MEDICAL UNIVERSITY – PLEVEN
FACULTY OF PUBLIC HEALTH
DEPARTMENT OF PUBLIC HEALTH SCIENCES

Lecture № 4

EPIDEMIOLOGY – PART 2

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LECTURE OUTLINE

1. **Types of epidemiological studies**
2. **Descriptive studies**
3. **Analytical studies**

TYPES OF EPIDEMIOLOGICAL STUDIES

Table 3.1. Types of epidemiological study

Type of study	Alternative name	Unit of study
Observational studies		
Descriptive studies		
Analytical studies		
Ecological	Correlational	Populations
Cross-sectional	Prevalence	Individuals
Case-control	Case-reference	Individuals
Cohort	Follow-up	Individuals
Experimental studies	***Intervention studies***	
Randomized controlled trials	Clinical trials	Individuals
Cluster randomized controlled trials		Groups
Field trials		
Community trials	Community intervention studies	Healthy people Communities

DESCRIPTIVE STUDIES

- Descriptive studies are usually the first phase of an epidemiological investigation.
- Descriptive studies are concerned with observing the distribution of disease or health-related characteristics in human populations and identifying the characteristics with which the disease in question seems to be associated.
- Descriptive studies basically ask the questions :
  - When is the disease occurring? - time distribution
  - Where is it occurring? - place distribution
  - Who is getting the disease? - person distribution

TIME DISTRIBUTION

- Short-term fluctuations
- Periodic fluctuations
- Long-term trends

By monitoring of time trends, the epidemiologist seeks which diseases are increasing, which are decreasing and which are emergency health problems and what is the effectiveness of measures to control old ones.

Three epidemiological transitions in human history

First - occurred around 10,000 years ago

- Human societies shifted from hunting and gathering to agriculture
- Marked by the emergence of novel infectious and nutritional diseases

Second - about 200 years ago

- Improved nutrition and living standards, public health measures, and medical advances in developed societies led to a decline in infectious diseases and a rise in chronic and degenerative diseases

Third – beginning now

- Resurgence of infectious diseases previously thought to be under control
- The potential for the spread of infectious diseases has been significantly enhanced in today's world by the globalization of trade and travel

PLACE DISTRIBUTION

- International variations
- National variations
- Rural-urban variations
- Local distributions (Snow's study)

PERSON DISTRIBUTION

- Age
- Sex
- Ethnicity
- Marital status
- Occupation
- Social class
- Behaviour

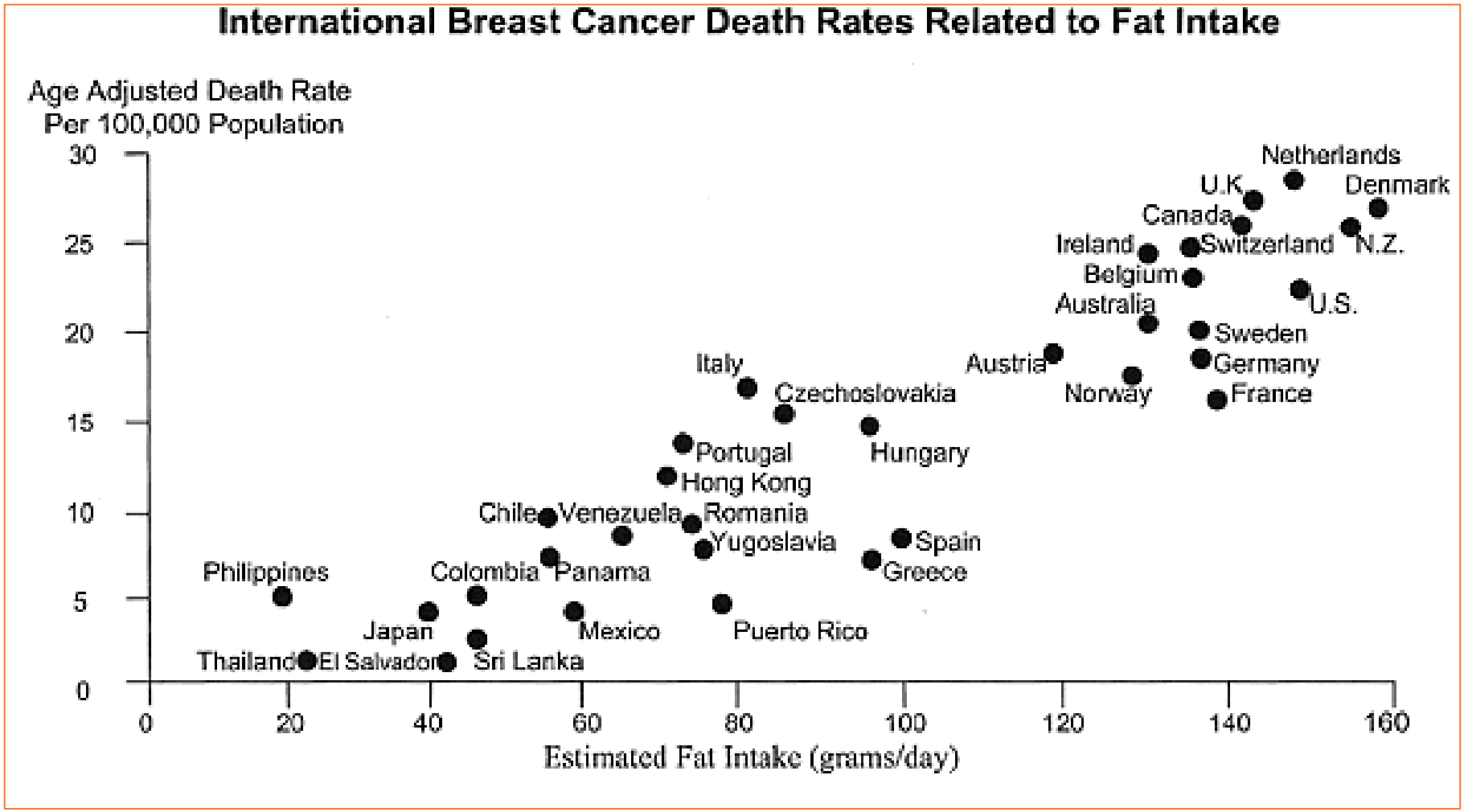
Uses of descriptive epidemiology

- Provides data regarding the magnitude of the disease load /amount of disease/ and types of disease problems of the community in terms of morbidity and mortality rates and ratios.
- Provides clues to disease etiology, and help in the formulation of an etiological hypothesis.
- Provides background data for planning, organizing and evaluating preventive and curative services.
- Contributes to research by describing variations in disease occurrence by time, place and person.

ANALYTIC STUDIES

ECOLOGICAL STUDIES

- The units of study are populations or groups of people rather than individuals.
- Compare disease frequencies between different groups during the same period of time or
- in the same population at different points in time - may avoid some of the socioeconomic confounding that is the potential problem in ecological studies.


