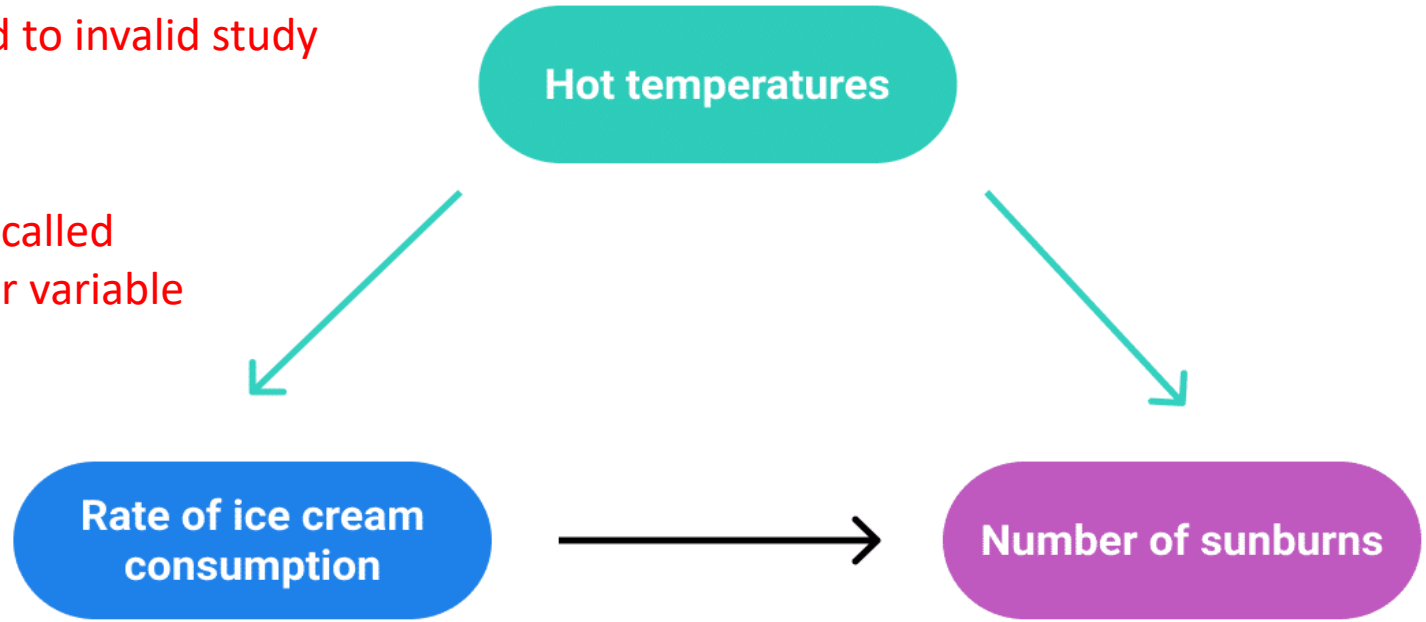
Types of Associations

- Is it a true (real) association or a false (spurious/artifactual) one?



اذا واحد اقترح ان كل ما اكل ايسكريم
اكتر بصير حروق اكتر وهاي علاقه
غير منطقيه لانه ما اخد بعين الاعتبار
الحرارة العالية عامل مشترك بينهم
Which lead to invalid study

