Case Control Study

Course Title: Research Methodology

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Submitted by: Group One

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Group One Members

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- **Definition:**
  - An observational study comparing individuals with a condition (cases) to those without (controls).
  - Purpose: To identify whether past exposures potentially linked to the condition.
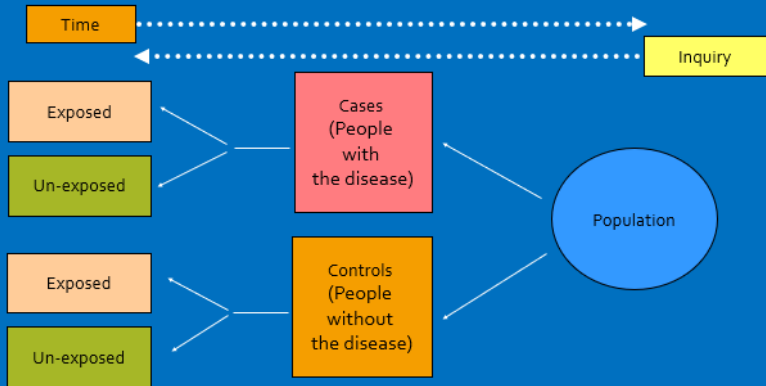- **Key Features:**
  - Retrospective design (looks backward in time)
  - Compares exposure history between cases and controls.
  - Commonly used for rare diseases or outbreak investigations
- **Example:**
  - Studying Association of Lung Cancer and Cigarette Smoking

Methodological Considerations

- **Case and Control Selection:**
  - Cases: Clearly defined, confirmed diagnosis
  - Controls: Similar in age, sex, geography, etc., but without disease
  - Matching helps control confounding
- **Exposure Assessment:**
  - Use standardized, reliable methods (e.g., interviews, records)
  - Apply blinding where possible to reduce interviewer bias
- **Bias and Confounding:**
  - Recall bias: Inaccurate memory of past exposures
  - Selection bias: Non-comparable case/control groups
  - Confounding: Unmeasured variables influencing exposure and outcome

Key Inputs:

- Expected odds ratio (OR) for exposure
- Prevalence of exposure in controls
- Desired power (typically 80–90%)
- Significance level (α), usually 0.05
- Case-to-control ratio (e.g., 1:1, 1:2, 1:4)

Tools:

- *Epi Info*, *OpenEpi*, *G*Power*

Retrospective case-control studies rely on existing records (medical records, databases) for data collection.

- **Data Collection:** Existing data sources like medical records, databases, etc.
- **Retrospective Element:** Data collected based on past events and records
- **Examples:**
  - Analyzing existing medical records to compare patients with a specific disease to those without, based on past risk factors identified in the records.

Study: H. pylori and Stomach Cancer (Uemura et al. 2001)

- **Design:** Retrospective case-control
- **Cases:** Patients with gastric cancer
- **Controls:** Patients without gastric cancer, undergoing endoscopy
- **Exposure:** H. pylori infection
- **Result:** Strong correlation between H. pylori infection and gastric cancer

Control
Case

Subcohort

Cases

Case-cohort data

Full cohort
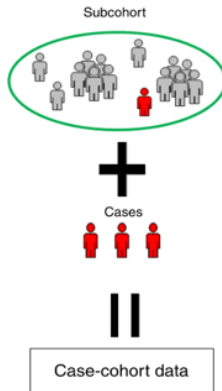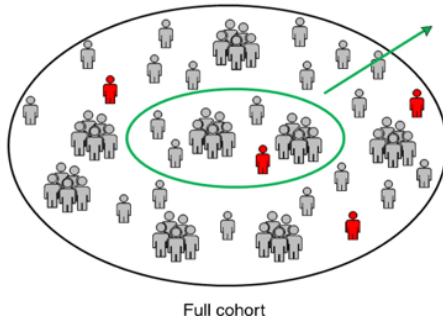
Advantages:

- Efficiency
- Cost-effectiveness
- Flexibility
- Reduced bias

Disadvantages:

- Statistical complexity
- Potential for reduced efficiency

Published Example

Study: Occupational Risk Factors for Bladder Cancer in Men – A Dutch Case-Cohort Study (Zeegers et al. 2001)

- **Design:** Case-Cohort Study
- **Cases:** 532 men from the total cohort who developed bladder cancer
- **Controls:** 1,630 men from the original cohort of 58,279 men
- **Exposure:** Paint components; Polycyclic aromatic hydrocarbons (PAHs); Diesel exhaust
- **Result:**
  - High exposure to paint, PAHs, diesel, and aromatic amines showed slightly increased bladder cancer risk, but not statistically significant.
  - The interaction with cigarette smoking was more consistent than the effect of occupational exposures alone.

