Cohort studies

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OUTLINE

- Overview
- Definitions
- Study design
- Basic measures
- Advantages and disadvantages
- When to apply a cohort design
- Practical considerations

Overview

Two major categories of Epidemiological studies:

- **Observational studies:**
  - **Cohort studies**
  - **Case-control studies**
  - **Cross-sectional study**
  - *Have no control over exposures, simply observe what happens to groups of people.*
  - *Examine associations between risk factors and outcomes*
- **Experimental studies**
  - ***Randomized controlled trials (RCT)***
  - ***Non-randomized trial***
  - *Explore the association between interventions and outcomes.*

Definitions

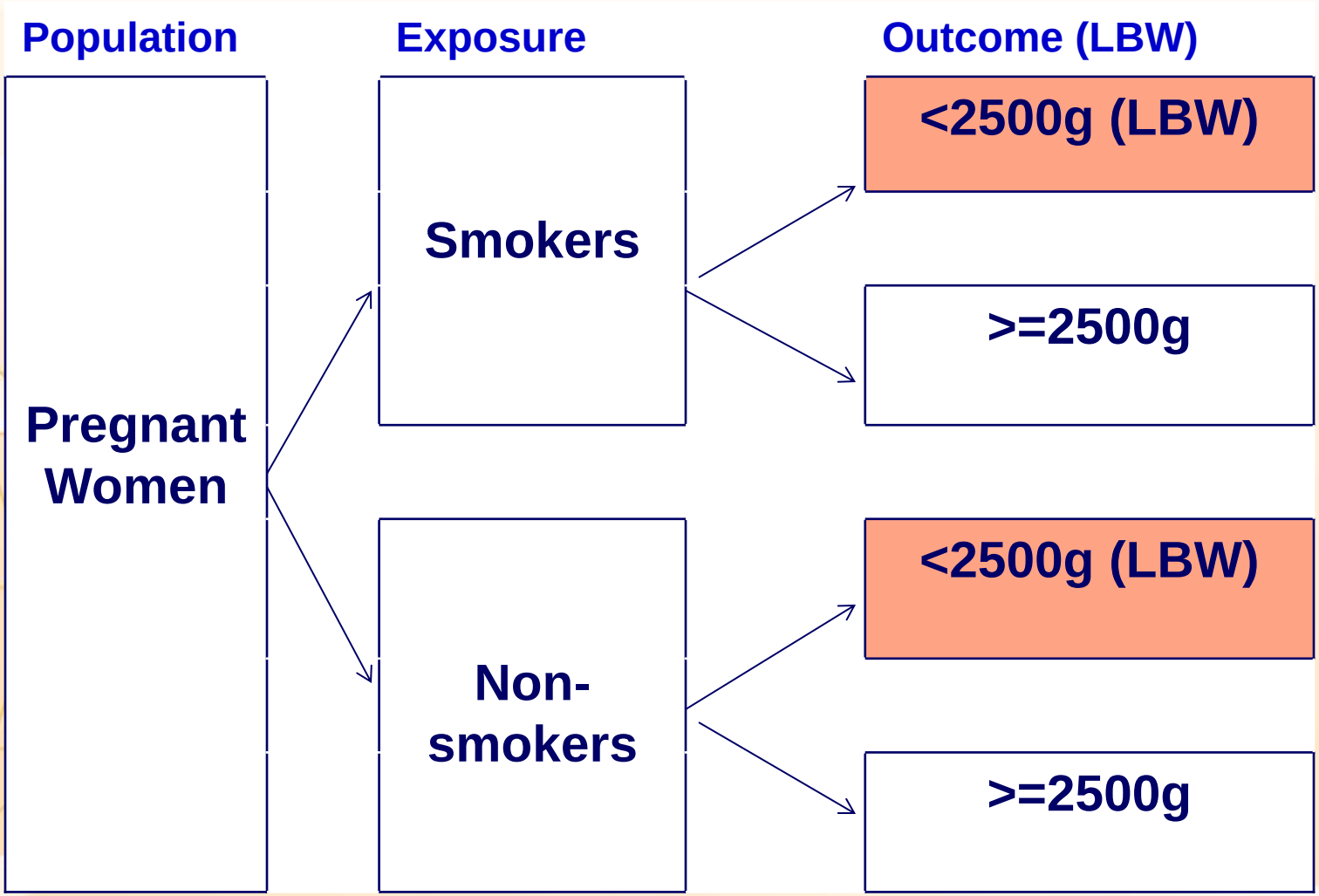
- **Cohort:**
  - **A group of individuals who have characteristics in common**
  - ***Examples of cohorts:***
    - ***Birth cohort:*** all individuals in a certain geographic area born within a given period of time (usually a year).
    - ***Marriage cohort:*** All persons married within a given period of time
    - ***Exposuse cohort:*** individuals assembled as a group based on some common exposure (e.g. radiation exposure during desert testing, smoking exposure…)