Confounding variable



Hot temp. called
confounder variable

Scribbr

Coffee consumption and pancreatic cancer

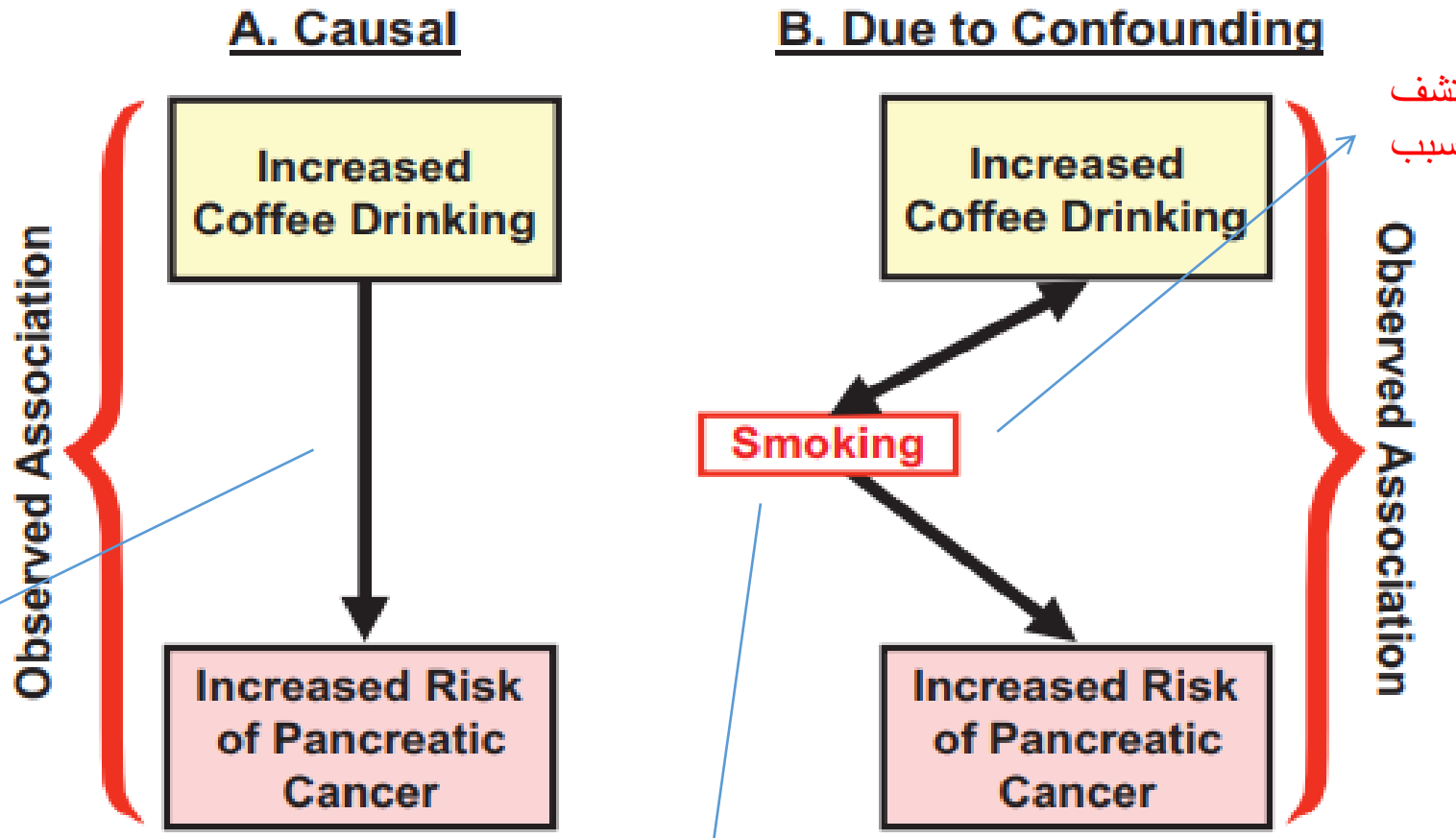


Fig. 14.5 Interpreting an observed association between increased coffee drinking and increased risk of pancreatic cancer.

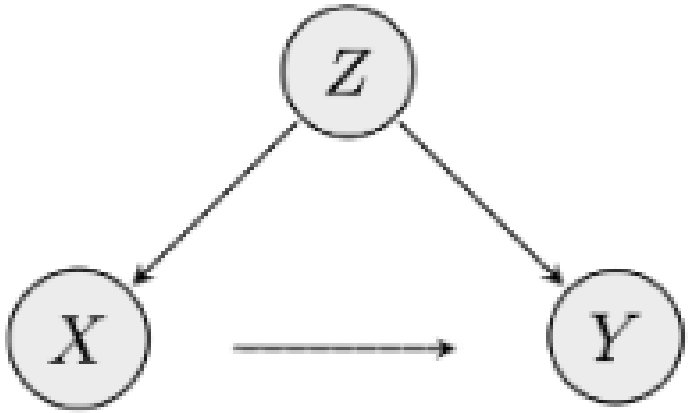
بعد التدقيق اكتشف التدخين هو السبب

Bec. There is defect on the study design when researcher select indiviual in the study
ف صار عندي bias

وجدوا ان الناس بتشرب قهوه كتير هم ال Heavy smoker

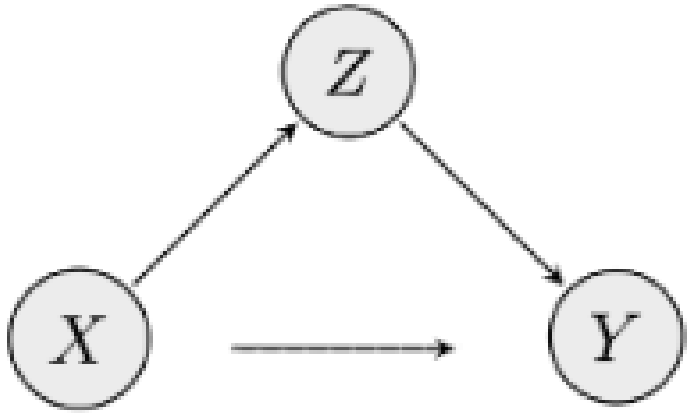
Three types of associations

Confounding



Common cause

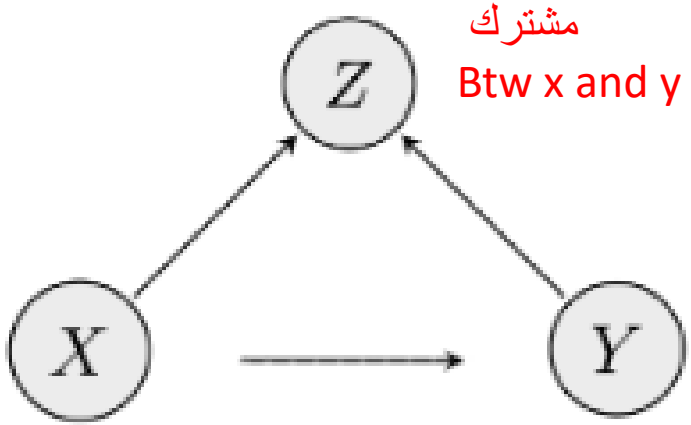
Causation



Mediation

Collision

Factor z
مشترك
Btw x and y



Selection / Endogeneity

When to suspect a spurious relationship? (false relationship)

- Differences or changes in the interest in identifying the disease.
  Intrest bec. Of trend like now “covid 19”

يعني اي شي حاليا مندرسه رح يكون في اله علاقه بالكوفيد

- Differences or changes in the ability to identify the disease.

As ex we have diagnostic test and with time its be more accurate , sensitive less detection limit so we can know case more than before

As ex before HbA1C there was people have DM but undiagnosed but after of it the same people are diagnosed bec. Previously I can not detect them

يعني لما طورت اداه للتعرف على المرض تغيرت الارقام وتأثرت نتائج الدراسة طبعا بالتغيير

- Differences or changes in the definition of the disease.

Like autism previously it was dis. Not syndrome so diagnostic criateria was clear but when they change it to syndrome they include more mild symptome so the no. of cases increased

هون الي تغير هو مفهوم المرض وليس دخول ترند جديد او اداة دراسة جديده للمرض

- Poor study design : Bias incorrect selection
- Unmeasured confounding factor.

Types of Causal Relationships

- A causal pathway can be either direct or indirect.