International Breast Cancer Death Rates Related to Fat Intake
Age Adjusted Death Rate
Per 100,000 Population
30
25
20
15
10
5
0
Netherlands
U.K
Denmark
Canada
Ireland
Switzerland
N.Z.
Belgium
Australia
U.S.
Sweden
Austria
Germany
Italy
Norway
France
Czechoslovakia
Hungary
Portugal
Hong Kong
Chile
Venezuela
Romania
Yugoslavia
Spain
Greece
Philippines
Colombia
Panama
Japan
Mexico
Puerto Rico
Thailand
El Salvador
Sri Lanka
0
20
40
60
80
100
120
140
160
Estimated Fat Intake (grams/day)

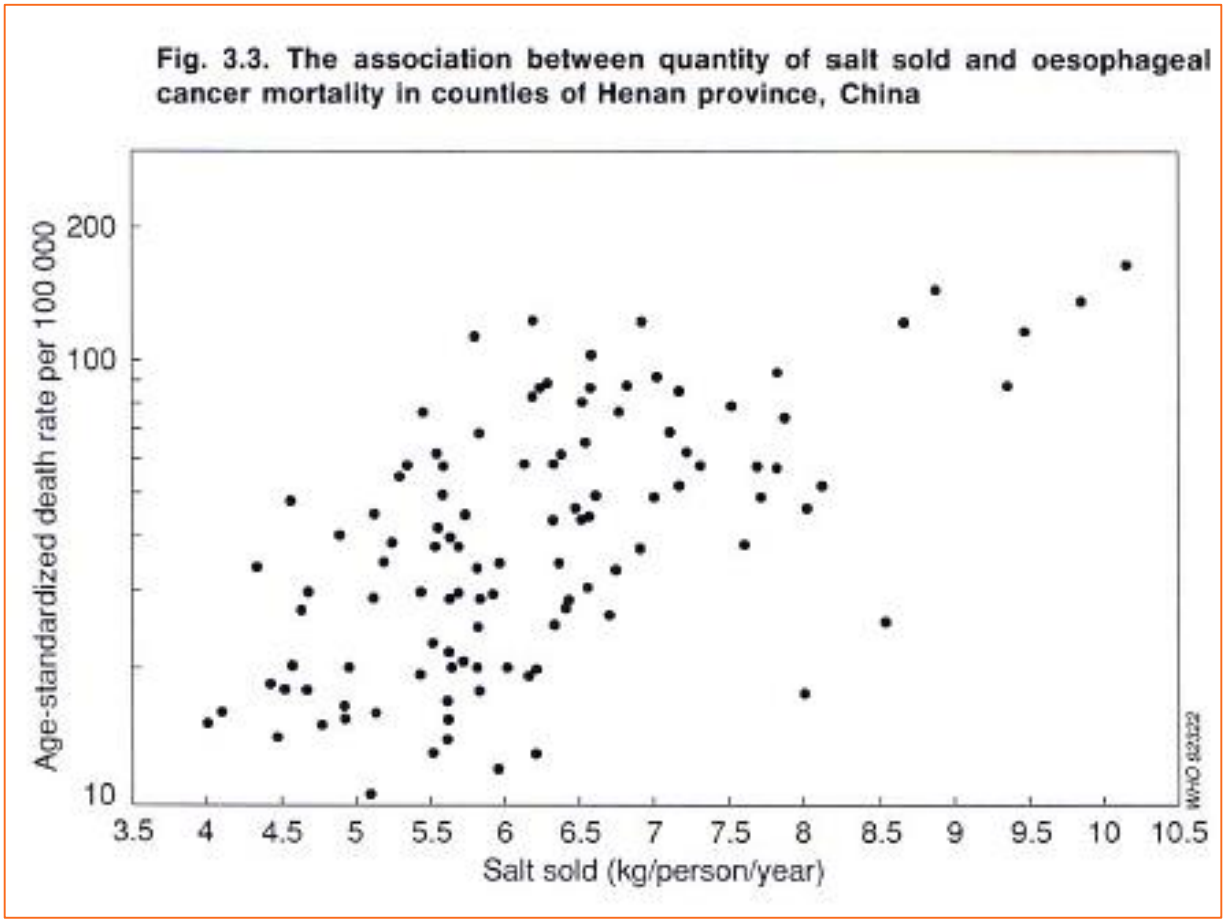


Fig. 3.3. The association between quantity of salt sold and oesophageal cancer mortality in counties of Henan province, China
Age-standardized death rate per 100 000
200
100
10
3.5
4
4.5
5
5.5
6
6.5
7
7.5
8
8.5
9
9.5
10
10.5
Salt sold (kg/person/year)
WHO 92322

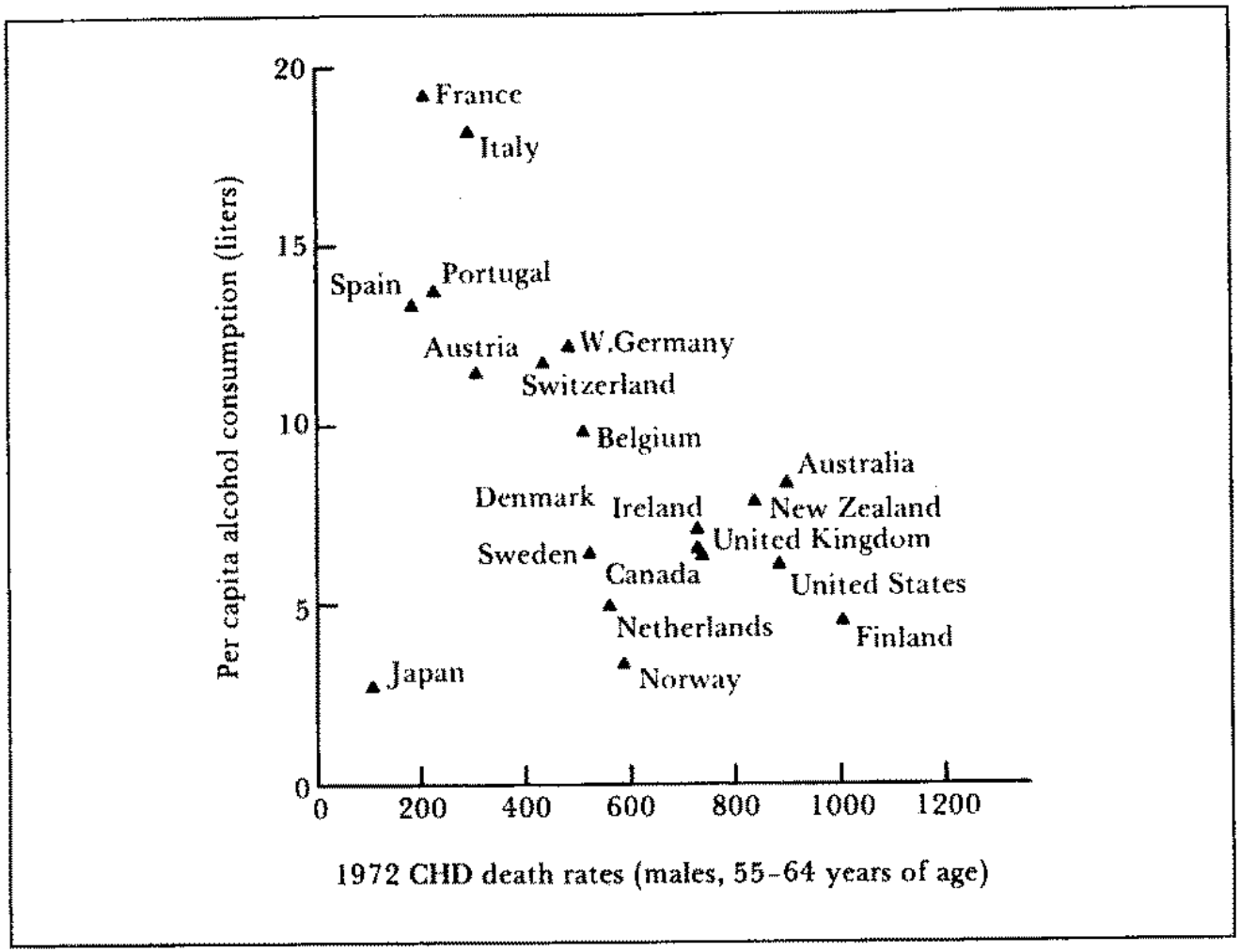


Fig. 5-2. Per capita alcohol consumption and coronary heart disease mortality rates in 20 countries in 1972. (From R. E. LaPorte, J. L. Cresanta, and L. H. Kuller, The relation of alcohol to CHD and mortality: Implication for public health policy. *J. Public Health Policy* 1:198, 1980.)