Definitions

- **Cohort study:**

  A study in which two or more groups of individuals those are free of disease and those differ according to the extent of exposure to a factor of interest, are followed over a period of time to see how their exposures affect their outcomes.

Study design



Type of cohort studies

- **Prospective cohort studies**
- **Retrospective cohort studies**

- **C**lassification is based on the temporal relationship between the initiation of the study (sample defined) and occurrence of the outcome, i.e. outcome before initiation (retrospective)
- Both start by identifying subjects based upon the presence or absence of the exposure of interest, without knowing the outcome at the time their exposure status is defined

Prospective cohort studies

- Sample defined prospectively during or before exposure and before outcome occurrence

Example:

(Ramchand, R., Lalongo, N.S., and Chilcoat, H.D. (2007). The effect of working for pay on adolescent tobacco use. American Journal of Public Health, 97(11),2056-2062)

- Cohort: High school students from Baltimore, Maryland
- Exposure: Working for pay
- Outcome: Initiation of tobacco use
- Results: Adolescents who work for pay have a higher risk of initiating tobacco use

Prospective cohort studies

Example:

(Doll R, Hill AB. Mortality in relation to smoking: 10 years observation of British docs. Br Med J.1964;1:1399-1410)

- Cohort: British doctors responding to a survey in 1950
- Exposure: smoking
- Outcome: Lung cancer
- Periodic follow-up and review of death records
- Results: Smoking increased risk of lung cancer

Prospective cohort studies

Example:

(Selikoff IJ, et al. Latency of asbestos dz among insulation workers in the US and Canada. CANCER. 1980;46:736+)

- *Exposed*: 17,800 males in Asbestos Insulation Workers union in North America
- Unexposed : General population of males matched by age
- Outcome: Lung cancer
- Results: Positive association between asbestos and lung cancer

Prospective cohort studies

Example:

(Nichol, K.L., Nordin, J.D., Nelson, D.B., Mullooly, J.P., and Hak, E. (2007). Effectiveness of influenza vaccine in the community –dwelling elderly. New England Journal of Medicine, 357(14), 1373-1381)

- Exposed: Vaccinated elderly
- Unexposed: Unvaccinated community-dwelling elderly
- Outcome: Hospitalization for pneumonia or influenza
- Results: The elderly who were vaccinated have a reduced risk of hospitalization for pneumonia or influenza

Retrospective cohort studies

- Both exposure and disease have occurred at the start of study.
- Data already collected for other purposes.
- The cohort is followed up retrospectively.
- It depends on the availability of previous study factor information.
- It is more feasible for studying a disease with a long latent period.
- The study period may be many years but the time to complete the study is only as long as it takes to collate and analyse the data.

Retrospective cohort studies

Example:

(Klung et al. article. Ann Pharmacother. 2002; 36:751-7)

- Begin study in 2000 using data already collected via health plan.
- Cohort surviving myocardial infarction (MI) 1986-1996
- Exposed: Lipid lowering therapy use
- Outcome: Cardiovascular events during 6 months following MI

Basic measures

- **Measures of disease occurrence:**
  - Cumulative Incidence
  - Incidence Rate (IR)

- **Measures of association between a factor and a disease:**
  - Relative Risk (RR)
  - Attributable Risk (AR)

Basic measures

- ***Cumulative Incidence:***
  - Risk of developing disease
  - # new cases of disease/# persons at risk (during the same time period)

Basic measures

- ***Cumulative Incidence:***
  - Risk of disease in exposed: a/a+b
  - Risk of disease in non-exposed: c/c+d

	Disease	Non-disease	
Exposed	a	b	a + b
Non-exposed	c	d	c + d
	a + c	b + d	

Basic measures

- ***Incidence Rate (IR)***
  - Risk per unit of time
  - # new cases of disease/Persons at risk*Duration
  - *Duration (Person-time):* sum of time at risk for all individuals (time until the date of the event of interest or date of censoring, i.e. death, end of FU, drop out). e.g.1 person FU for 2 years=2 person-year.
  - *Persons "at risk"* who do not have the disease of interest and are capable of developing the disease.