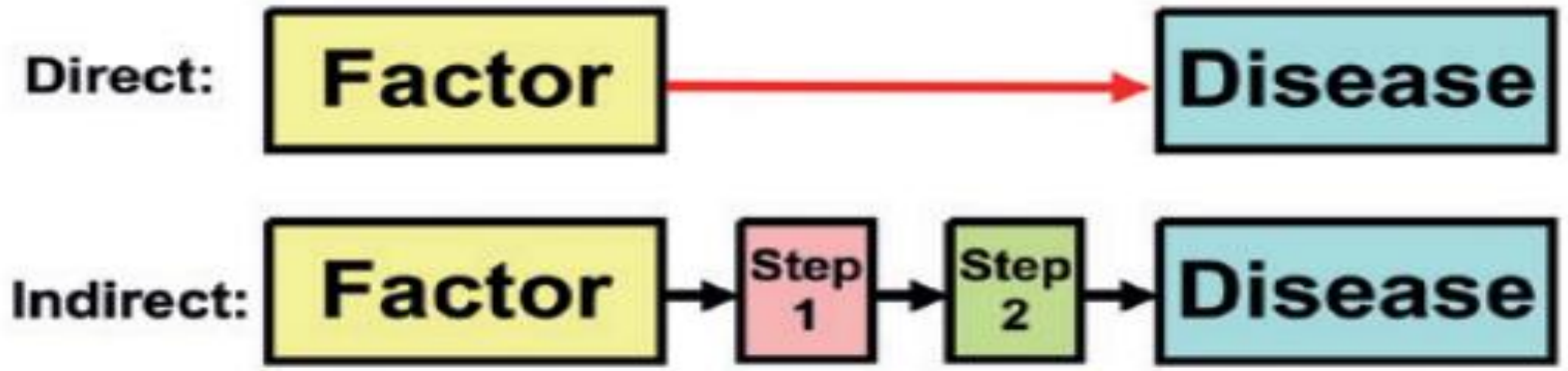


Fig. 14.11 Direct versus indirect causes of disease.

In direct causation a factor directly causes a disease without any intermediate step.
In indirect causation a factor causes a disease but only through an intermediate step or steps.

- If a relationship is causal, **four types of causal relationships are possible:**

    A. Necessary and sufficient
    B. Necessary but not sufficient
    C. Sufficient but not necessary
    D. Neither sufficient nor necessary

NECESSARY AND SUFFICIENT

كافي ووجوده لوحده يكفي لظهور المرض

المرض لا يحدث دون وجوده

- Without that factor, the disease never develops **(the factor is necessary),** and in the presence of that factor, the disease always develops **(the factor is sufficient).**

Fig. 14.12 Types of causal relationships: I. Factor A is both necessary and sufficient.

الفيروس موجود اذا يوجد مرض حتى بدون وجود عوامل اخرى

Most infectious diseases follow this model.

NECESSARY BUT NOT SUFFICIENT

- Each factor is necessary but not in itself sufficient to cause the disease. Thus multiple factors are required, often in a specific temporal sequence.

H. Pylori is a necessary cause for gastric adenocarcinoma, not every individual with H.pylori develop Gastric cancer. Thus, in addition to H. pylori, individuals have to be exposed to other risk factors (e.g., smoking and intake of foods containing nitrates) to develop gastric cancer.

Here its necessary to present cluster of factors to cause disease
If just one factor present it will not cause dis.

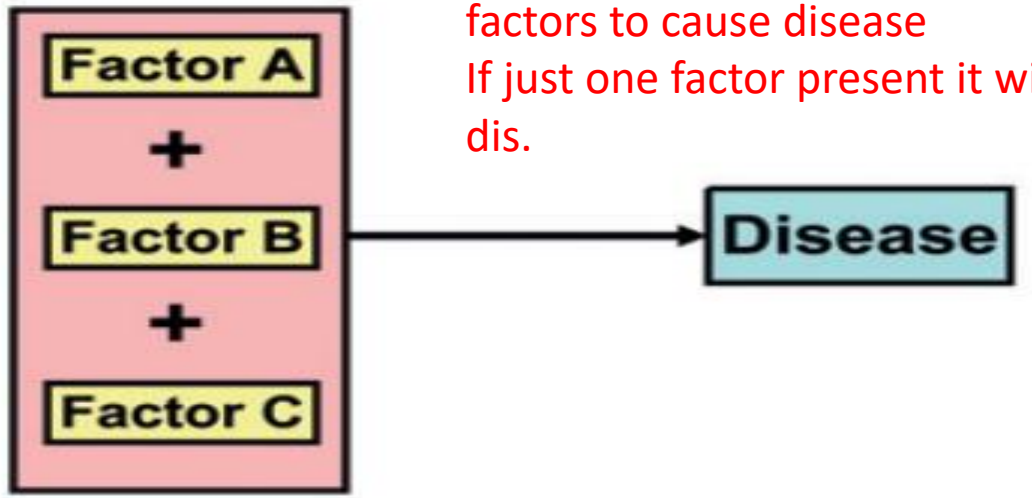


Fig. 14.13 Types of causal relationships: II. Each factor is necessary, but not sufficient.

SUFFICIENT BUT NOT NECESSARY (very rare and mainly environmental exposure)

- In this model the factor alone can produce the disease but so can other factors that are acting alone.

وجوده كافي لظهور المرض ولكن يمكن اي يحدث المرض بوجود عامل اخر غيره

Mostly in environmental exposure. Ex. radiation exposure or benzene exposure can each produce leukemia without the presence of the other. Although both factors are not needed, other cofactors probably are. The criterion of sufficient is rarely met by a single factor.

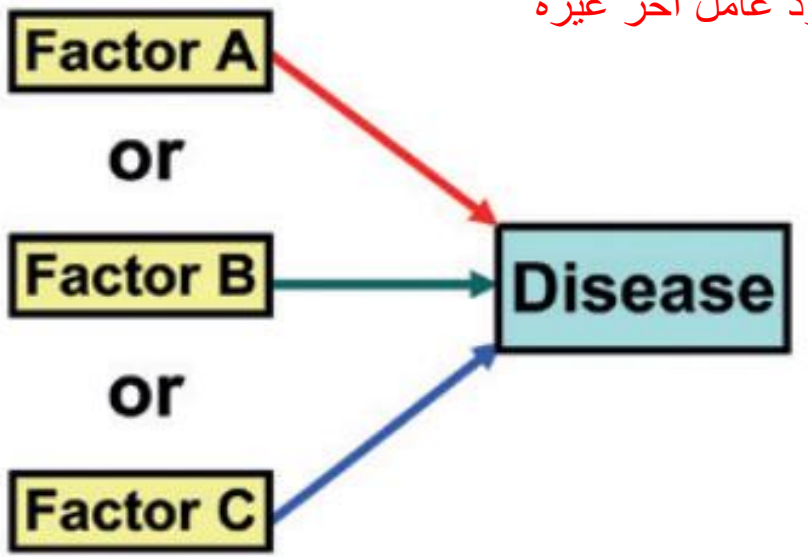


Fig. 14.14 Types of causal relationships: III. Each factor is sufficient, but not necessary.