ECOLOGICAL STUDIES

ADVANTAGES

- simple to conduct
- useful for the formulation of hypotheses

DISADVANTAGES

- lack of ability to control potential confounding factors
- cannot be used to test the hypotheses
- difficult to interpret - since correlational studies refer to whole populations rather than to individuals, it is not possible to link exposure to occurrence of disease in the same person - **ECOLOGICAL FALLACY**

On the contrary, BIOLOGICAL FALLACY is an error that may occur when the attempt to explain variations in population groups is based on individual study results.

CROSS-SECTIONAL STUDIES

Cross-Sectional Study as a Descriptive Study

Purpose: To learn about the characteristics of a population at one point in time (like a photo “snap shot”)

Design: No comparison group

Population: All members of a small, defined group or a sample from a large group

Results: Produces estimates of the prevalence of the population characteristic of interest

When to Conduct a Cross-Sectional Study

- To estimate prevalence of a health condition or prevalence of a behavior, risk factor, or potential for disease
- To learn about characteristics such as knowledge, attitude and practices of individuals in a population
- To monitor trends over time with serial cross-sectional studies

ADVANTAGES TO CROSS-SECTIONAL STUDIES

- Does not require follow-up and is therefore less costly and quicker than other designs.
- Helpful for programme planning and policy development.
- Hypotesis generating.

DISADVANTAGE OF CROSS-SECTIONAL STUDIES

Since exposure and disease status are measured at the same time it is not possible to determine the direction of the association. In other words, it is not known if the exposure preceded the disease and is therefore a potential cause of disease.

EXAMPLES OF CROSS-SECTIONAL STUDIES

A cross-sectional study can be used to look at the association between **obesity and television watching.** A sample of people from the population that you are interested in can be polled and asked about their height/weight ratio and the number of hours of television the person watches each week. This study will give insight as to whether obesity and television watching are associated, but it will not help to determine which might cause the other. In other words, it is not known if obesity causes more television watching or if more television watching causes obesity.

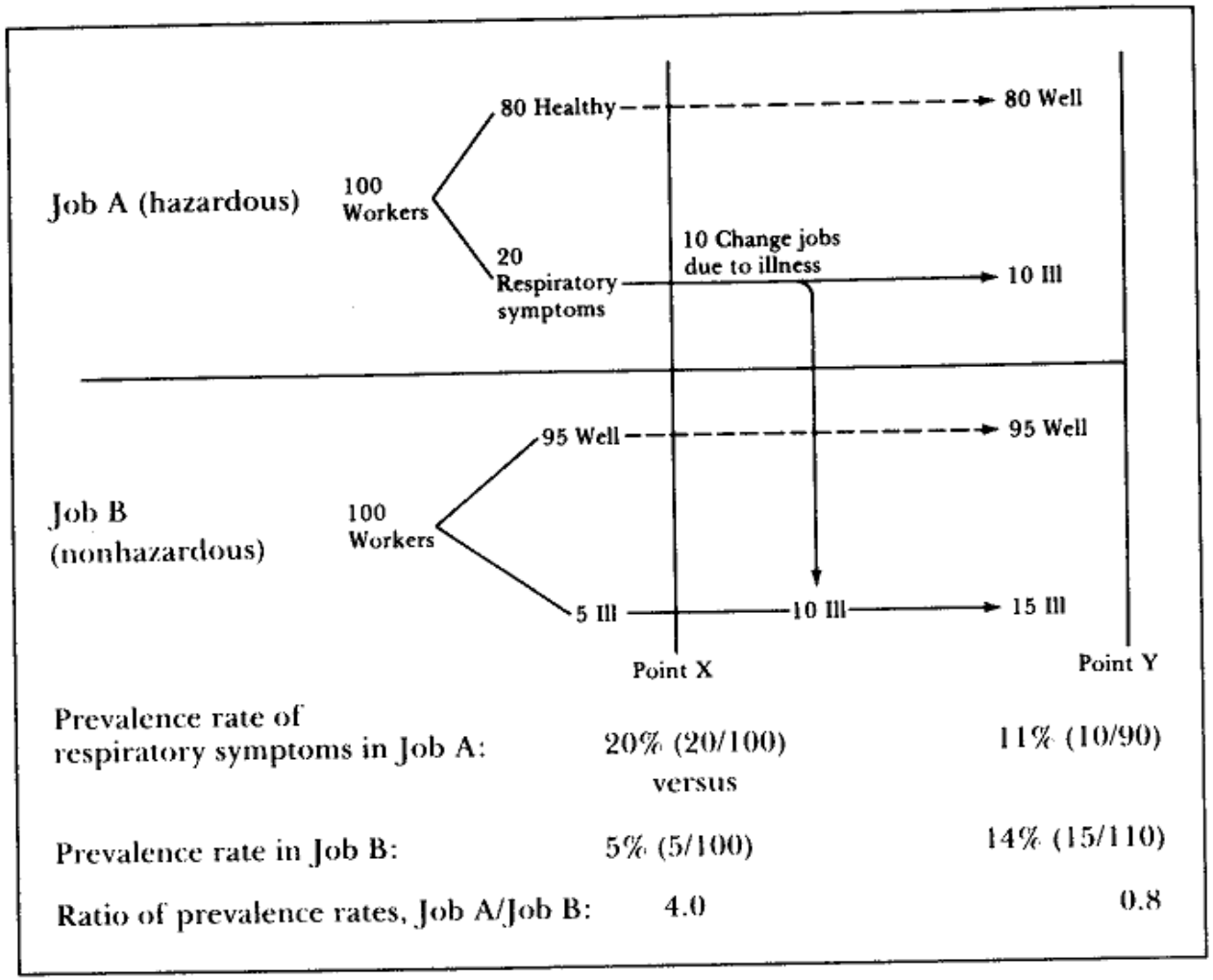


Fig. 5-3. Hypothetical illustration of the interrelationship between an occupational exposure and prevalence of disease, as measured by a cross-sectional survey. (Adapted from A. J. McMichael et al., Chronic respiratory symptoms and job type within the rubber industry. *J. Occup. Med.* 18:611, 1976.)

Eur J Clin Nutr. 2003 Oct;57(10):1250-3.

Beer and obesity: a cross-sectional study.

Bobak M[1], Skodova Z, Marmot M.

Author information

Abstract

OBJECTIVE: There is a common notion that beer drinkers are, on average, more 'obese' than either nondrinkers or drinkers of wine or spirits. This is reflected, for example, by the expression 'beer belly'. However, the few studies on the association between consumption of beer and abdominal obesity produced inconsistent results. We examined the relation between beer intake and waist-hip ratio (WHR) and body mass index (BMI) in a beer-drinking population.

DESIGN: A cross-sectional study.

