

Cohort studies

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OUTLINE

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



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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.*



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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
 - **Exposure cohort:** individuals assembled as a group based on some common exposure (e.g. radiation exposure during desert testing, smoking exposure...)



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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.



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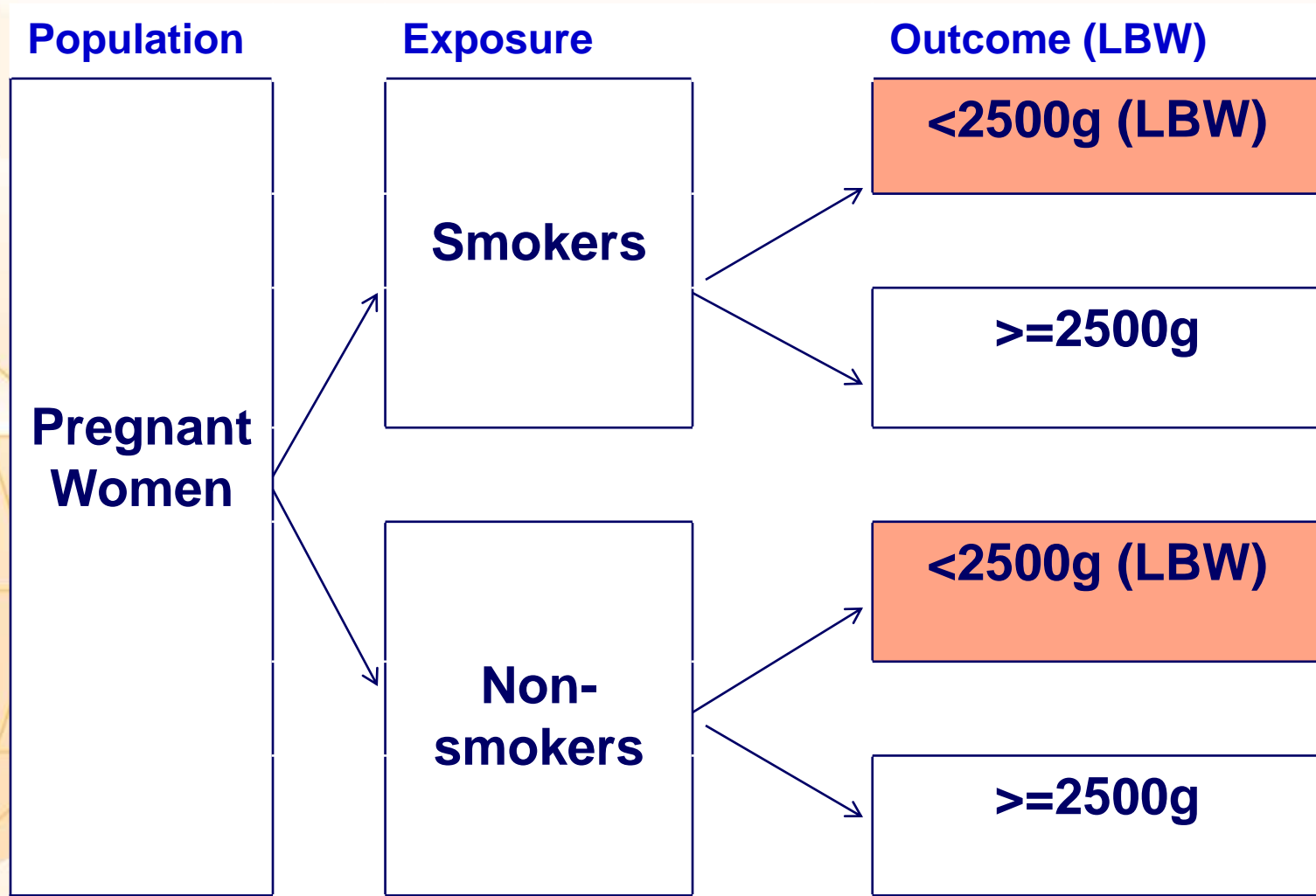


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Study design



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Type of cohort studies

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



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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



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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



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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



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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



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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.



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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



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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)



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Basic measures

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



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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	



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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.



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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:* $2 \text{ events} / 26.3 \text{ person-years} = 0.076/\text{year}$ (or 76/1000/year)



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Basic measures

- **Relative 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)



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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



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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

- $IR_{\text{exposed}} = 41/28011 = 1.5/1000$ woman-years
- $IR_{\text{non-exposed}} = 15/19025 = 0.8/1000$ woman-years
- $RR = IR_{\text{exposed}}/IR_{\text{non-exposed}} = 1.9$
- Results: Women exposed to fluoroscopies had 1.9 times the risk of breast cancer compared to unexposed women.



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Basic measures

- ***Attributable Risk (AR):***

- The excess risk of disease observed among exposed subjects.
- $AR = IR_{\text{exposed}} - IR_{\text{non-exposed}}$

Example:

(Tuberculosis treatment and breast cancer study)

- $IR_{\text{exposed}} = 1.5/1000$ woman-years
- $IR_{\text{non-exposed}} = 0.8/1000$ woman-years
- $AR = IR_{\text{exposed}} - IR_{\text{non-exposed}} = 1.5 - 0.8 = 0.7/1000w/y$
- Excess IR of breast cancer among women exposed to fluoroscopies was 0.7/1000 woman-year



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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



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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)



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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



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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.*



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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



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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)



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THANK YOU VERY MUCH



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