التنتين مع بعض او كل واحد لحال بيعمل كانسر
وجود اي واحد فيهم او التنين مع بعض بيعمل كانسر

NEITHER SUFFICIENT NOR NECESSARY

- In the fourth model a factor by itself is neither sufficient nor necessary to produce disease.

Mostly represent Chronic diseases, more complex model. Ex. risk factor clusters for the development of CHD; for instance, individuals may develop CHD if they are exposed to smoking, diabetes, and low high-density lipoprotein (HDL) **or** to a combination of hypercholesterolemia, hypertension, and physical inactivity.

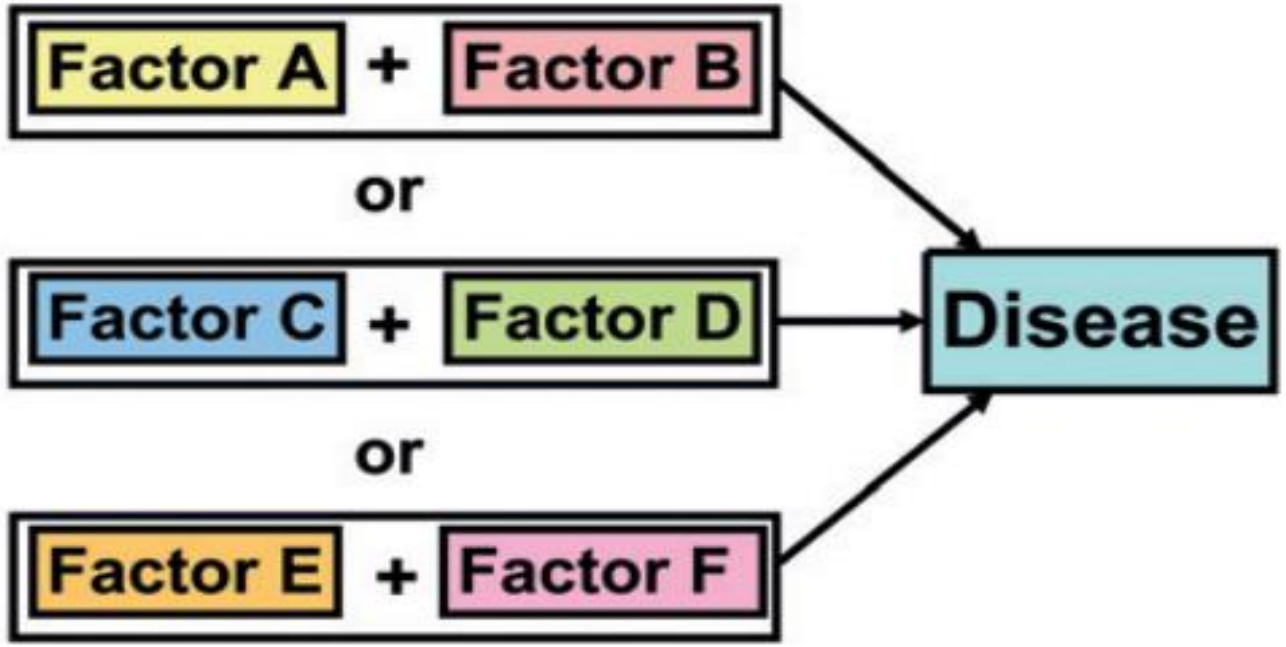


Fig. 14.15 Types of causal relationships: IV. Each factor is neither sufficient nor necessary.

Rothman's Pie Chart

A "sufficient cause" is formed by a constellation of risk factors, termed by him "component causes."

Thus Rothman's "sufficient cause" is actually a cluster of "component causes."