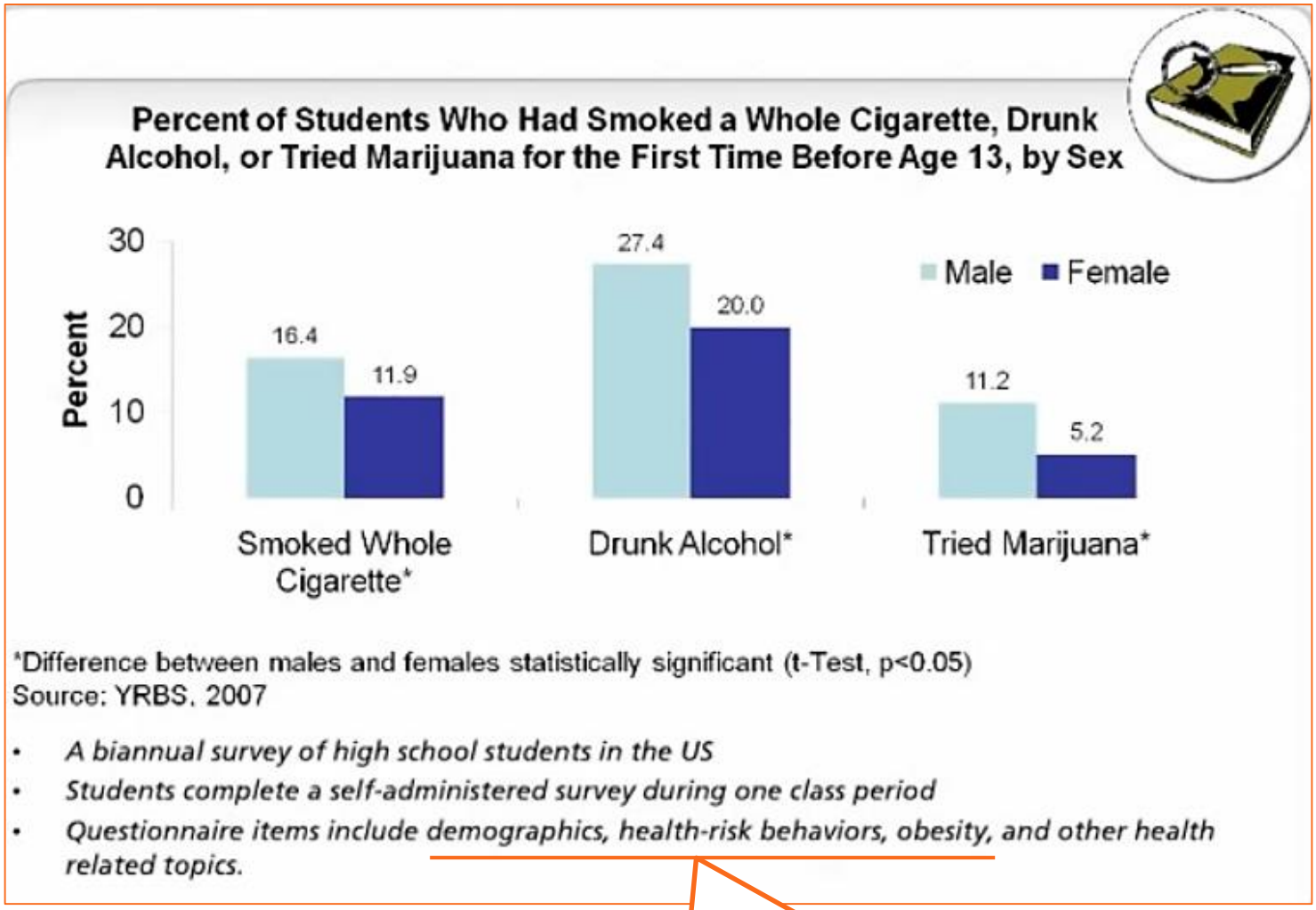
SETTINGS: General population of six districts of the Czech Republic.

SUBJECTS: A random sample of 1141 men and 1212 women aged 25-64 y (response rate 76%) completed a questionnaire and underwent a short examination in a clinic. Intake of beer, wine and spirits during a typical week, frequency of drinking, and a number of other factors were measured by a questionnaire. The present analyses are based on 891 men and 1098 women who where either nondrinkers or 'exclusive' beer drinkers (ie they did not drink any wine or spirits in a typical week).

RESULTS: The mean weekly beer intake was 3.1 l in men and 0.3 l in women. In men, beer intake was positively related to WHR in age-adjusted analyses, but the association was attenuated and became nonsignificant after controlling for other risk factors. There appeared to be an interaction with smoking: the relation between beer intake and WHR was seen only among nonsmokers. Beer intake was not related to BMI in men. In women, beer intake was not related to WHR, but there was a weak inverse association with BMI.

CONCLUSION: It is unlikely that beer intake is associated with a largely increased WHR or BMI.

PMID: 14506485 [PubMed - indexed for MEDLINE]



- *A biannual survey of high school students in the US*
- *Students complete a self-administered survey during one class period*
- *Questionnaire items include demographics, health-risk behaviors, obesity, and other health related topics.*

Allows studying more than one variable

COHORT STUDIES

Cohort Studies

What is a cohort?

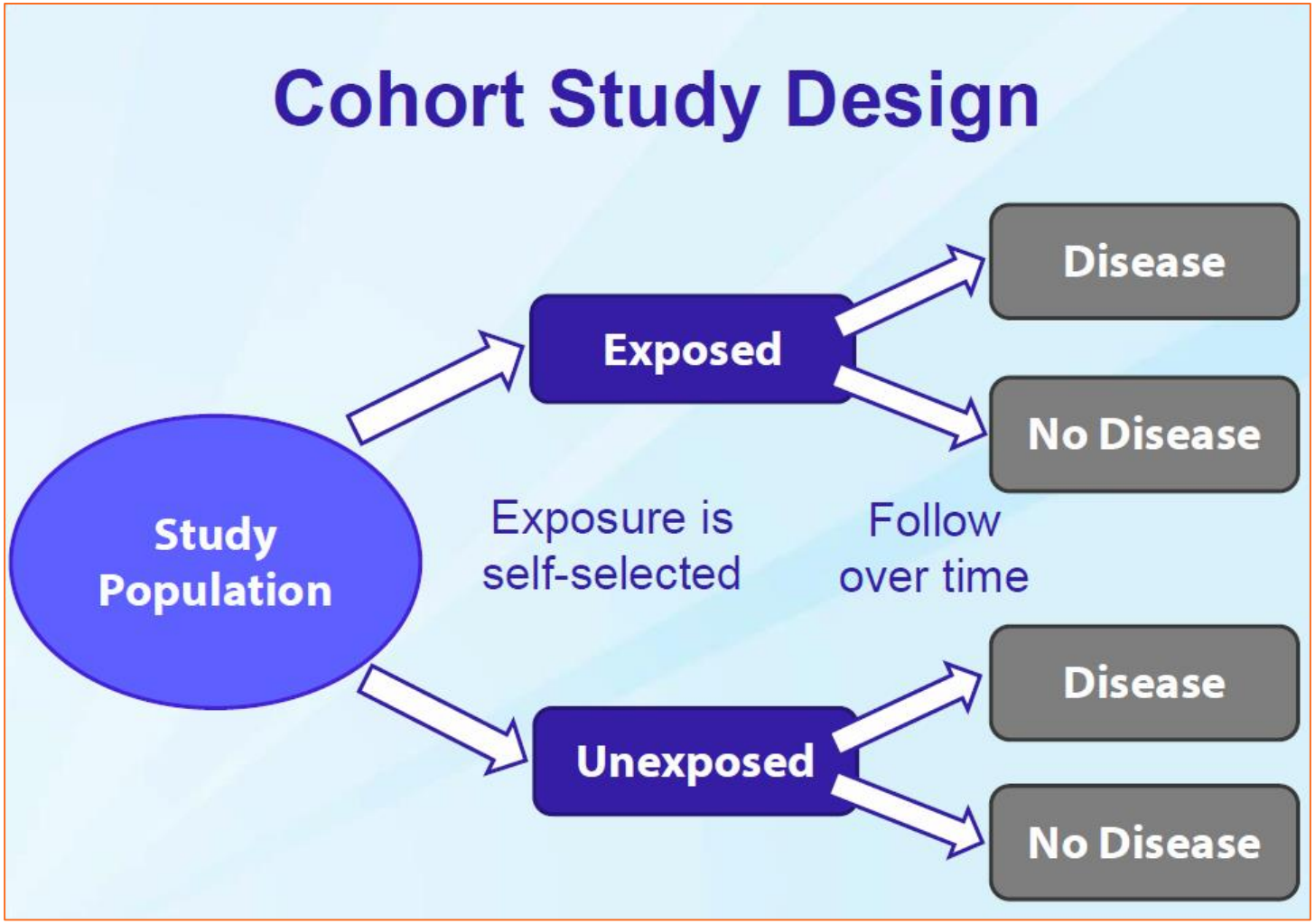
A well-defined group of individuals who share a common characteristic or experience

- Example: Individuals born in the same year

What are other examples of cohorts?

