



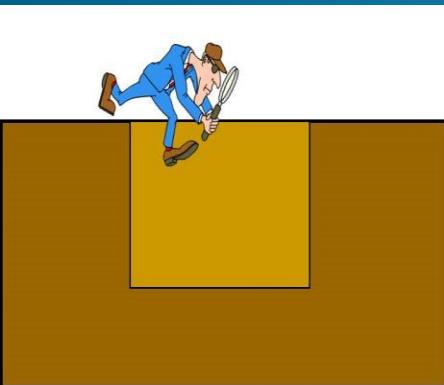
# Public Health

Title : *Analytic Epidemiology*

Lec no : *13 / File 10*

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# ANALYTIC EPIDEMIOLOGY

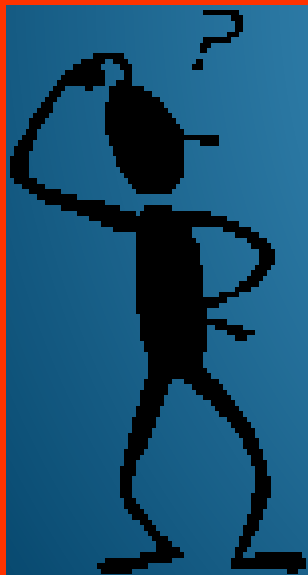
## L10

In descriptive epidemiology lecture, we discussed the factors that determine the occurrence of a disease regarding the (host, agent & environment) ... in this lecture we're gonna discuss WHY some individuals have the disease & others do not.

We need to know what makes the individual liable for a disease.

Descriptive epidemiology: ( who, when and where), forms the initial basis for Analytical epidemiology.

Analytical epidemiology: (why and how).



# Learning Objectives:

At the end of this lecture ,the student is able to:

1. Describe the **difference between descriptive and analytic** epidemiologic studies in terms of information/evidence provided for medicine and public health.
2. to estimate the **differences or variations** in the occurrence of diseases or health related events regarding exposure.
3. Give **explanations** for these variations.
4. Understand the **role of analytic** epidemiology in describing the population and helping in the exploration of variation to aid in the planning of the health services.
5. Understand the **association between risk factors and the outcome**, and the criteria of association.

- We search for the determinants of health outcomes, first, by relying on descriptive epidemiology to generate hypotheses about associations between exposures and outcomes.
- Analytic studies are then undertaken to test specific hypotheses.
- Samples of subjects are identified and information about exposure status and outcome is collected.
- The essence of an analytic study is that groups of subjects are compared in order to estimate the magnitude of association between exposures and outcomes.

Enhancing people's health can be achieved by understanding the individual factors that predispose them to developing the illness.

In descriptive epidemiology, we formulate a hypothesis that serves as the foundational basis (starting point) for analytical epidemiology to subsequently investigate and validate (testing the hypothesis).

Ex: a hypothesis (anemia is common in pregnant women)  
By performing analytical studies we accept or reject it.

\*Descriptive studies focus on **one group** (e.g., medical students, school children), describing disease occurrence with factors like age and gender.

\*Analytical studies, involving **two groups**, delve deeper into differences (e.g., sex, age) to validate descriptive hypotheses. This is why it's considered a **comparative study**, as it involves comparing two groups according to the exposure of a certain risk factor that is related to the outcome

slide # 3

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The objective is to determine if there is a **connection or correlation** between a specific risk factor and the rise or reduction of a particular disease's frequency.

Ex: : Does hypercholesterolemia increase the chance of having CVDs ?

slide 4

# ANALYTIC EPIDEMIOLOGY

TESTING

Investigating a hypothesis about the cause of disease by studying how exposures relate to disease.

## DEFINITION OF BASIC TERMS

**Risk:** A probability that an individual will become ill or die within a specified period of time or age. It is used to denote **incidence rate**. Risk and incidence are synonymous

✘ Physical activity reduces the occurrence of CVDs, while lack of physical activity increases the occurrence of CVDs.

**Risk factor:** is a variable associated with an increased risk of disease or infection. Sometimes, **determinant** is also used, being a variable associated with either ✘ increased or decreased risk.

## *Risk factors*

● A risk factor refers to an aspect of **personal habits** or an **environmental or occupational exposure**, **nutritional factors**, that is associated with an **increased probability of occurrence of a disease**. **Early detection and interventions (modifying risk factors)** lead to change in the progression of diseases.

● Since risk factors can usually be **modified**, intervening to **alter** them in a favorable direction **can reduce the probability of occurrence of disease**.

