Epidemiological Concepts

Epidemiological Study Design

1. PECO
2. Study design
   2.1 Randomized Controlled Trials (RCT)
   2.2 Observational studies
   - Cohort study
   - Case-control study
   - Cross-sectional study

ORIGINAL CONTRIBUTION

Aspirin Use and All-Cause Mortality Among Patients Being Evaluated for Known or Suspected Coronary Artery Disease

A Propensity Analysis

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Context Although aspirin has been shown to reduce cardiovascular morbidity and short-term mortality following acute myocardial infarction, the association between its use and long-term all-cause mortality has not been well defined.

Objectives To determine whether aspirin is associated with a mortality benefit in stable patients with known or suspected coronary disease and to identify patient characteristics that predict the maximum absolute mortality benefit from aspirin.

Design and Setting Prospective, nonrandomized, observational cohort study conducted between 1990 and 1998 at an academic medical institution, with a median follow-up of 3.1 years.

Patients Of 6174 consecutive adults undergoing stress echocardiography for evaluation of known or suspected coronary disease, 2310 (37%) were taking aspirin. Patients with significant valvular disease or documented contraindication to aspirin use, including peptic ulcer disease, renal insufficiency, and use of nonsteroidal anti-inflammatory drugs, were excluded.

Main Outcome Measure All-cause mortality according to aspirin use.

Results During 3.1 years of follow-up, 276 patients (4.5%) died. In a simple univariable analysis, there was no association between aspirin use and mortality (4.5% vs 4.5%). However, after adjustment for age, sex, standard cardiovascular risk factors, use of other

ASPIRIN HAS BEEN SHOWN TO be associated with decreased cardiovascular morbidity in multiple clinical trials[1,2] but the association between aspirin use and all-cause mortality has been less well defined except in the setting of acute myocardial infarction.[3] Although a few observational analyses have suggested a longer-term survival benefit,[4-6] it is not clear whether this benefit persists after accounting for

Let's design a study !

Study Hypothesis: Taking an aspirin will reduce the risk of dying from cardiovascular disease.

Which study design do you choose?

1. Divide a group of patients who were seen at outpatient clinics at Osaka University Hospital this year; and follow them for the next 20 years to observe cardiovascular related death.
2. Compare frequency aspirin use between patients who died of cardiovascular related death at Osaka University Hospital in the last 5 years and those who did not die of cardiovascular related death.
3. Survey a group of patients who are seen at Osaka University Hospital for asking frequency of their Aspirin use in the last 5 years and also asking if they have a cardiovascular disease.
4. Randomly allocated people who live in Osaka, half to taking an aspirin, and the other half to not taking aspirin. Then follow them over the next 20 years to observe cardiovascular related death.
5. Look into electric medical record, and identify patients who were taking an aspirin at time of hospitalization, and see if they died of cardiovascular related death. Compare them to those who without taking aspirin at the time of hospitalization for the frequency of their cardiovascular related death.

Always Start with PECO

- **P**opulation/Patients
- **E**xposure / Intervention
- **C**ontrol / Comparison
- **O**utcome

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Population?
Patients with an echo for possible coronary disease

Exposure?
Use of Aspirin at the index visit (baseline)

Control?
No use of Aspirin at the index visit (baseline)

Outcome?
Long term mortality (median FU of 3.1 years)

Classification of Clinical Studies

Epidemiologic Studies

- Experimental (Intervention)
  - Randomized Controlled Trials (RCT)
  - Non-randomized Trials
- Observational
  - Cohort studies
  - Case-control studies
  - Cross-sectional studies

Importance as an evidence

Non-epidemiologic Studies

- Case-study（Case-series）
- Opinion from a specialist based on biological and clinical principles

Classification of Epidemiologic Studies

- Experimental Studies
  - Randomized Clinical Trials
  - Non-Randomized Clinical Trials
- Observational Studies
  - Cohort Studies
  - Case-Control Studies
  - Cross-Sectional Studies