Cohort Study
(longitudinal study, follow-up study)

- Participants classified according to exposure status and followed-up over time to ascertain outcome
- Can be used to find multiple outcomes from a single exposure
- Appropriate for rare exposures or defined cohorts
- Ensures temporality (exposure occurs before observed outcome)


Cohort Study Design
Disease
Exposed
No Disease
Study Population
Exposure is self-selected
Follow over time
Disease
Unexposed
No Disease

Types of Cohort Studies

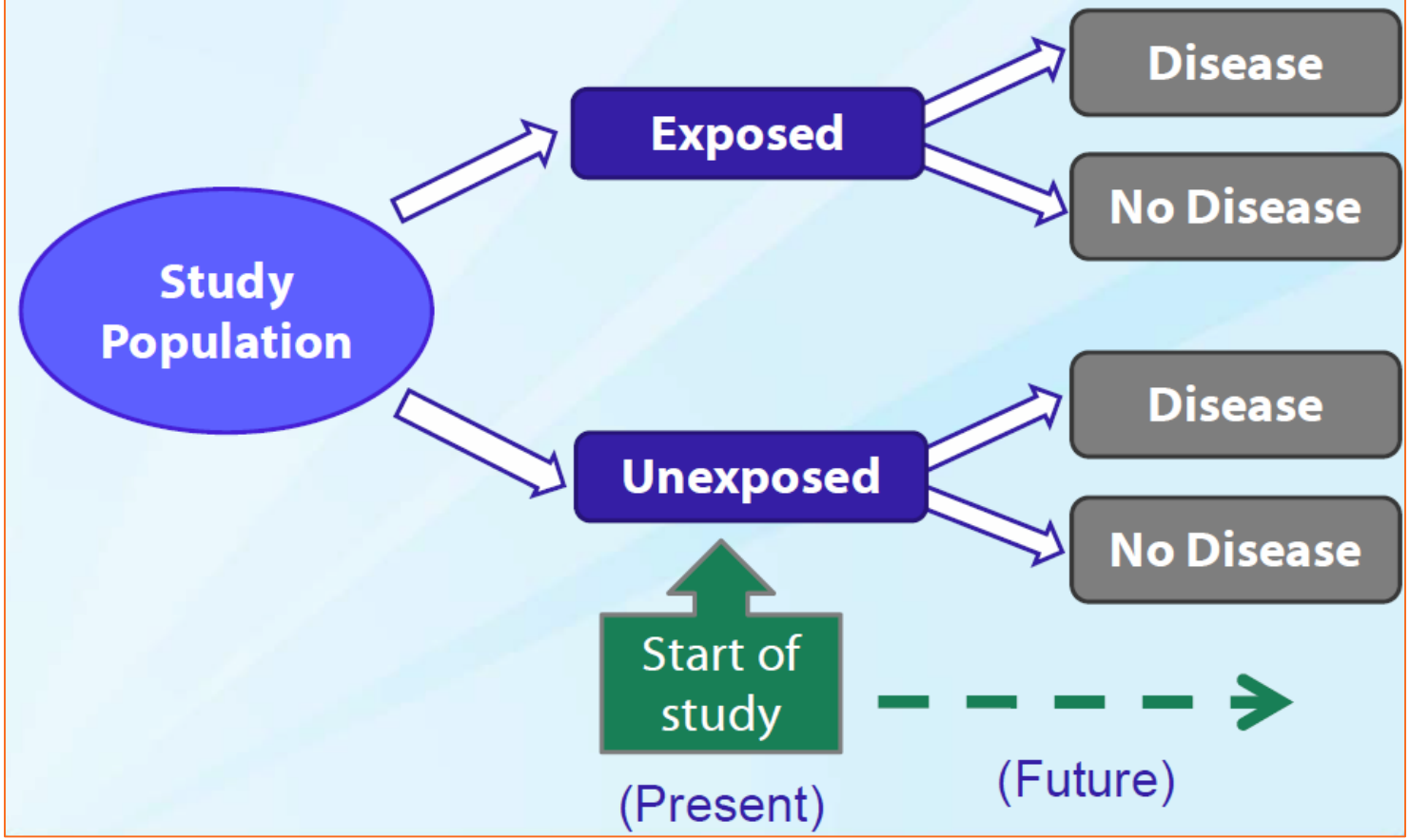
Prospective cohort studies

- Group participants according to past or current exposure and follow-up into the future to determine if outcome occurs

Retrospective cohort studies

- At the time that the study is conducted, potential exposure and outcomes have already occurred in the past

Prospective Cohort Studies



EXAMPLE: RELATION BETWEEN SMOKING AND LUNG CANCER /DOLL AND HILL/

Beginning 1951	Cohorts	Replies	Follow-up	Outcome under study
59,600 British doctors questionnaire about smoking habits	**smokers** **non-smokers**	**40,701 physicians** **34,494 men** **6,207 women**	**4 years and 5 months**	**deaths due to lung cancer**

Lung cancer death rates among smokers and non-smokers	Deaths per 100,000 person-years
Heavy smokers	224 exposed to suspected factor
Non-smokers	10 non-exposed to suspected factor
Total population	74
Individual RR	224/10 = 22.41
Population AR	74-10/74 = 86%