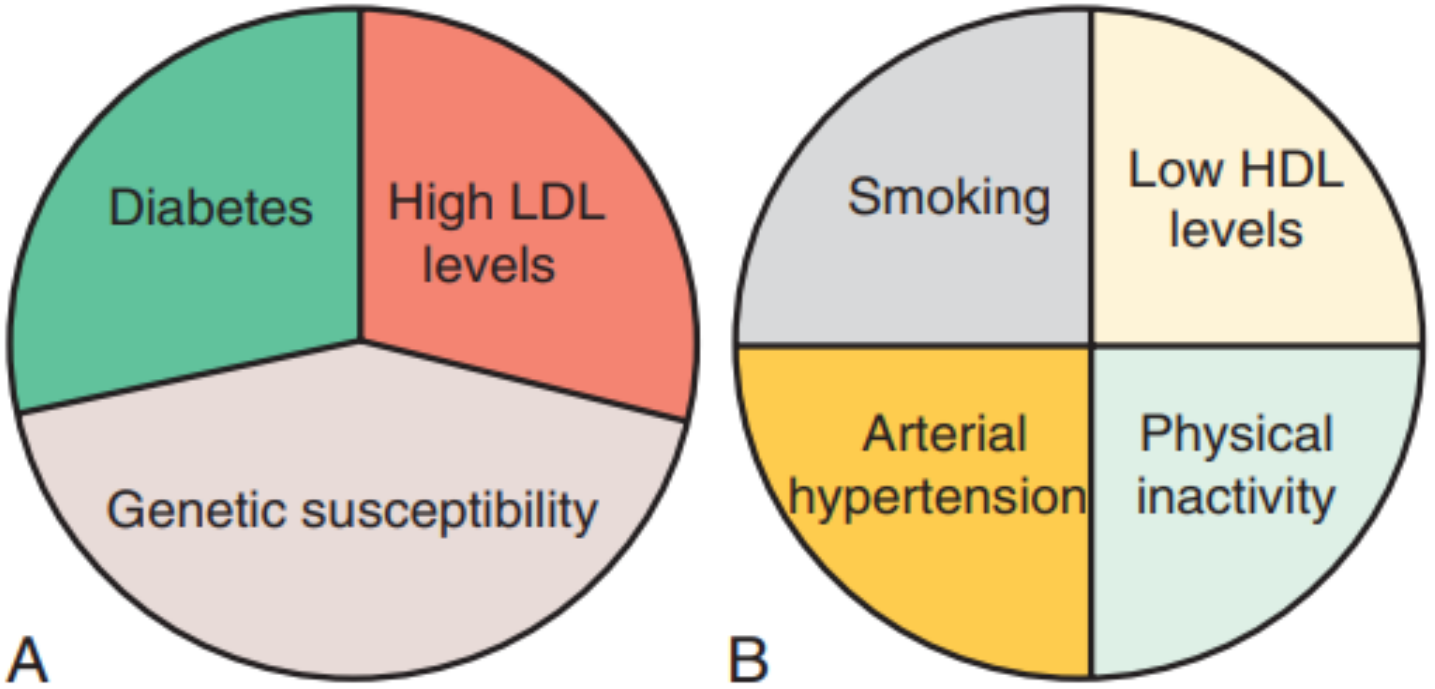


Fig. 14.16 (A–B) Hypothetical examples of of sufficient causes of atherosclerotic disease. *HDL*, High-density lipoprotein; *LDL*, low-density lipoprotein.

From record

Neither sufficient nor necessary Mostly with chronic disease

وجود فاكتورA

لحاله ما بيعمل مرض ضروري يكون في

Cluster of factors lead.to the disease

يعني

Factor A doesn’t cause disease but with factor b as group can cause it

مثال عليه ال

DM and metabolic syndrome which is insulin resistant ,obesity , dyslipidemia and hypertension

وجود عامل واحد متل الضغط ما بسبب السكري ولكن وجود عاملين او كلهم ممكن يسبب المرض

Evidence for a Causal Relationship

صعب اني اصنف العلاقات بالطريقة
السابقة لهيك بدي شي
More subjective

Hill's criteria for causality

هون بتساعد احكم على طبيعة العلاقة
بشكل اسهل

BOX 14.1 GUIDELINES FOR JUDGING WHETHER AN OBSERVED ASSOCIATION IS CAUSAL

1. Temporal relationship
2. Strength of the association
3. Dose-response relationship
4. Replication of the findings
5. Biologic plausibility
6. Consideration of alternate explanations
7. Cessation of exposure
8. Consistency with other knowledge
9. Specificity of the association

بالاعتماد على ال
Hills criteria
بدي احكم على هاي العلاقm
اذا هي
Cause and effect
او لا

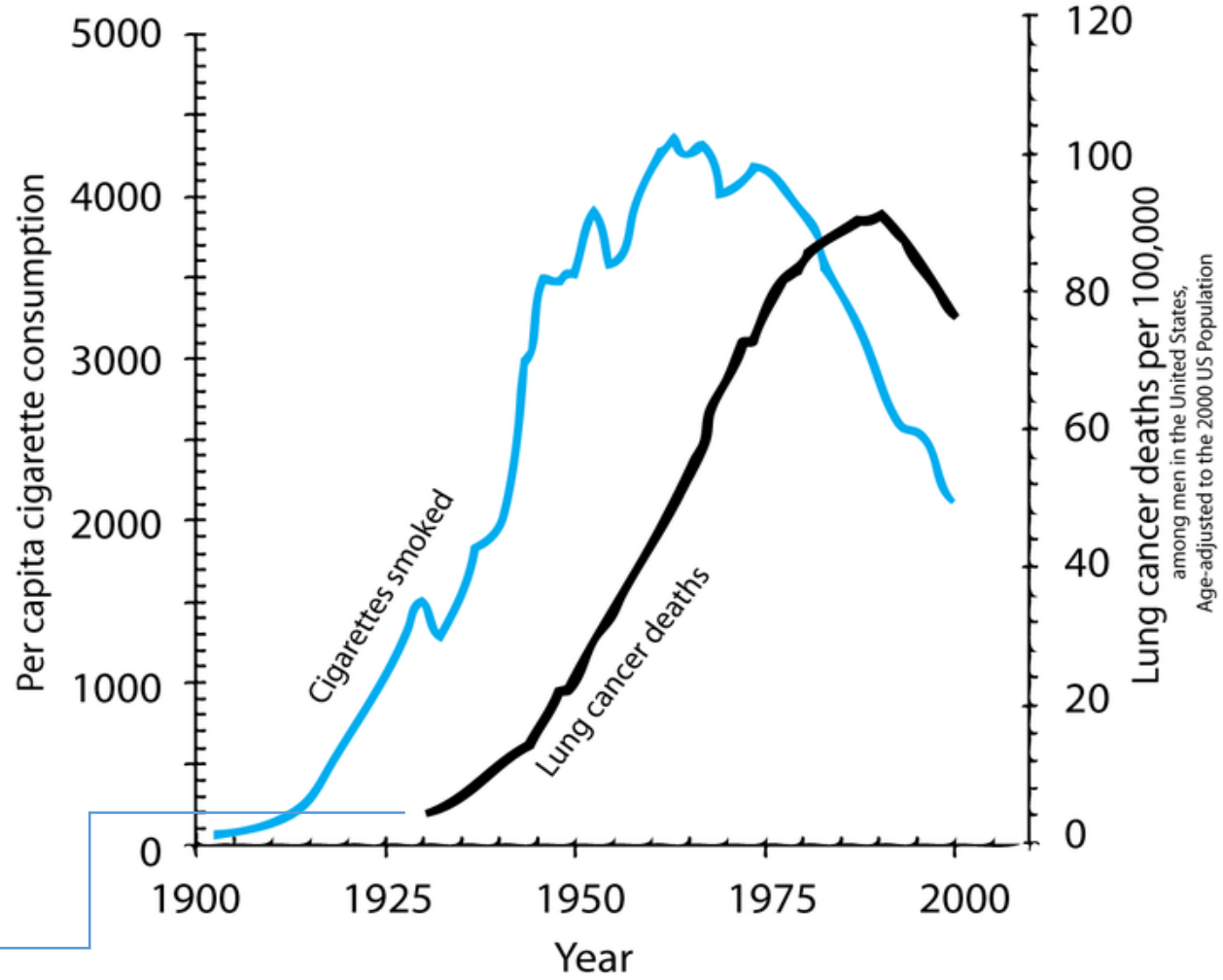
Back to our smoking story …

The observed increase of lung cancer associated with smoking cigarettes make scientist think that smoking is the cause?