Basic measures

Example:

(IR, Person-time calculation, a 9-year follow-up study)

Subject	Years of follow-up	Outcome
1	→ 2.1	Event
2	→ 4.8	Die
3	→ 3.2	Die
4	→ 9.0	End of FU
5	→ 7.2	Event

- *Person time:* 2.1+4.8+3.2+9.0+7.2=26.3 years
- *Incidence rate:* 2 events/26.3 person-years=0.076/year (or 76/1000/year)

Basic measures

- **R*elative Risk (RR):***
  - Incidence of disease in exposed compared to the incidence of disease in unexposed
  - RR= **(a/a+b)/(c/c+d)**

	Disease	Non-disease	
Exposed	a	b	a + b
Non-exposed	c	d	c + d
	a + c	b + d	

Basic measures

- ***Relative Risk (RR):***
  - Determine the strength of the association between exposure and disease
  - RR=1 (no association)
  - RR>1 (exposure increases risk for disease, e.g. RR=2.0 can be interpreted as two fold increase in risk)
  - RR<1 (exposure decreases risk for disease, e.g. RR=0.7 can be interpreted as 30% decrease in risk)

Basic measures

Example:

(Tuberculosis treatment and breast cancer study)

- Exposed: women were treated with air collapse therapy and exposed to numerous fluoroscopic examinations (radiation)
- Unexposed: women who received other treatment.
- Outcome: A total of 47036 woman-years of follow-up were accumulated during which 56 breast cancer cases occurred

Basic measures

Example:

(Tuberculosis treatment and breast cancer study)

	Breast Cancer	Non-disease	Total	Women-years of FU
Exposed	41	1006	1047	28,011
Non-exposed	15	702	717	19,025
	56	1708	1764	47,036

- IR_exposed=41/28011=1.5/1000 woman-years
- IR_non-exposed=15/19025=0.8/1000 woman-years
- RR=IR_exposed/IR_non-exposed=1.9
- Results: Women exposed to fluoroscopies had 1.9 times the risk of breast cancer compared to unexposed women.

Basic measures

- ***Attributable Risk (AR):***
  - The excess risk of disease observed among exposed subjects.
  - AR=IR_exposed - IR_non-exposed

Example:

(Tuberculosis treatment and breast cancer study)

- IR_exposed=1.5/1000 woman-years
- IR_non-exposed=0.8/1000 woman-years
- AR=IR_exposed - IR_non-exposed=1.5-0.8=0.7/1000w/y
- Excess IR of breast cancer among women exposed to fluoroscopies was 0.7/1000 woman-year

Advantages

- Gold standard for studying the association between risk factor and outcome
- Useful for looking at multiple exposures and their interactions
- Can evaluate multiple outcomes /diseases
- Clear time sequence (temporal relationship between exposure and outcome) strengthens the inference about cause

Advantages

- Less bias due to prospective evaluation of exposures
- Efficient for rare exposures
- The best or only ethical way, sometimes, to do the study (situations where randomization is not possible)

Disadvantages

- Time consuming
- The problem of attrition: loss of subjects (e.g. migration or death from other causes)
- Unexpected changes over time:
  - Changes to the environment can influence the association of disease and possible cause
  - Changes in diagnostic criteria and methods
  - Changes of staff
- Financial problems: lack of funding and the high costs of record keeping

When to apply a cohort design

- In many cases, *cohort studies are preferred to RCT because they do not require strict random assignment of subjects*, which is unethical or improbable.
- Sometimes they are the only methods available. (e.g. testing the effect of smoking on health, random assignment would be infeasible and unethical. A *reasonable alternative* would be a cohort study with *two groups smokers and non-smokers* and *follows them forward through time to see what health problems they develop*.

Practical considerations

- **Selection of comparable groups:**
  - Select a comparison (unexposed) group as similar as possible to the exposed group with respect to all factors except the exposure
- **Comparable ascertainment of the outcome in both groups:**
  - Blind the investigator conducting follow-up and confirming the outcome

Practical considerations

- **Minimize "lost to follow-up"**
  - Exclude those likely to become "lost" (e.g. Planning to move, unwilling to return)
  - Obtain complete tracking information (address, phone number of subjects as well as of close friends and relative)
  - Maintain periodic contact (reminders, updates)

THANK YOU VERY MUCH