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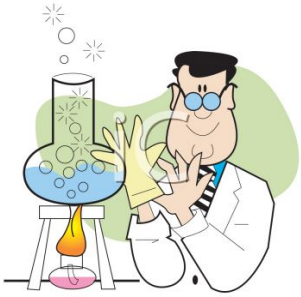
Experimental vs Observational Studies

- Who will receive a study exposure（i.e.,new drug vs standard of drug) is determined by a researcher

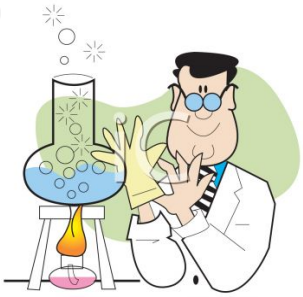
Yes → Experimental

No → Observational



Experimental Study Classification

- Randomized Clinical Trials
- Non-Randomized Clinical Trials



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Epidemiologic Study Classification

- Cohort Studies
- Case-Control Studies
- Cross-Sectional Studies

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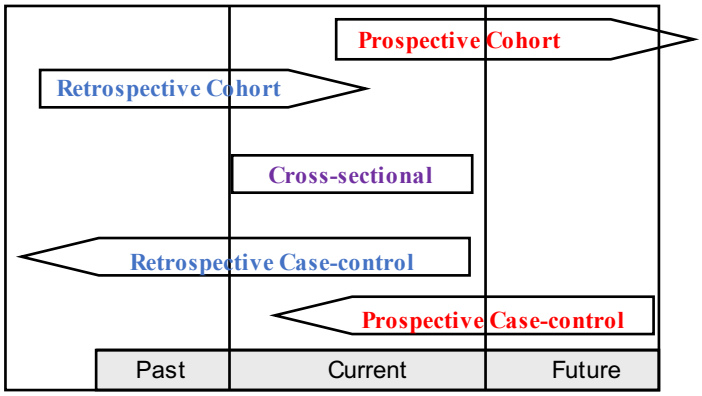
Classification of Study Design



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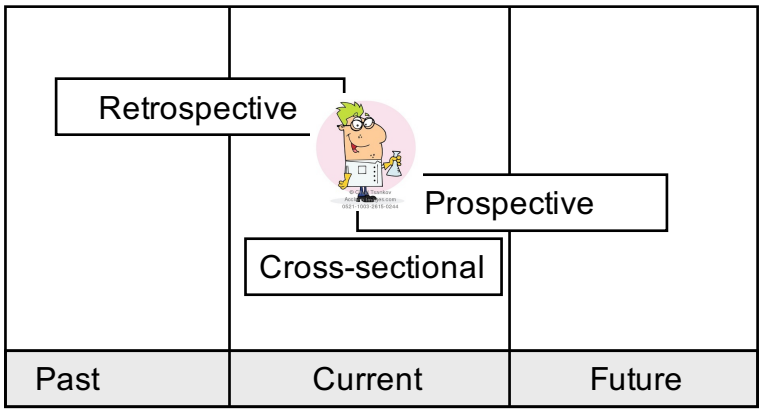
Classification of study design: Factors to consider

- Timing of Data Collection
- Data Sampling method

Timing of Data Collection



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Sampling method

Cohort: A group of people who share a common characteristics

Cohort Study – sample subjects without knowing their outcome status

Follow to observe their outcome

Case-Control Study

Need to know who has an outcome when deciding which subjects to include in a study.