Examples:

- 1) Studying hypercholesterolemia's link to cardiovascular disease: If screened and dietary changes made, heart disease risk drops.
- 2) Vision screening in school kids, as poor eyesight affects academics.
- 3) Higher breast cancer risk in contraceptive pill users.

● The impact of these interventions can be determined by repeated measures using the same methods and definitions.

We should evaluate these interventions to see whether they're beneficial in decreasing occurrence and progression of the disease or not.

● Risk factors can include tobacco and alcohol use, diet, physical inactivity, blood pressure and obesity ect. ....

● Since risk factors can be used to predict future disease, their measurement at a population level is important. After recognizing the link between tobacco use and lung cancer risk, we need to quantify tobacco's contribution. This allows us to modify this risk factor and prevent lung cancer occurrence.



**Relative risk (RR):** is a measure of strength of association between an **exposure** and an **outcome**.

Its value is an indicator of the significance of the exposure in the etiology of the outcome.

The relative risk is calculated by relating the **incidence rate (IR) of the disease among those exposed** to the risk factor to the **incidence rate of the disease among those not exposed**.

$$\text{Relative risk (RR)} = \frac{\text{Incidence rate among exposed}}{\text{Incidence rate among non exposed}}$$

Relative risk tells us What is the strength of association between smoking and lung cancer, what is the strength of association between breastfeeding and natural immunity of babies.

Infants who are breastfed have a lower likelihood of experiencing respiratory and gastrointestinal infections compared to those who are fed with bottles.

Breastfeeding is the exposure, RT and GIT infections are the outcome.

When comparing breastfeeding to formula feeding and their impact on infectious diseases, we're essentially contrasting two groups: one with exposure and the other without.

The risk factor is (not breastfeeding); the exposed group comprises bottle-fed infants, The outcome we're observing is infection.

We analyze infection rates among breastfed and bottle-fed infants separately, then compare the incidence of infections between these groups.

The **value** of the relative risk depends on the difference in the incidence rates of the disease in the two groups (exposed group and non exposed group).

- a. If the value is 1, then no association exists,
- b. if it is below 1, the factor may be protective,
- c. when it is greater than 1, then the association exists and positive.

The greater the value of the relative risk is, **the stronger the association is and the** more likely that the association is causal.

Incidence rate (IR) of lung Ca among smokers is 100/1000, IR of lung Ca among non-smokers is 20/1000,

$$\text{Relative risk} = \frac{100}{20} = 5 \quad \{ \text{RR} > 1 \}$$

*a strong* **→ there is association between smoking and lung Ca}**

This means that smokers develop lung Ca 5 times more than non-smokers

## Attributable risk (AR):

It refers to the fraction of the incidence rate of the disease that can be attributed to the exposure to the risk factor.

It is calculated by the following formula:

$$\text{Attributable risk (AR)} = \text{IR among exposed} - \text{IR among non exposed} .$$

The **significance of the attributable risk** is that it gives an idea about the expected gain in health and life or the expected reduction in incidence rate if the risk factor is eliminated.

Attributable risk involves determining the extent to which a risk factor contributes to the development of a disease. It aims to understand the connection between the factor and the disease's occurrence.

$$\text{Percentage reduction} = \frac{\text{IR among exposed} - \text{IR among non exposed}}{\text{IR among exposed}} \times 100$$

The expected reduction can be expressed as **percentage** out of the incidence rate among the exposed (Attributable risk proportion) as follows:

IR of lung Ca among smokers is 100/1000, IR of lung Ca among non- smokers is 20/1000,

$$AR = 100 - 20 = 80/1000$$

Smoking attributed to 80/1000 cases of lung Ca.

$$\text{Percentage reduction} = \frac{80}{100} \times 100 = 80 \%$$

That means , we can prevent 80% of lung ca by preventing smoking, or by implementation of smoking cessation program we prevent 80% of lung Ca among smokers.

In the earlier instance, we indicated an incidence of 100 cases of lung cancer among smokers. Now, the question arises: out of these 100 cases, how many were directly attributed to smoking rather than another factor like asbestos exposure? Furthermore, by eliminating smoking, what extent of reduction can we achieve in lung cancer occurrences among smokers?

Certain illnesses involve multiple contributing factors. It's important to understand the individual impact of each factor on disease occurrence and incidence.