Framingham Study

Objectives

To study the impact of several factors on incidence of cardiovascular diseases

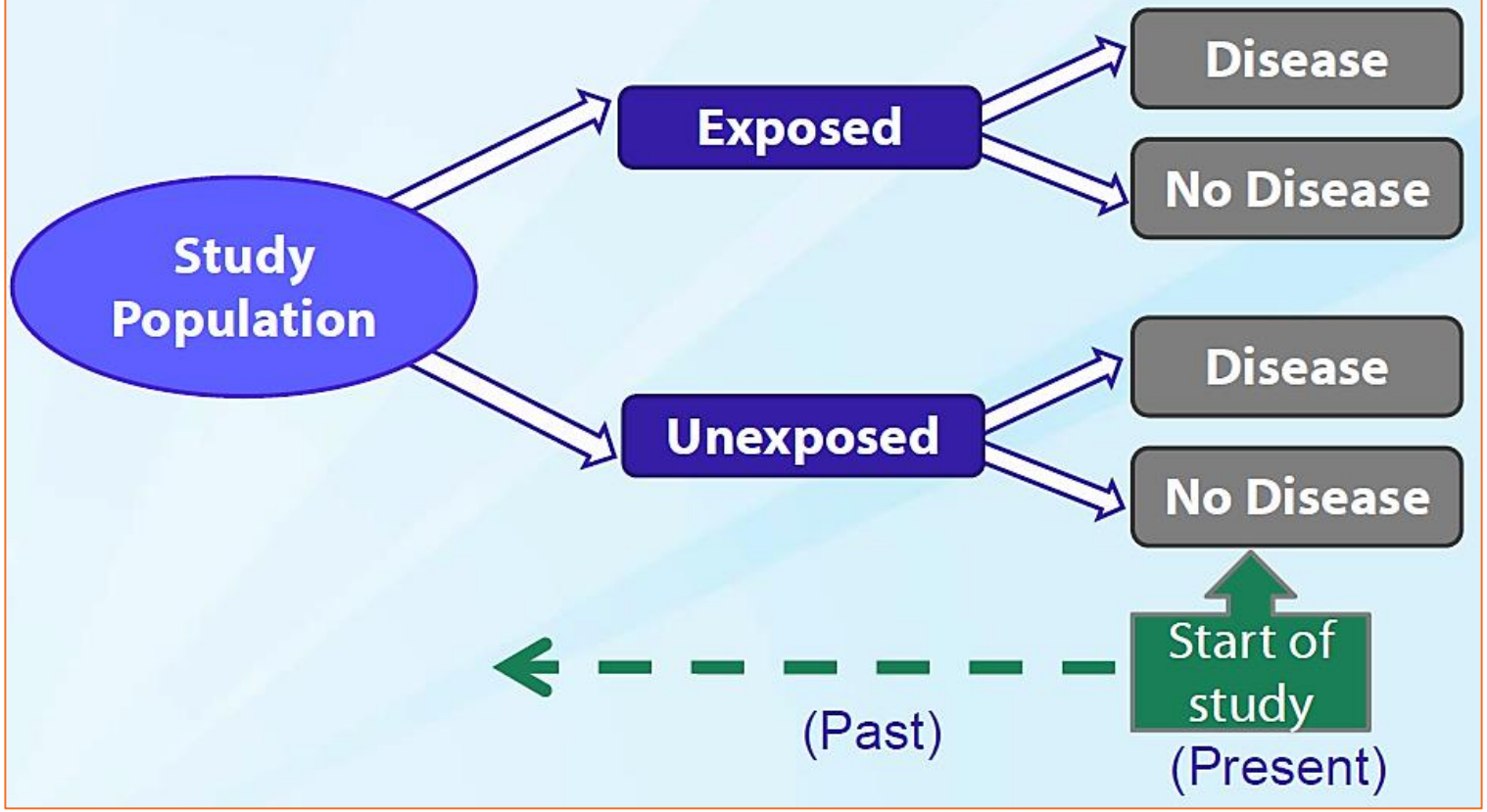
Exposures

Blood pressure, smoking, body weight, diabetes, exercise, etc.

Prospective cohort study - Framingam Heart Study on association between lifestyle and coronary heart disease /CHD/

Beginning 1948	Collected information	Follow - up	Results
cohort of 5127 • men + women • 30 - 59 years • free from CHD	• **demographic variables** • **medical history** • **cigarette smoking** • **clinical and laboratory parameters**	**reexamination every 2 years** **monitoring the development of cardiovascular events**	**identification risk factors for CHD** • **cigarette smoking** • **hypertension** • **level of blood cholesterol**

Retrospective Cohort Studies



Retrospective cohort study on association between hazardous working conditions /radiation in a nuclear shipyard/ and death from leukemia

1952	Information from personnel records	1977	Information about vital status as of August 15, 1977
	Classifying each worker with respect to length of employment and annual radiation	cohort of **24,545** white males employed in the shipyard at any time during 1952 to 1977	Comparing the mortality experience of shipyard workers exposed to radiation and workers with no such exposure

Example 8.8. *In the early 1950s, Case and his co-workers set up a cohort study to assess whether men engaged in the manufacture of certain dyestuff intermediates had an excess risk of bladder cancer. They began by constructing a list of all men who had ever been employed in the chemical industry in the United Kingdom for at least six months since 1920. The age and the dates between which exposure to dyestuffs occurred were recorded. A search was made retrospectively for all bladder cancer cases occurring among men who had been employed in the chemical industry, in or after 1921 until 1 February 1952. The number of observed bladder cancer cases among these workers was then compared with the number that would have been expected if these workers had the same mortality experience as the general population of the United Kingdom (Case* et al.*, 1954; Case & Pearson, 1954).*

AMBISPECTIVE COHORT STUDY

Combined Prospective and Retrospective Cohort Study

- Investigator uses existing data collected in the past to:
  - Identify the population and the exposure status (exposed/not exposed groups)
  - **Follow them into the future** for the development of the disease
- Investigator
  - Spends a relatively short time to assemble study population (and the exposed/not exposed groups) from past data
  - Will spend additional time following them into the future for the development of disease

Ambispective cohort study on the possible deleterious consequences of exposure to dioxin of Air Force personnel conducted by U.S. Air Force School of Aerospace Medicine

Exposure period	Retrospectively	Cohorts	Follow - up
1962 1971	**short-term effects** • dermatologic conditions	**1264 exposed** /pilots involved in defoliant spraying in Vietnam/	**long-term effects**
	• infertility • birth defects • liver abnormalities • phychological effects	**1264 non-exposed** /pilots in cargo missions in Southeast Asia during the same period/	development of cancer

NESTED CASE-CONTROL DESIGN

- A cohort is identified and followed untill sufficient number of cases develop.
- More detailed information is then collected and analysed but only for "cases" and for a sample from disease-free individuals ("controls"), not for all members of the cohort.
- Particularly useful if complex and expensive procedures are being applied.

Example 8.16. *In 1972, a cohort of 42 000 children was established in the West Nile District of Uganda in order to investigate the etiological role of the Epstein–Barr virus (EBV) in Burkitt's lymphoma. A blood sample was obtained from each child at the time of entry into the study. By the end of the follow-up in 1979, 16 new Burkitt's lymphoma cases had been detected among the cohort members. The level of EBV antibodies in the serum sample taken at entry from each of these cases was then compared with the levels in the sera of four or five children of the same age and sex who were bled in the neighbourhood at the same time as the Burkitt's lymphoma case but who did not develop the disease ('controls')* (Geser et al., *1982).*

DESIGN OF A COHORT STUDY

1. **Selection of study subjects**

- General population - when the exposure or cause of death is fairly frequent in the population.
- Special groups :
  - selected gropus - professional groups /*Doll and Hill - British doctors*/, government employees, insured persons etc. - homogeneous population, accessible and easy follow-up
  - exposure groups - when the exposure is rare

DESIGN OF A COHORT STUDY

2. Obtaining data on exposure

- Directly from the cohort members - personal interviews or mailed questionnaires */Doll and Hill/*
- Review of records - dose of radiation, kinds of surgery, details of medical treatment, etc.
- Medical examination or special tests - blood pressure, serum cholesterol, etc.
- Environmental surveys - information on exposure levels of the suspected factor

DESIGN OF A COHORT STUDY

3. **Classification of cohort members on the basis of received information**

- According to whether or not they have been exposed to the suspected factor
- According to the level or degree of exposure

DESIGN OF A COHORT STUDY

4. Selection of comparison groups:

- Internal comparisons - the members of the cohort may be classified into several comparison groups according to the degrees or levels of exposure to risk before the development of the disease in question. The groups, so defined, are compared in terms of their subsequent morbidity and mortality rates.
- External comparisons - when information on degree of exposure is not available, it is necessary to put up an external control, to evaluate the experience of the exposed group / *for example, smokers and non-smokers*/. The study and control cohorts should be similar in demographic and possibly important variables.
- Comparison with general population rates - if none is available, the mortality experience of the exposed is compared with the mortality experience of the general population in the same geographic area as the exposed people.

DESIGN OF A COHORT STUDY

5. Follow-up:

- periodic medical examination of each member of the cohort
- reviewing physician and hospital records
- routine surveillance of death records
- mailed questionnaires, telephone calls, periodic home visits

DESIGN OF A COHORT STUDY

6. Analysis:

- Incidence rates of outcome among exposed and non-exposed groups
- Estimation of risk:
  - Relative risk
  - Risk difference
  - Ethiologic fraction

Advantages	Disadvantages
1. Is of particular value when the exposure is rare 2. Can examine multiple effects of a single exposure */for example, cohort studies designed to study the association between smoking and lung cancer also showed association of smoking with coronary heart disease, peptic ulcer, cancer esophagus/.* 3. Can show temporal relationship between exposure and disease 4. Allows direct measurement of incidence of disease in the exposed and nonexposed groups 5. Provide a direct estimate of relative risk 6. Since comparison groups are formed before disease develops, certain forms of bias can be minimized like misclassification of individuals into exposed and non-exposed groups	1. Inefficient for the evaluation of rare diseases 2. Expensive and time consuming - prospective 3. Requires the availability of adequate records - retrospective 4. Validity of the results can be seriously affected by losses to follow-up 5. Ethical problems - as evidence accumulates about the implicating factor in etiology of disease, we are obliged to intervene and if possible to reduce or eliminate this factor.