Compare their exposure status

Cohort study

Gene A Present
N = 3000

Lung Ca+
N = 80

Lung Ca-
N = 2920

Gene A Absent
N = 5000

Lung Ca+
N = 90

Lung Ca-
N = 4910

Risk 80/3000 = 2.7% 90/5000 = 1.8%

Risk Ratio = 2.7% /1.8% = 1.5

Having gene A increase the risk of having a lung cancer by 50%

P = 0.009

Case-control study

With Lung Cancer
N = 170

Gene A Present
N = 80

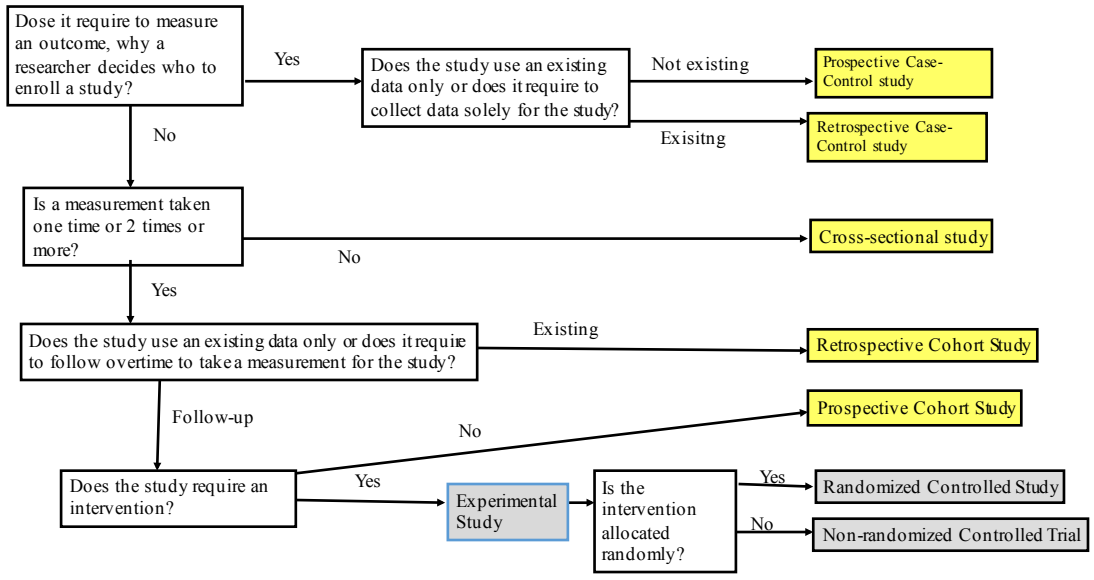
Gene A Absent
N = 90

Without Lung Cancer
N = 170

Gene A Present
N = 63

Gene A Absent
N = 107

Flow-chart of identifying a study design



Which study design do you choose?

1. Divide a group of patients who were seen at outpatient clinics at Osaka University Hospital this year; and follow them for the next 20 years to observe cardiovascular related death. Prospective cohort
2. Compare frequency aspirin use between patients who died of cardiovascular related death at Osaka University Hospital in the last 5 years and those who did not die of cardiovascular related death. Case-control
3. Survey a group of patients who are seen at Osaka University Hospital for asking frequency of their Aspirin use in the last 5 years and also asking if they have a cardiovascular disease. Cross-sectional
4. Randomly allocated people who live in Osaka, half to taking an aspirin, and the other half to not taking aspirin. Then follow them over the next 20 years to observe cardiovascular related death. Prospective cohort, RCT
5. Look into electric medical record, and identify patients who were taking an aspirin at time of hospitalization, and see if they died of cardiovascular related death. Compare them to those who without taking aspirin at the time of hospitalization for the frequency of their cardiovascular related death. Retrospective cohort

Cross-sectional

- Exposure (E) and Outcome (O) at one moment in time
  - Prevalence of disease
  - Prevalence of exposure
- Efficient
  - But
- Often biased for questions involving time between exposure and outcome.

Advantage of a cohort study

Rare exposure (exposures)
Several outcomes
Exposure precedes disease
Less sensitive for selection bias (compared with a case-control study)
Less sensitive for information (recall) bias

Disadvantage of a cohort study

Costly and time consuming
If cohort: loss of subjects due to migration, death
Selection bias can be severe in a retrospective cohort study

Case – Control study

Advantages:

* Efficient due to sampling approach
* Rare disease (e.g. side effects)
* When exposure measurements are expensive
  Blood measurements such as genome or bio-marker data
  Radiographic readings

Disadvantages:

- One outcome
- Rare exposure
- Risk cannot be estimated
- More sensitive to selection bias
- More sensitive to information (recall) bias