Penelitian IKM/Epidemiologi

Oleh : Suyatno, Ir. MKes

Contact:
E-mail: suyatnofkmundip@gmail.com
Blog: suyatno.blog.undip.ac.id
Hp/Telp: 08122815730 / 024-70251915
Epidemiologic Study Designs

I. Experimental (RCTs)
II. Observational
   - Analytical
     - Case-Control
     - Cohort
   - Descriptive
     + cross-sectional & ecologic
Epidemiologic Study Designs

Descriptive studies
Examine patterns of disease

Analytical studies
Studies of suspected causes of diseases

Experimental studies
Compare treatment modalities
Epidemiologic Study Designs

Did investigator assign exposures?

- Yes
  - Experimental study
    - Random allocation?
      - Yes: Randomised controlled trial
      - No: Non-randomised controlled trial

- No
  - Observational study
    - Comparison group?
      - Yes: Analytical study
      - No: Descriptive study

Exposure → Outcome

Exposure and outcome at the same time

- Cohort study
- Case-control study
- Cross-sectional study

Grimes & Schulz, 2002
Hierarchy of Epidemiologic Study Design

- Case reports
- Case series
- Ecologic studies
- Cross-sectional studies
- Case-control studies
- Cohort studies
- Randomized controlled trials

Generate hypotheses

Establish causality

Tower & Spector, 2007 (www)
Observational Studies
(no control over the circumstances)

- **Descriptive**: Most basic demographic studies
- **Analytical**: Comparative studies testing an hypothesis
  * cross-sectional
    (a snapshot; no idea on cause-and-effect relationship)
  * **cohort**
    (prospective; cause-and-effect relationship can be inferred)
  * case-control
    (retrospective; cause-and-effect relationship can be inferred)
Epidemiologic Study Designs

Figure 2: Schematic diagram showing temporal direction of three study designs
Analytical Studies
(comparative studies testing an hypothesis)

* **cohort** (prospective)

  *Begins with an exposure (smokers and non-smokers)*

* **case-control** (retrospective - trohoc)

  *Begins with outcome (cancer cases and healthy controls)*
Cohort Studies

Population ➔ People without disease ➔ Exposed ➔ Disease

People without disease ➔ Not exposed ➔ Disease

Exposed ➔ No disease

Not exposed ➔ No disease
Advantages of Cohort Studies

- Can establish population-based incidence
- Accurate relative risk (risk ratio) estimation
- Can examine rare exposures (asbestos > lung cancer)
- Temporal relationship can be inferred (prospective design)
- Time-to-event analysis is possible
- Can be used where randomization is not possible
- Magnitude of a risk factor’s effect can be quantified
- Selection and information biases are decreased
- Multiple outcomes can be studied
  (smoking > lung cancer, COPD, larynx cancer)
Disadvantages of Cohort Studies

- Lengthy and expensive
- May require very large samples
- Not suitable for rare diseases
- Not suitable for diseases with long-latency
- Unexpected environmental changes may influence the association
- Nonresponse, migration and loss-to-follow-up biases
- Sampling, ascertainment and observer biases are still possible
Presentation of cohort data: Presentation of cohort data: Population at risk

Does HIV infection increase risk of developing TB among a population of drug users?

<table>
<thead>
<tr>
<th>Population (follow up 2 years)</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV +</td>
<td>215</td>
</tr>
<tr>
<td>HIV -</td>
<td>289</td>
</tr>
</tbody>
</table>

Source: Selwyn et al., New York, 1989
Does HIV infection increase risk of developing TB among drug users?

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Population (f/u 2 years)</th>
<th>Cases</th>
<th>Incidence (%)</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV +</td>
<td>215</td>
<td>8</td>
<td>3.7</td>
<td>11</td>
</tr>
<tr>
<td>HIV -</td>
<td>298</td>
<td>1</td>
<td>0.3</td>
<td></td>
</tr>
</tbody>
</table>
Presentation of cohort data: Person-years at risk

Tobacco smoking and lung cancer, England & Wales, 1951

<table>
<thead>
<tr>
<th></th>
<th>Person-years</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoke</td>
<td>102,600</td>
<td>133</td>
</tr>
<tr>
<td>Do not smoke</td>
<td>42,800</td>
<td>3</td>
</tr>
</tbody>
</table>