- Whether it is real or not further investigation using scientific methods were used to know long delay and/or a need for long-term exposure to cigarettes before lung cancer developed.

1. **Temporal Relationship.** The “cause” precedes the “effect” in time. That is, the potential “cause” is present at an earlier time than the potential “effect.”

Therefore, we need to establish that cigarette smoking comes before the development of lung cancer.



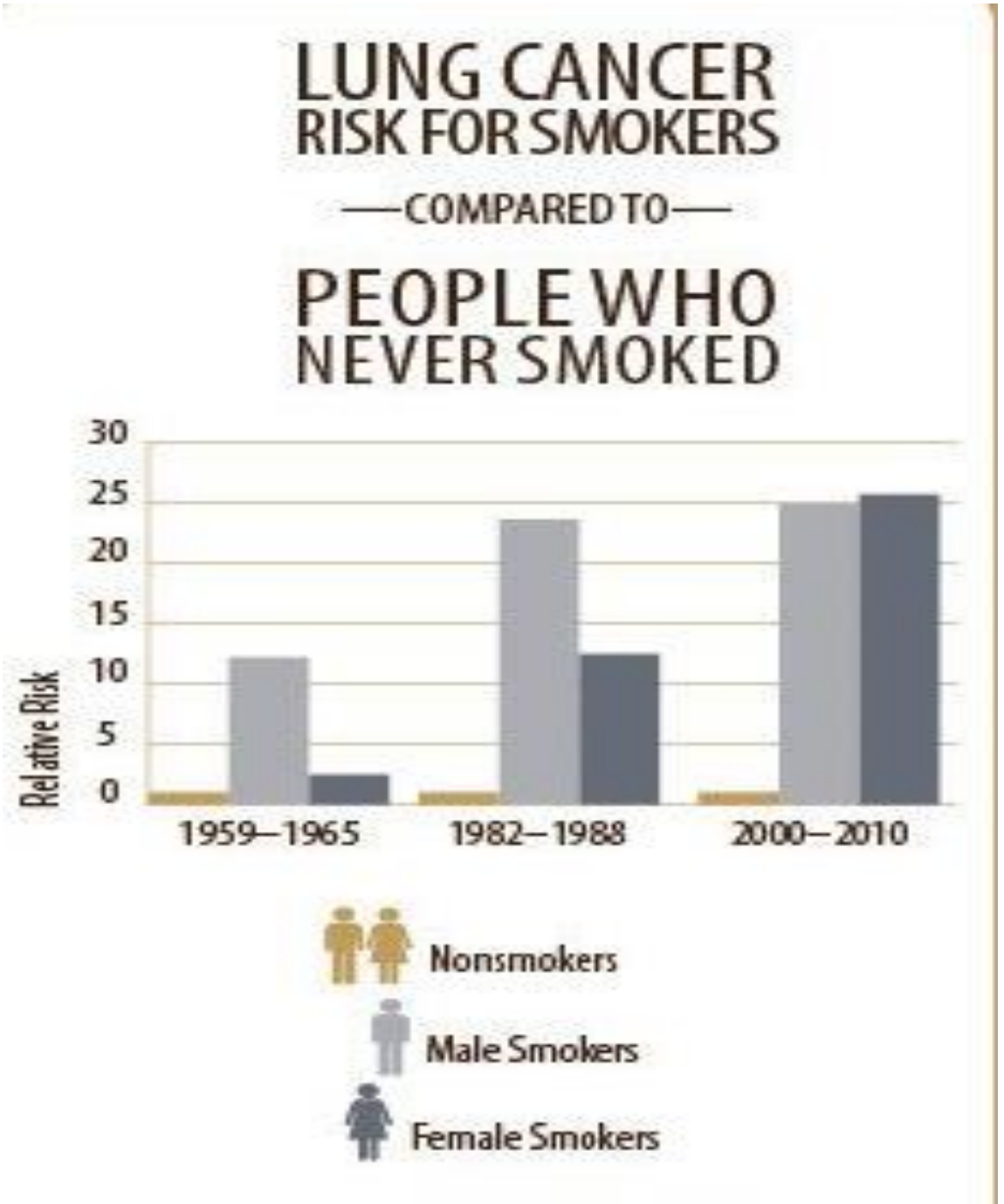
فارق زمني كبير ولكن غير كافي لوحده دون باقي العوامل

2. Strength of the Association.

The strength of the association is measured by the relative risk (or odds ratio).

The stronger the association, the more likely it is that the relation is causal.

يعني هون ببين قوة العلاقة بين العوامل بالارقام وهون بين العلاقة القوية بين زيادة المصابين ب سرطان الرئة وعدد المدخنين



	Smokers	Non-smokers	RR	AR	AR%
Lung cancer	140	10	14.0	130	92.9
CHD	669	413	1.6	256	38.3

Smoking has a much stronger association with lung cancer mortality than CHD mortality, however…

death from CHD is much more common than lung cancer, hence higher attributable risk associated with smoking.

حسب الRR
RR=1 mean there is no association
RR >1 or <-1 mean there is association
وكل ما كان اكبر من 1 او اقل من -1 كانت العلاقة اقوى بغض النظر عن الاشارة
الاشارة+ اي علاقة طردية اما – اي علاقة عكسية

3. Dose-Response Relationship. As the dose of exposure increases, the risk of disease also increases.

As smoking intensity increase lung cancer increase

RRالي بدخن 5 سجائر باليوم ال اقل من الي بدخن 15 باليوم وبكون اقل م الي بدخن 20 واكتر