POTENTIAL BIASES IN COHORT STUDIES

A systematic error in a study that leads to a distortion of the results

- **Selection bi**
  - Select pa … sed groups based on … the outcome
- **Information bias**
  - Collect different quality and extent of information from exposed and not exposed groups
  - Loss to follow-up differs between exposed and not exposed (or between disease and no disease)
- **Misclassification bias**
  - Misclassify exposure status or disease status

The effects of nonparticipation - in practically every cohort study, only a proportion of those who are eligible to participate actually agree to do so and are entered into the study. Those who agree to participate are likely to differ from nonparticipants in a number of important ways, including basic levels of motivation and attitudes towards health as well as risk factor status. For example, nonparticipants are more likely than participants to be current smokers. The effect of this difference between these groups concerns the generalizability of the study results.

Ways to Maintain Follow Up

1. Collect baseline information that will facilitate tracking subjects, e.g., addresses, phone numbers and email addresses not only for the subject, but also for possible contacts such as next of kin or close friends.
2. When feasible, use subjects who are easier to track. Studies sometimes use doctors or nurses or other professionals because they are more likely to remain interested in the study, and because they belong to professional organizations that make it easer to track them down if they relocate.
3. Maintain regular contact via personal contact, mail, phone, or email.
4. Send participants newsletters periodically to keep them updated on the study' progress.
5. Send multiple requests to non-responders.
6. Employ tracking resources, such as telephone directories, the US Postal Service's National Change of Address system, or Internet tracking resources.

The healthy worker effect

The healthy worker effect is another potential form of selection bias in cohort studies, particularly affecting occupational studies. In an occupational cohort study where disease rates among individuals from a particular occupational group are compared with an external standard population, bias may be introduced if membership of the exposed cohort is partly dependent upon health (which may be related to the presence or absence of the health outcome under investigation).

Individuals who are employed, for example, are generally healthy by nature of their ability to work. Therefore, mortality or morbidity rates in the occupation group cohort may be initially lower than in the population as a whole, which includes individuals who are too ill to work.

MULTIPLE COMPARISON GROUPS

When we cannot be sure that any single group will be sufficiently similar to the exposed group in terms of the distribution of potential confounding variables. In such circumstances, the study results may be more convincing if a similar association were observed for a number of different comparison groups.

Example 8.7. *A cohort of workers in a major tyre-manufacturing plant in Akron, Ohio (USA) was set up to examine their overall and cause-specific mortality. A total of 6678 male rubber workers aged 40 to 84 at 1 January 1964 were identified retrospectively from pension, payroll, death claims and other company files. These workers were followed from 1964 to 1972. The age-specific mortality experienced by this cohort was then compared with that experienced by three comparison groups–an industrial cohort of steel workers, the population of the state where the plant is located (Ohio) and the US national population (Table 8.1) (McMichael* et al.*, 1974).*

	Age-specific mortality rate (per 100 000 pyrs)			
Age-group (years)[b]	Rubber worker cohort (1964–72)	Steel worker cohort (1953–61)	Ohio state (1972)	USA (1968)
45–54	852	907	940	980
55–64	2317	2166	2365	2370

[a] Data from McMichael *et al.* (1974).

[b] Only data for these two age-groups were available for all the four populations.

Table 8.1.
Male age-specific mortality rates from all causes in the rubber worker cohort and in three other comparison groups: steel workers, Ohio state population and USA national population.[a]

When Is a Cohort Study Warranted?

- When the (alleged) exposure is known
- When exposure is rare and incidence of disease among exposed is high (even if the exposure is rare, determined investigators will identify exposed individuals)
- When the time between exposure and disease is relatively short
- When adequate funding is available

CASE-CONTROL STUDIES

DEFINITION

Type of observational analytic epidemiologic investigation in which subjects are selected on the basis of whether they do /case/ or do not /controls/ have a particular disease under study. The groups are then compared with respect to the proportion having a history of an exposure or characteristic of interest.

Purpose:

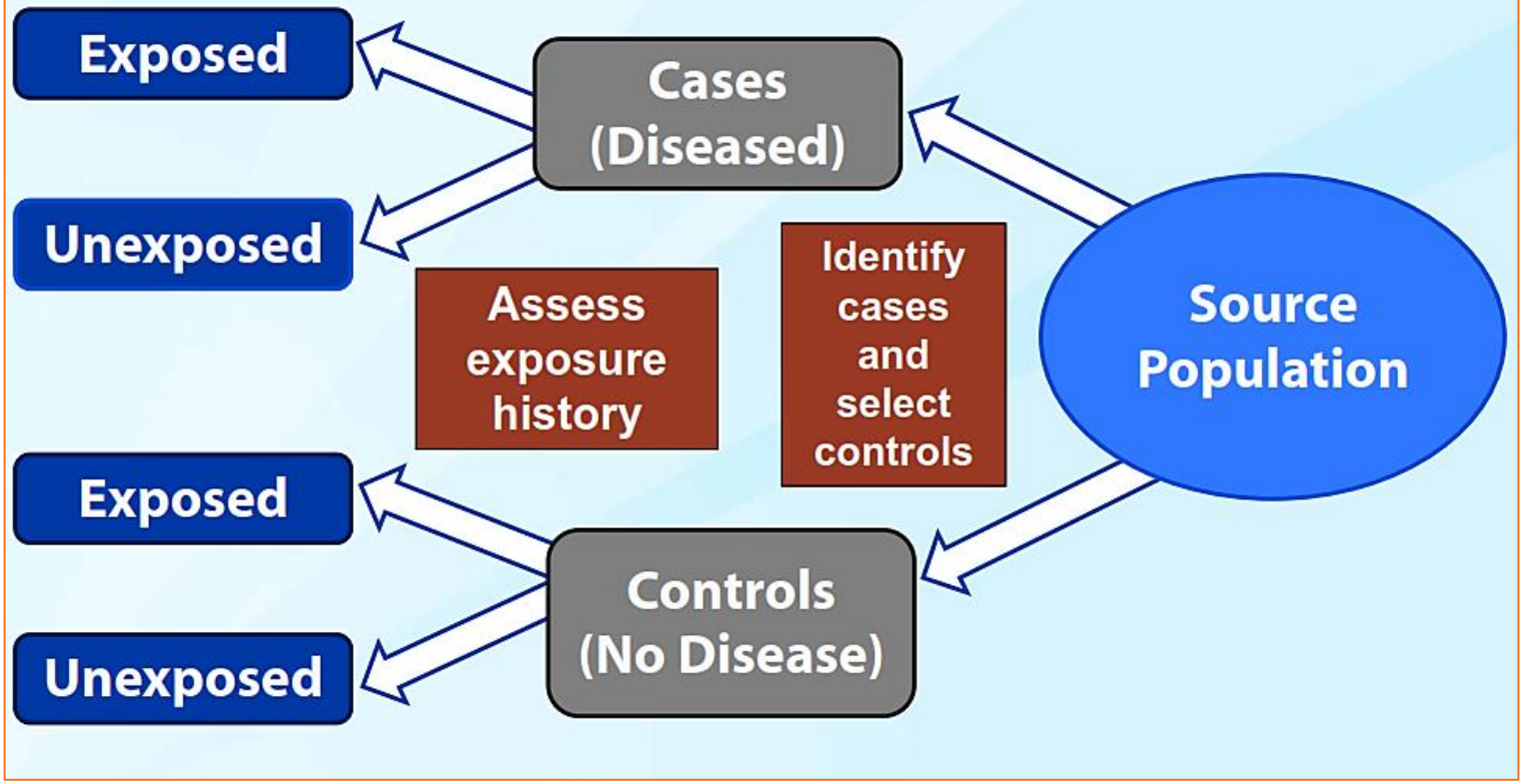
- To study rare diseases
- To study multiple exposures that may be related to a single outcome