Source: Doll & Hill
## Presentation of data:
### Various exposure levels

<table>
<thead>
<tr>
<th>Daily number of cigarettes smoked</th>
<th>Person-years at risk</th>
<th>Lung cancer cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 25</td>
<td>25,100</td>
<td>57</td>
</tr>
<tr>
<td>15 - 24</td>
<td>38,900</td>
<td>54</td>
</tr>
<tr>
<td>1 - 14</td>
<td>38,600</td>
<td>22</td>
</tr>
<tr>
<td>none</td>
<td>42,800</td>
<td>3</td>
</tr>
</tbody>
</table>

EPIET (www)
### Cohort study: Tobacco smoking and lung cancer, England & Wales, 1951

<table>
<thead>
<tr>
<th>Cigarettes smoked/d</th>
<th>Person-years at risk</th>
<th>Cases</th>
<th>Rate per 1000 p-y</th>
<th>Rate ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 25</td>
<td>25,100</td>
<td>57</td>
<td>2.27</td>
<td>32.4</td>
</tr>
<tr>
<td>15 - 24</td>
<td>38,900</td>
<td>54</td>
<td>1.39</td>
<td>19.8</td>
</tr>
<tr>
<td>1 - 14</td>
<td>38,600</td>
<td>22</td>
<td>0.57</td>
<td>8.1</td>
</tr>
<tr>
<td>none</td>
<td>42,800</td>
<td>3</td>
<td>0.07</td>
<td>Ref.</td>
</tr>
</tbody>
</table>

Source: Doll & Hill
Prospective cohort study

Exposure → Study starts → Disease occurrence

time
Retrospective cohort studies

- Exposure
- Disease occurrence
- Study starts

(time)
Cohort Studies

Figure 2: Schematic diagram of concurrent, retrospective, and ambidirectional cohort studies

Grimes & Schulz, 2002 (www) (PDF)
Cohort Studies

Panel 2: **Features to look for in a cohort study**

**How much selection bias was present?**
1. Were only people at risk of the outcome included?
2. Was the exposure clear, specific, and measurable?
3. Were the exposed and unexposed groups similar in all important respects except for the exposure?

**What steps were taken to minimise information bias?**
1. Was the outcome clear, specific, and measurable?
2. Was the outcome identified in the same way for both groups?
3. Was determination of outcome made by an observer blinded as to treatment?

**How complete was the follow-up of both groups?**
1. What efforts were made to limit loss to follow-up?
2. Was loss to follow-up similar in both groups?

**Were potential confounding factors sought and controlled for in the analysis?**
1. Did the investigators anticipate and gather information on potential confounding factors?
2. What method(s) were used to assess and control for confounding?
Case-Control Studies

Exposed
Not exposed
Cases
Exposed
Not exposed
Controls
Population
Case-Control Studies

Schulz & Grimes, 2002 (www) (PDF)
Advantages of Case-Control Studies

- Cheap, easy and quick studies
- Multiple exposures can be examined
- Rare diseases and diseases with long latency can be studied
- Suitable when randomization is unethical
  (alcohol and pregnancy outcome)
Disadvantages of Case-Control Studies

- Case and control selection troublesome
- Subject to bias (selection, recall, misclassification)
- Direct incidence estimation is not possible
- Temporal relationship is not clear
- Multiple outcomes cannot be studied
- If the incidence of exposure is high, it is difficult to show the difference between cases and controls
- Not easy to estimate attributable fraction
- Reverse causation is a problem in interpretation - especially in molecular epidemiology studies
Epidemiologic Study Designs

Figure 3: Algorithm for distinguishing rates, proportions, and ratios
Sources of Error in Epidemiologic Studies

Random error

*Large sample size, replication*

Bias

*Be careful*

Confounding

Effect Modification

Reverse Causation
Confounding can be controlled by:

- **Randomization**: assures equal distribution of confounders between study and control groups

- **Restriction**: subjects are restricted by the levels of a known confounder

- **Matching**: potential confounding factors are kept equal between the study groups

- **Stratification** for various levels of potential confounders

- **Multivariable analysis** (does not control for *effect modification*)
Effect modification can be assessed by:
- Stratification for various levels of potential confounders
- Multivariable analysis (by assessing interaction)

Reverse causation can be assessed by:
- Mendelian Randomization