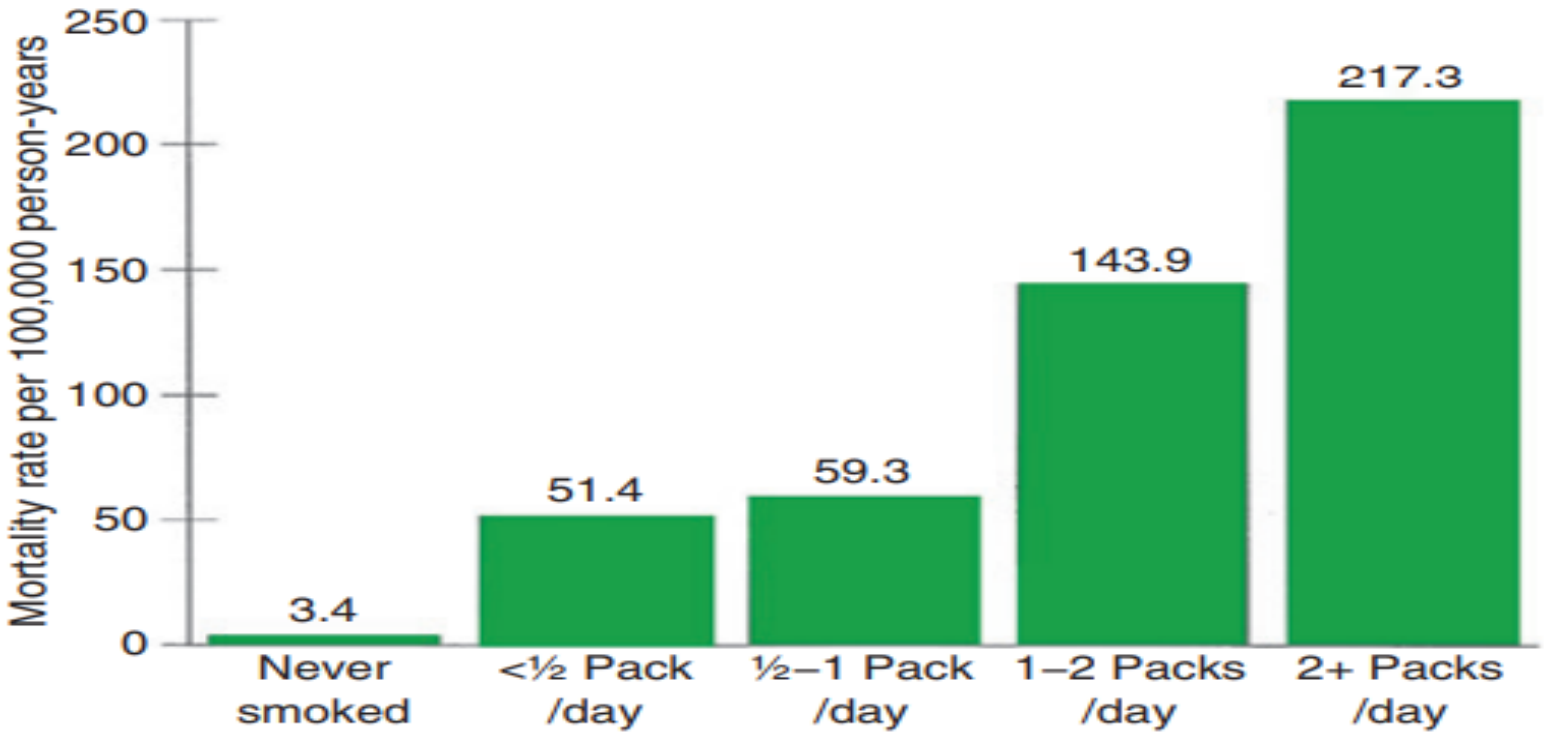


Fig. 14.18 Age-standardized death rates due to well-established cases of bronchogenic carcinoma (exclusive of adenocarcinoma) by current amount of smoking. (Modified from Hammond EC, Horn D. Smoking and

4. Replication of the Findings. If the relationship is causal, we would expect to find it consistently in different studies and in different populations.واحد قرر يعمل دراسة بالاردن رغم انها موجودة ب امريكا لكن على غير ببيوليشن

هل رح تطلع الدراسة بنفس النتائج ؟

المفروض بغض النظر عن الRR

لازم تطلع نفس طبيعة العلاقة ونفس النتائج

5. Biologic Plausibility. Biologic plausibility refers to coherence with the current body of biologic knowledge. I can explain the relationship and mechanism by biology scinence

Ex: smoking increase oxidative stress so lead to make changes in the cell then cause cancer

ف عرفت العلاقة من خلال البيولوجي لهيك رفضنا دراسة الايسكريم والحروق لانه ما في منطق علمي بيولوجي

6. Consideration of Alternate Explanations. Taking other possible explanations into account and the extent to which they have ruled out. Especially the effect of confounding. Mean no bias no confounding factors no another explanations that explain the relationship especially confounders

7. 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.

بمثال التدخين لو حفزت الناس تترك التدخين
Risk of lung cancer will decrease
لازم اشوفه بال Epidemiologic study
اذا ما شفته اذا ما حقق هاد الشرط