Study Subjects

Participants selected based on outcome status:

- Case-subjects have outcome of interest
- Control-subjects do not have outcome of interest

Case-Control Study Design



DESIGN OF A CASE-CONTROL STUDY

1. Selection of cases and controls:

CASES	CONTROLS
1. Definition of case : • diagnostic criteria of the disease and the stage of the disease to be included in the study • eligibility criteria 2. Sources of data : • hospitals • general population	1. Requirements : • must be free from the disease under study • must be as similar to the case as possible 2. Sources of controls : • hospital - patients with different illness • relatives • neighborhood - living in the same locality, working in the same factory, attending the same school • general population - random sample of individuals free from the study disease 3. How many controls are needed? • if the study is large and many cases are available - one control for each case • if the study group is small - 2, 3 or even 4 controls can be selected for each study subject

DESIGN OF A CASE-CONTROL STUDY

2. Matching

- Definition - process by which we select controls in such a way that they are similar to cases with regard to certain appropriate selected variables which are known to influence the outcome of disease and which if not adequately matched for comparability, could distort or confound the results.
- If the confounding factor is age matching will involve taking equal proportion of each age group in case and control groups.
- The suspected etiological factor we wish to measure should not be matched /**overmatching**/.

3. Measurement of exposure

4. Analysis

ADVANTAGES	DISADVANTAGES
1. Relatively easy to carry out 2. Rapid and inexpensive 3. Suitable for rare diseases 4. Suitable for disease with long latent period 5. Allows the study of several aetiological factors for a single disease	1. Inefficient for the evaluation of rare exposures 2. Cannot directly compute incidence rates 3. The temporal relationship between exposure and disease may be difficult to establish 4. Problems of bias /selection, recall/

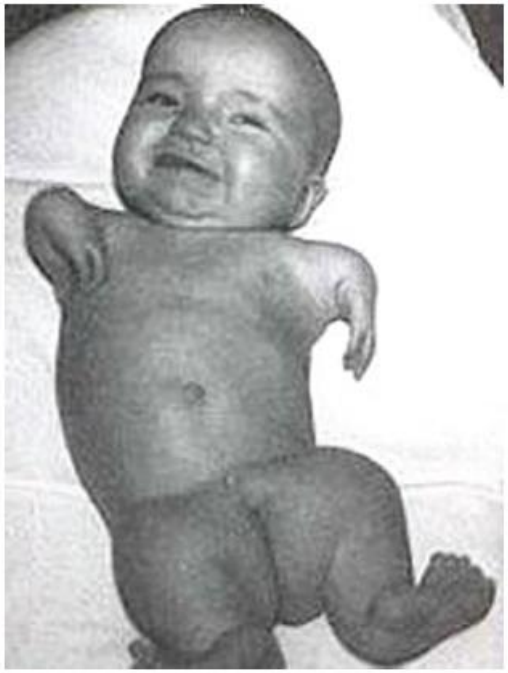
Example 9.14. *Adenocarcinoma of the vagina in young women was recorded rarely until the report of several cases treated at the Vincent Memorial Hospital (in Boston, MA, USA) between 1966 and 1969. The unusual diagnosis of this tumour in eight young patients led to the conduct of a case–control study to search for possible etiological factors. For each of the eight cases with vaginal carcinoma, four matched female controls born within five days and on the same type of hospital service (ward or private) as the case were selected from the birth records of the hospital in which the case was born. All the mothers were interviewed personally by a trained interviewer using a standard questionnaire (Herbst* et al., *1971).*

Information acquired retrospectively	Cases /8/	Controls /32/
Maternal age	26.1	29.3
Maternal smoking	7	21
Antenantal radiology	1	4
Oestrogen exposure	7	-

EXAMPLE 2 : Oral contraceptives and thromboembolic disease

By August 1965, the British Committee on Safety of Drugs had received 249 reports of adverse reactions and 16 reports of death in women taking oral contraceptives. It became apparent that epidemiologic studies were needed to determine whether women who took OC were at greater risk of developing thromboembolic disease. In 1968 and 1969, Vassey and Doll reported the findings of their case-control study in which they interviewed women who had been admitted to hospitals with venous thrombosis or pulmonary embolism without medical cause and compared the history with that obtained from other women who had been admitted to the same hospital with other diseases and who were matched for age, marital status and parity.

	Number	Per cent who used oral contraceptives
Cases /venous thrombosis and pulmonary embolism/	84	50
Controls	168	14



Thalidomide victim

EXAMPLE 3 : Thalidomide tragedy

Thalidomide was first marketted as a safe, non-barbiturate hypnotic in Britain in 1958. In 1961, at a congress of Gynaecologist, attention was drawn to the birth of large number of babies with congenital abnormalities /unusual limb defects/, which was previously rare. In the same year, it was suggested that Thalidomide might be responsible for it.

	Number	Per cent who used Thalidomide
Cases /mothers who had delivered deformed babies /	46	89.13
Controls	300	0

Case-Control Study: Analysis Format

Exposure	Cases	Controls
Yes	a	b
No	c	d

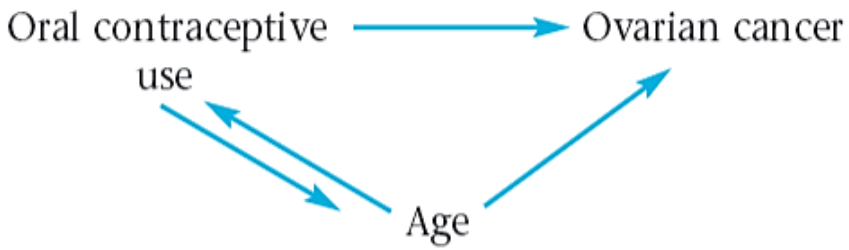
Exposure odds ratio (OR) ≈ RR when disease is rare

Odds of being exposed among the cases = a/c
Odds of being exposed among the controls = b/d

Exposure odds ratio = (a/c)/(b/d) = (a*d)/(b*c)
(Cross-product ratio)

POTENTIAL BIASES IN CASE-CONTROL STUDIES
CONFOUNDING

Let us suppose that we are interested in examining the relationship between current use of oral contraceptives and ovarian cancer. In this example, it is appropriate to match on age, since age is associated with the exposure of interest (current oral contraceptive use) and is an independent risk factor for ovarian cancer. In other words, age is a confounding factor. Failure to match, or otherwise control, for age would result in a biased assessment of the effect of oral contraceptive use.



- An alternate explanation for observed association between an exposure and disease.
- A mixing of effects. The association between exposure and disease is distorted because it is mixed with the effect of another factor that is associated with the disease.

POTENTIAL BIASES IN CASE-CONTROL STUDIES
RESPONDER BIAS

- Occurs when the validity of the information provided by the subjects differs for cases and controls.
- Subjects with serious disease are likely to have been thinking hard about possible causes of their condition and so cases may be inclined to give answers that fit with what they believe (or think is acceptable to say) is the cause of their illness. = **RECALL BIAS**
- Can be minimized by keeping study subjects unaware of the hypotheses under study and, where possible, ensuring that both cases and controls have similar incentives to remember past events.

When to Conduct a Case-Control Study

- The outcome of interest is rare
- Multiple exposures may be associated with a single outcome
- Funding or time is limited

Cohort vs. Case-Control Studies

Study Comparison	Cohort Study	Case-Control Study
Preferred Study Design When…	Members are easily identifiable Members are easily accessible Exposure is rare There may be multiple diseases involved	Identifying entire cohort would be too costly or time consuming Accessing entire cohort would be too costly or time consuming Illness is rare There may be multiple exposures involved
Study Group	Exposed persons	Persons with illness (cases)
Comparison Group	Unexposed persons	Persons without illness (controls)