



PHC 6010

EPIDEMIOLOGY METHODS I

Selection Bias in Cohort Studies

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Selection bias in Cohort Studies

- In a typical cohort study, exposed and unexposed individuals are followed over time to determine whether they experience the outcome of interest
- At the end of the study, information on both groups is gathered to assess the association between exposure status and the outcome using relative risk measure.



Selection bias in Cohort Studies

- The assumptions made in a cohort study include the following:
 1. At baseline, disease-free individuals are enrolled into the study
 2. Exposed and unexposed groups are comparable except for the exposure
 3. Information obtained is comparable for both groups

Deviation from these assumptions could lead to selection bias



Selection Bias in Cohort Study

- Types of selection bias in a Cohort Study:
 1. Front-end bias
 2. Population Choice bias
 3. Loss to follow-up bias
 4. Other forms of selection bias: control group bias; contamination bias/spillover effect; co-intervention bias; compliance bias;etc.



Selection bias in cohort study

- What is a cohort study?

Definition: A cohort study is one in which a group of individuals with similar characteristics, except for the exposure of interest, is followed over time to determine how the exposure of interest affects a specific or group of outcomes



Selection bias in cohort study

- A fundamental assumption in a cohort study is that the two groups (exposed and unexposed) will differ only with respect to the exposure.
- Consequently, differences in the outcome is attributed to the exposure status.
- There are two main types: (1) observational and (2) experimental (also known as clinical trial).



Selection bias in cohort study

- The difference between an observational cohort and a randomized trial is that in the latter the investigator controls the assignment of exposure status.
- For observational cohort, nature (e.g., genetic pre-disposition) or self-selection (e.g., smoking habits) rather than the investigator determines exposure status.



Selection bias in cohort study

- In this lecture, we will examine the various types of selection bias that affect cohort studies
- We will also discuss ways to handle or minimize the influence of the sources of these biases on measures of effects.
- Most of our examples will be either from an observational longitudinal cohort or a randomized trial



Front-End Bias

- **Definition:** This is a type of selection bias in which at study baseline in a cohort study, truly diseased persons are unknowingly enrolled into the study.
- This usually occurs when the screening instrument used for detecting the disease at baseline is not very sensitive.
- Let's illustrate this by means of an example given in the next slide.



Front-End Bias

- We will illustrate an example using two types of study that involve a cohort design.
- One is a randomized clinical trial and the other is an observational cohort study.
- In both study design, the hypothesis is to test the effectiveness of electric cigarettes in preventing lung cancer among individuals that have been smoking for at least 10 years.



Front-End bias

- Individuals must be at least 60 years of age and screened free of lung cancer by the absence of lesions on a chest-xray at baseline.
- Randomized Trial: For the randomized study, consented individuals were randomly assigned to electric cigarette consumption or left to continue with conventional smoking.



Front-End bias

- In addition, both groups received smoking cessation counseling.
- Study participants were then followed for 10 years to document the occurrence of lung cancer.
- Patients who developed lung cancer were appropriately treated according to standard of care.



Front-End bias

- For the cohort study, individuals were selected from a tobacco treatment center where electric tobacco was offered to patients as alternative to conventional cigarettes.
- Similar to the randomized trial, consented patients received smoking cessation counseling and X-ray screening for lung cancer lesions
- The eligibility criteria and follow-up were similar as in the randomized design



Front-End bias

- Unknown to the study investigators, however, some of the patients recruited into the study had “occult” lung cancer that was not captured by the chest X-ray.
- This implies that selection bias could occur on the front-end during the process of choosing study participants since diseased individuals were unknowingly entered into the study.



Front-End bias

- Now, let's examine what will happen starting with the randomized trial.
- Randomization bears the inherent property of equalizing distinct characteristics of study participants .
- With perfect random assignment, we will expect the proportion of individuals with occult disease in both treatment arms to be the same.
- Consequently, effects of front-end bias will be canceled.



Front-end bias

- However, if random assignment is sub-optimal, individuals in both arms of the study may differ based on “occult” disease status at baseline.
- In the electric cigarette example, with imperfect randomization, we may inadvertently have a greater or lesser proportion of individuals with occult disease in the control than in the treatment arm.



Front-end bias

- What will happen if the former is the case (more occult disease in the control group or conventional smokers)?
- If the electric cigarette is truly protective against lung cancer then the effect estimate (relative risk) will be amplified and distanced farther away from the null.



Front-end bias

- But what will be the influence of the front-end bias If the electric cigarette does not protect against lung cancer but has the same effect as conventional smoking?
- Since as a result of selection bias (i.e., front-end bias), we will have more individuals than expected developing lung cancer in the control group
- As a result, the effect measure will spuriously portray electric cigarette to be protective (away from the null).



Front-end bias

- Now what happens if more occult disease occurs among those randomized to the treatment group?
- Obviously, if the electric cigarette is truly protective against lung cancer as compared to conventional smoking, the effect will be blunted or erased (toward the null).
- If the treatment is no different from conventional smoking, depending upon the magnitude of the front-end bias, the electric cigarette may appear worse than conventional smoking regarding cancer causation (away from the null).



Front-end bias

- The same effects will be observed in the cohort study as described for the randomized clinical trial.
- Now, how can we prevent front-end bias from happening or how can we best handle it?
- Subsequent slides discuss how to prevent or remedy front-end bias using the study on the effectiveness of electric cigarette to reduce lung cancer as an example.



Front-end bias

PREVENTION OF FRONT-END BIAS

- As with any other type of selection bias, the best way to handle front-end bias is to prevent it at the design stage
- This is feasible by ensuring that a more sensitive instrument is used to ascertain the absence of the outcome at baseline
- In the previous example, instead of using chest X-ray, investigators should have used a more sensitive imaging procedure such as CAT SCAN to minimize the impact of front-end bias



Front-End Bias

- In certain circumstances use of a more sensitive instrument may be prohibitively costly (e.g., CAT SCAN)
- In such instances, use of a low cost instrument or procedure may be the only viable option, and front-end bias cannot be avoided
- Consequently, the prevention of front-end bias in this case is only feasible at the data analysis stage



Front-end bias

- How do we then minimize the impact of front-end bias when data has already been collected and the study has ended?
- A number of experts have proposed the exclusion of early outcomes as a way of removing cases of occult disease from both exposed and unexposed groups.
- This sounds rational since individuals who already had the disease would manifest symptoms earlier than those who did not have the disease



Front-end bias

- In our example of the effectiveness of electric cigarette in preventing lung cancer, we could decide to exclude all lung cancer cases as well as lung-cancer related mortality that occurred within the first 1 year after commencement of the 10-year study.
- This will remove cases of early lung cancer which probably started before the commencement of the study
- Usually, to decide a cut-off point, knowledge of the natural history of the disease is important.