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### Slide (16) ↓

**prospective study:** Study in the future, for example we screen a group of people for anemia before the disease's onset. We then maintain the study by conducting subsequent assessments.

we start with the risk factor, **EX: women who are on contraceptive pills are subsequently monitored over time to ascertain the incidence of breast cancer within this group.** These women are exposed to the exposure and under investigation but don't necessarily develop the disease.

**Retrospective:** people already have the disease.

we start with the outcome, **ex; women diagnosed with breast cancer, we look for history of using contraceptive pills.**



★ بهادي الدراسة انا ما بحتاج الي عندهم المرض، انا باخد المجموعة اللي ما عندها المرض  
وبضلني متابعتها.

**prospective study** : is a type of **study** where participants are enrolled into the study **before they develop the disease or outcome** under study and follow up for a period of time (depend on the type of disease), to estimate the risk of exposure (**incidence**).

**Retrospective:** A retrospective study looks **backwards** and examines exposures to suspected risk or protection factors in relation to an outcome **that is established at the start of the study**

# Association

A statistical (quantitative) **dependence** between two or more variables. Variables are said to be **associated if they tend to occur together more frequently** than could be explained by chance. The degree of association is determined by statistical tests.

## Types of association:

### A. statistical association

Association could be (real or by chance)

\*Real Association ;( if a certain risk factor is present the outcome will occur).

\*Association by chance;( not proved by statistics or studies.

### B. Biological association: Koch's Postulates

A specific risk factor is linked to a particular outcome, yet it isn't the direct cause; its connection is influenced by other confounding risk factors..

## Types of statistical association:

a. **Non causal** when the apparent association is due to **confounding process**, when a **third factor** is related both to the risk factor (the cause) and the outcome or effect (the disease).

b. **Causal** which is either **direct** A  $\longrightarrow$  B  
i.e.,: vit. A deficiency causes night blindness

*↳ Proved by statistical studies.*

or **indirect**: A  $\longrightarrow$  B  $\longrightarrow$  C

Vit D deficiency causes osteoporosis ,  $\longrightarrow$  **bone fracture**

# Causal association

A statistical association is likely to be **causal** if the following **criteria** are fulfilled:

## Epidemiological criteria (Bradford Hill criteria):

1. **Strength of association**, as measured by the **relative risk** The higher the RR, the stronger the association and more likely its the causal factor
2. **Dose-response relationship**, The **larger the dose** and or the **longer the duration of exposure**, the **higher the risk** of disease.
3. **Time sequence**, Temporality, **Exposure** comes **before** the outcome. Smoking( exposure) is before lung.CA (outcome)
4. **Experimental evidence**, Elimination of risk factor reduces or eliminates the disease.

5. **Consistency**, Different studies have similar results regarding the association.

التوافق بنتائج الدراسات باختلاف وقت إجرائهم و مكانهم و اختلاف اعراق عينات الدراسة.

6. **Coherence**: Coherence between epidemiological and laboratory findings increases the likelihood of an effect. However, Hill noted that "... lack of such [laboratory] evidence cannot nullify the epidemiological effect on associations.

بنتعمد على ال epidemiological findings حتى لو ما كان عن نتائج مخبرية تدعمها.

7. **Biological plausibility**, Is the association consistent with another knowledge? (**mechanism of action**; evidence from experimental animals)

8. **Specificity**, The outcome or disease occurs only in relation to the risk factor..

## Strength of association

- Measures of association” used to quantify the strength of the association between an exposure and outcome  
*e.g.* Relative risk, odds ratio
- Strong associations are more likely to be causal than weak associations  
The larger the relative risk (RR) or odds ratio (OR), the greater the likelihood that the relationship is causal.
- Weak associations are more likely to be explained by undetected biases or confounders

- How large must a relative risk or odds ratio be to be considered 'strong':
  - 2 ? 4 ? 20 ? .....?
- No universal agreement regarding what constitutes a 'strong' or 'weak' association
  - An OR or RR > 2.0 is 'moderately strong'
  - An OR or RR > 5.0 is 'strong'
- The relationship between smoking and lung cancer is an excellent example of a 'strong association'
  - odds ratios and relative risks in different studies are in the 4 to 20 range

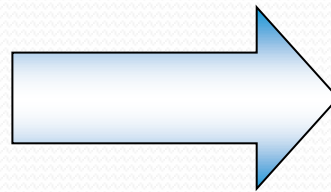
~~#~~ If the exposure to the risk factor wasn't before the occurrence of the disease, the risk factor is not causal