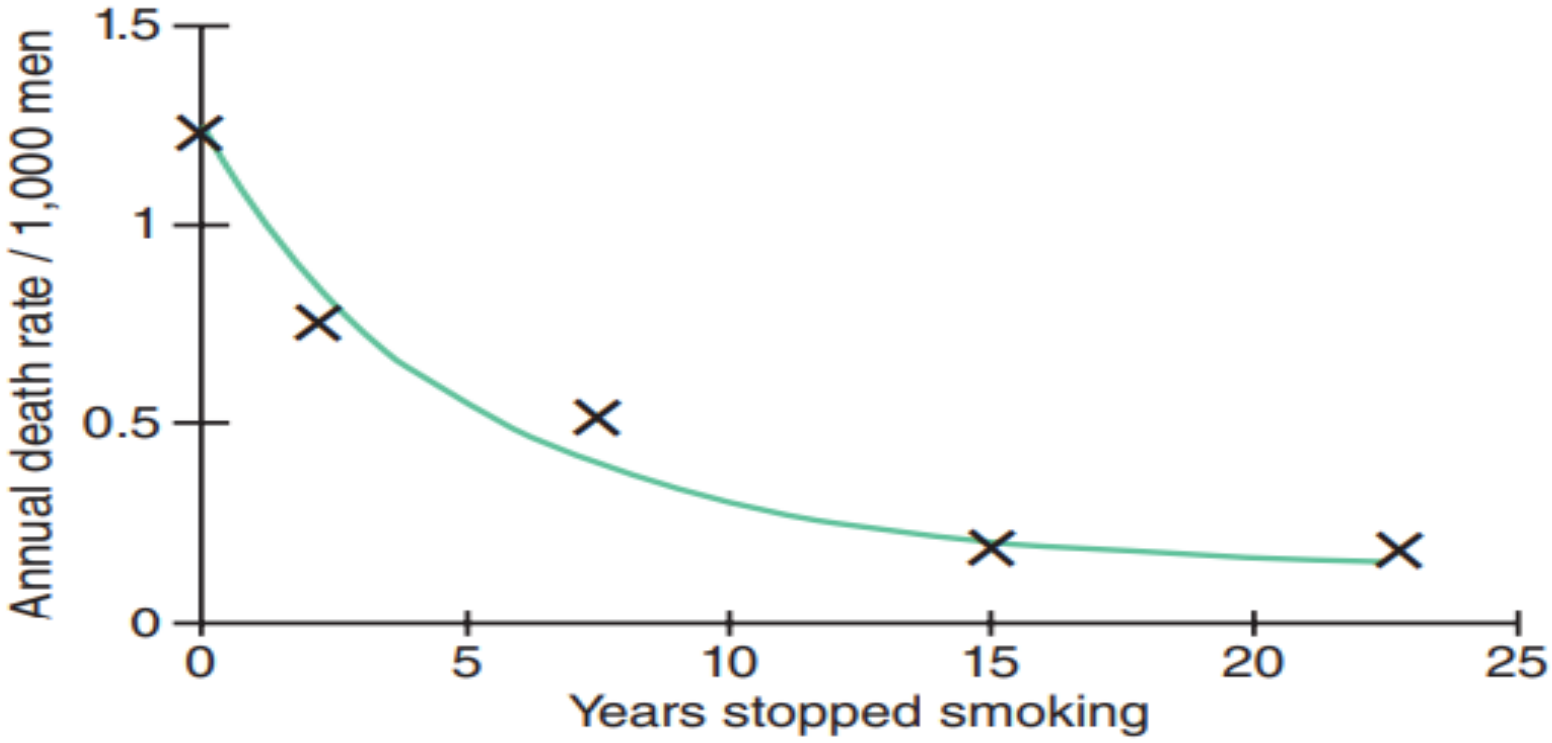


Fig. 14.19 Effects of terminating exposure: lung cancer death rates, standardized for age and amount smoked, among men continuing to smoke cigarettes and men who gave up smoking for different periods.

8. Consistency With Other Knowledge. If a relationship is causal, we would expect the findings to be consistent with other data.(stability of relationship)

We see a consistent direction in the curves, with the increase in lung cancer rates following the increase in cigarette sales for both men and women.

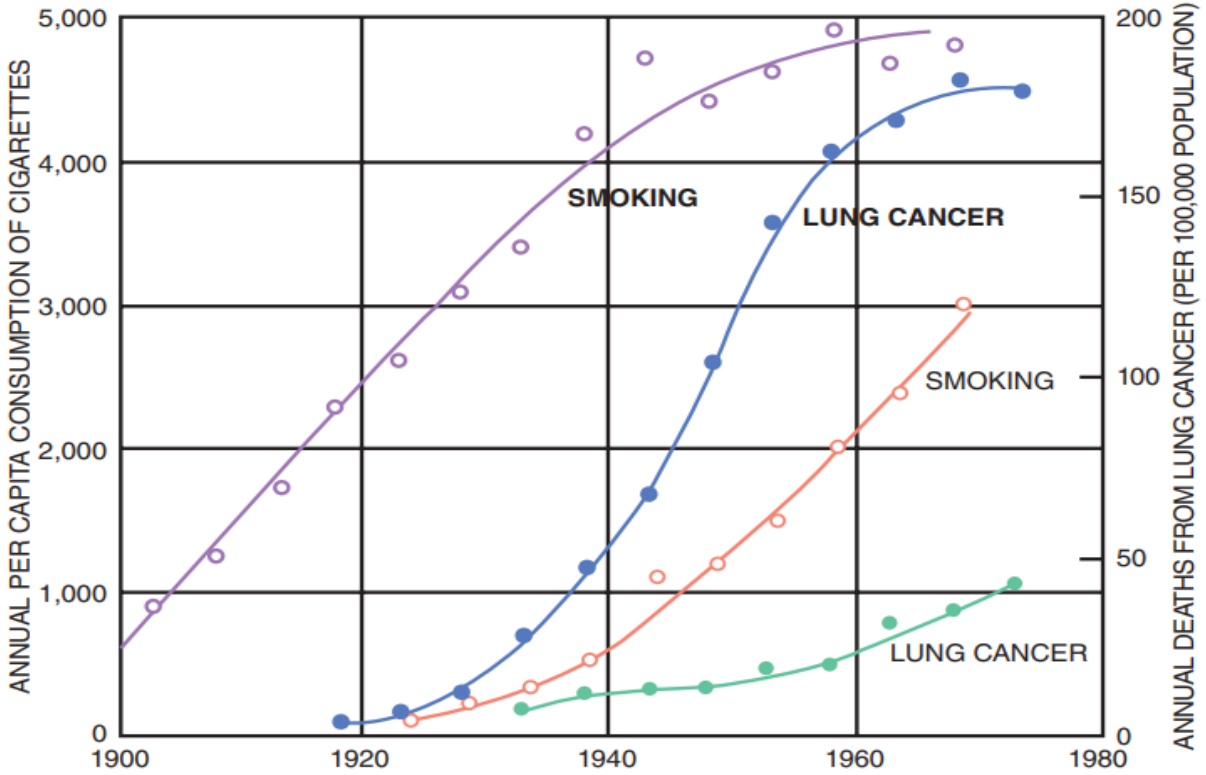


Fig. 14.21 Parallel trends between cigarette consumption and lung cancer in men *(two curves on left)* and in women *(two curves on right)* in England and Wales. (From Cairns J. The cancer problem. *Sci Am.* 1975;233:64–72, 77–78.)

9. Specificity of the Association. An association is specific when a certain exposure is associated with only one disease.

This is the weakest of all the guidelines and should probably be deleted from the list.

صعب جدا نحكم عليه لان فقط تنطبق على ال
Necessary sufficient relationship (infectious dis.)

اي دراسة لازم تحقق 70% من النقاط هدول لنعتبرها دراسة صحيحة

Question