Population Based Case-Control Study
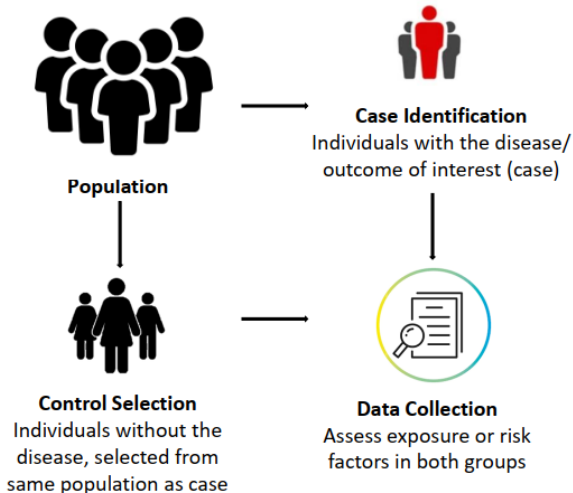
Population Based Case-Control Study

Strengths:

- Controls from same population as cases
- Suitable for rare diseases
- Helps identify exposure-disease associations

Weaknesses:

- Recall bias
- Selection bias (non-representative controls)
- Cannot directly calculate incidence/prevalence

Matched Case-Control Study

We compare matched and unmatched case-control design using targeted maximum likelihood estimation to assess which provides more information on the marginal causal effect.

Advantages:

- Helpful when confounding factors are strong
- May increase power of small studies
- Works well for studies focusing on one factor
- Case make finding controls easier

Disadvantages:

- Difficulty in analyzing matched data
- Increased study complexity
- Difficulty in assessing does-response relationship

Published Example

Study: Assessing Risk Factors Associated with Multiple Sclerosis in Kuwait (El Muzaini et al. 2020)

- **Data Collection:** Structured, pre-tested questionnaire via face-to-face interviews
- **Cases:** 110 confirmed MS patients
- **Controls:** 110 matched controls (matched on age ± 5 years, gender, and nationality)
- **Analysis:** Conditional logistic regression to identify significant associations
- **Result:**
  - A family history of MS significantly increased risk (adjusted matched odds ratio)
  - Vaccination against influenza A and B was associated with reduced MS risk

This study compares the exposure history of individuals with a specific disease (cases) to individuals without that disease (controls), all recruited from a hospital setting.

Strengths:

- Efficient for studying rare diseases
- Allow for a more focused investigation of risk factors within a specific healthcare setting

Weaknesses:

- Findings may not be generalizable to the broader population
- Selection bias (non-representative controls)
- Recall Bias

Published Example

Study: Case–Control Study of HPV & Oropharyngeal Cancer (D'Souza et al., 2007)

- **Design:** Hospital-based matched case-control study
- **Cases:** 100 patients
- **Controls:** 200 cancer-free patients (matched by sex and age group)
- **Exposure:**
  - Oral HPV infection (including HPV-16 DNA via oral rinse cytology)
  - Seropositivity for HPV-16 capsid protein L1 and oncoproteins E6/E7
- **Result:**
  - Oral HPV-16 infection associated with oropharyngeal cancer (OR 14.6; 95% CI 6.3–36.6)
  - Seropositivity for HPV-16 L1: OR 32.2 (95% CI 14.6–71.3)

Nested Case-Control Study
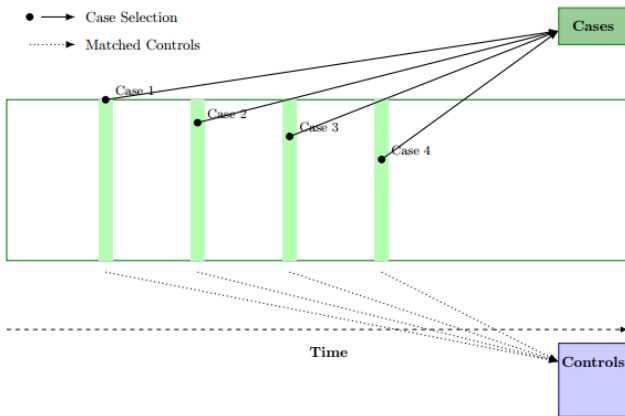
(Idea from **Prof. Javier Nieto** and **Prof. Moyses Szklo**)

Study: Serum Sex Hormone Levels and Breast Cancer (Drogan et al., 1997)

- **Actual Time Frame** From 1977 to 1987
- **Source Population** 3375 postmenopausal women
- **Cases:** 72 women with breast cancer
- **Controls:** 144 without breast cancer
- **Exposure:** Serum estrogen and androgen levels
- **Result:** Risk of breast cancer was positively and significantly associated with serum levels of estrogens and androgens. Relative Risk = 5.2 (estrogens); 6.2 (androgens)

Thank You!

Questions or Comments?

We appreciate your attention.