## Time sequence , Temporality:

- Exposure comes **before** the outcome.
- This refers to the necessity for the **exposure** to **precede** the **outcome** (effect) in time.
- Any claim of causation must involve the cause preceding in time the presumed effect
- Easier to establish in certain study designs
  - Prospective cohort study
- ~~#~~ Lack of temporality **rules out** causality



Exposure



TIME



Normal lung

Cancer

Outcome



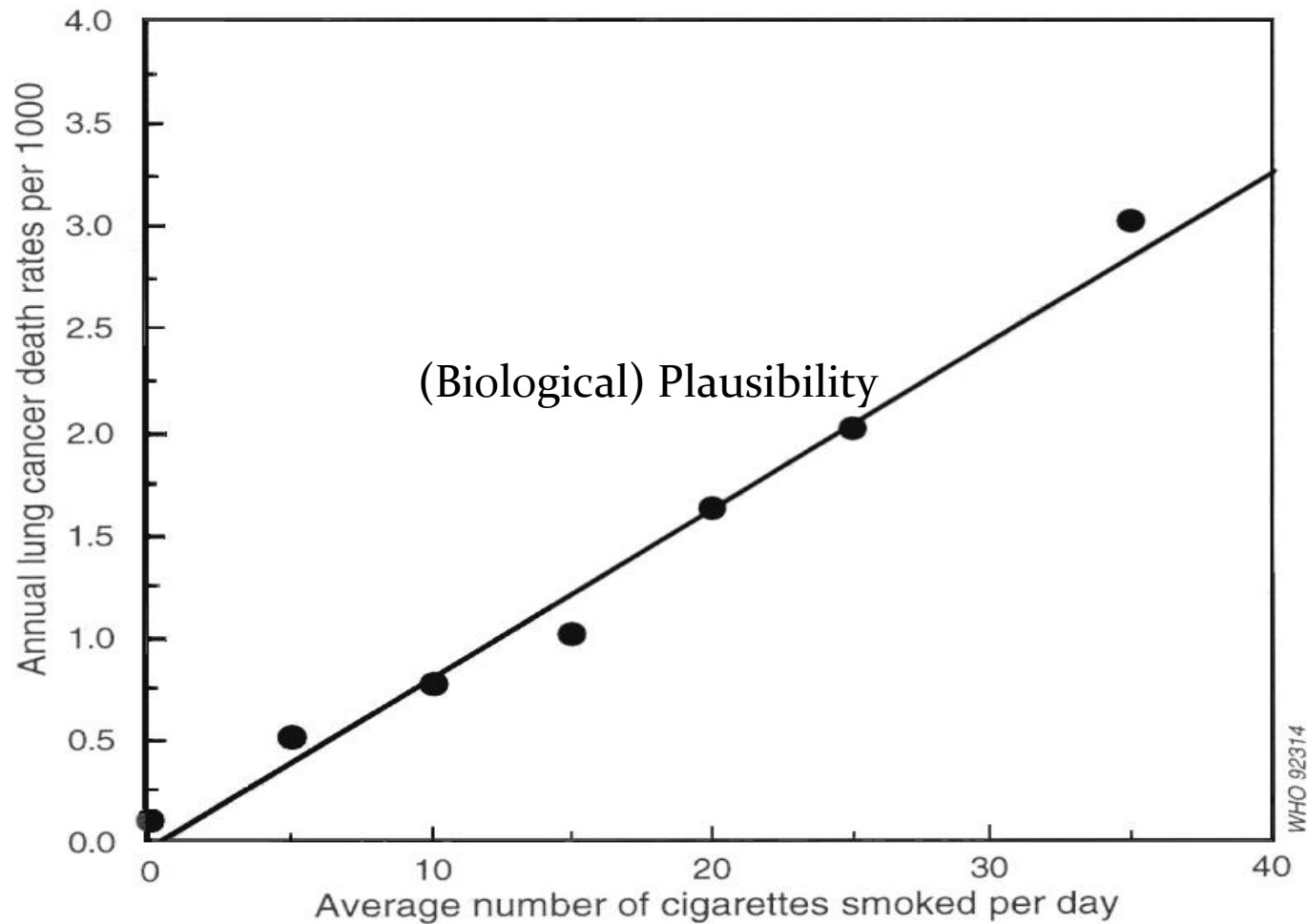
# Dose-response relationship

- Dose-response ('biological gradient') the relationship between the **amount of exposure (dose)** to a substance and the resulting changes in **outcome (response)**
- If an increase in the level of exposure increases the risk of the outcome.
- this strengthens the argument for causality.

Measuring the relationship between dosage and response varies according to the specific risk factor being studied. For instance:

1. When examining smoking, we focus on the years of smoking and the number of packs smoked daily.
2. For contraceptive pills, the dose-response relationship centers on the duration of pill usage.
3. In the context of breastfeeding, we consider the duration of breastfeeding and whether it's exclusive or mixed with other food sources like formula.
4. Radiologists employ continuous radiation monitoring devices to track their exposure levels.
5. Medications and drugs each possess a distinct recommended dosage; straying from this can lead to overdose and toxicity.

## Death rates from lung cancer (per 1000) by number of cigarettes smoked, British doctors, 1951–1961



# (Biological) Plausibility

Plausibility refers to the **biological** plausibility of the hypothesized causal relationship between the exposure and the outcome

*Is there a logical and plausible biological mechanism to explain the relationship?*

## OBSTETRICS

### Maternal caffeine consumption during pregnancy and the risk of miscarriage: a prospective cohort study

Xiaoping Weng, PhD; Roxana Odouli, MSPH; De-Kun Li, MD, PhD

“A high dose of caffeine could constrict a mother’s blood vessels reducing the blood flow to the placenta” (Biological

200 mg/day, and aHR of 2.23 (1.34 to 3.69) for intake of 200 or more mg/day. Key words: abortion, caffeine, miscarriage, pregnancy, risk factors, and Li D-K. Maternal caffeine consumption during pregnancy and the risk of miscarriage: a prospective cohort study.

Plausibility)



anthine, is a naturally occurring stimulant. Caffeine can be found in many sources, including coffee, tea, and energy drinks. Caffeine can be a stimulant, and it can increase heart rate and blood pressure. It can also be a diuretic, and it can increase the risk of dehydration. Caffeine can also be a vasoconstrictor, and it can reduce blood flow to the placenta.

feine could have an adverse effect on fetal development. Indeed, caffeine intake has been reported to increase the risk of miscarriage.<sup>7-10</sup>

Although numerous studies on mater-

sources of caffeine intake, including coffee, tea, and energy drinks, have been reported to increase the risk of miscarriage. However, the results of these studies are inconsistent, and the underlying mechanisms are unclear. Further research is needed to clarify the relationship between caffeine intake and miscarriage risk.



➤ Sometimes, “There is no accepted biological mechanism to explain the epidemiological results; indeed, the relation may be due to chance or confounding”

➤ **Biological gradient.** Is there a **dose response**?

➤ **Biological plausibility.** **Does it make sense?**

➤ **Coherence.** Does the evidence fit with what is known regarding the natural history and biology of the outcome?



➤ **Experimental evidence.** Are there any clinical studies supporting the association?

➤ **Reasoning by analogy.** Is the observed association supported by similar associations?

# Consistency

Repeated observation of an association in studies conducted on different populations under different circumstances

If studies conducted by....

- different researchers
- at different times
- in different settings
- on different populations
- using different study designs
- .....all produce consistent results,
- this strengthens the argument for causation.

*e.g.* The association between cigarette smoking and lung cancer has been consistently demonstrated in several and different types of epidemiological study (ecological, case-control, cohort)

## Is there a causal relationship between fluoride in water and bone fractures?

- 18 studies have investigated the association between hip fractures (outcome) and water fluoride level (exposure)
- 30 separate statistical analyses
- 14 analyses produced a 'positive association'
- 13 analyses produced a 'negative association'
- 3 'no association'
- The **inconsistency** of these results casts doubt on the hypothesised causal relationship between fluoride in water and bone fractures

■ The usual approach in **epidemiology is to begin with a disease** and **search for its causes**, although it is also possible to start with a **potential cause (such as air pollution)** and **search for its effects**.

عوامل مثل العمر و الجنس... بنعتبرهم confounding factors

■ For example, **social class is associated with a range of health problems**.

■ Low social class, as measured by **income, education, housing and occupation**, leads to a general **susceptibility to poor health**, rather than to a specific effect.

■ A **range of specific causes of disease could explain why poor people have poor health**, among them excessive exposure to infectious agents due to overcrowding, lack of clean water and sanitation, insufficient and unsafe food, and dangerous working conditions.







بعض الأمراض خاصة الأمراض المزمنة و السرطانات بتحتاج وقت طويل  
من ال follow up، هادا النوع من الأمراض بنفضل نستخدمه  
retrospective studies, خاصة انه ممكن نخسر بعض عناصر المجموعة  
بسبب الوفاة...الخ

*Thank You*