DESIGNING OBSERVATIONAL STUDIES

As we have discussed, for the purpose of establishing cause-and-effect relationships, observational studies have a distinct disadvantage in comparison to randomized comparative experiments. In some cases, however, researchers are not interested in assessing causality. Observational studies are appropriate for investigating these types of research questions. Furthermore, there are many cases in which designing an experiment is either unethical or impossible (we’ve already discussed a few examples like this). In such cases, we conduct an observational study, which can be useful for discovering trends and possible relationships.

Next, we will discuss various types of observational studies.

Types of Observational Studies

Observational studies are typically classified into one of three types according to the relevant time frame of the data collected: cross-sectional, case-control, and cohort studies.

**Cross-sectional Study**

In a **cross-sectional study**, a sample of individuals is ascertained at one point in time, and measurements are taken at that point. This type of study provides a picture of both the outcome(s) of interest and associated characteristics at a single point in time.

**Example: Cross-sectional Study of Mentoring Relationships**


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**A Cross-sectional Descriptive Study of Mentoring Relationships Formed by Medical Students**

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**Abstract**

To describe medical students’ mentoring relationships and determine characteristics associated with having mentors, 232/302 (77%) of third- and fourth-year medical students at the University of California at San Francisco (UCSF) were surveyed. Twenty-six percent of third-year and 45% of fourth-year students had mentors. Most met their mentors during inpatient clerkships (28%), research (19%), or sought them on the basis of similar interests (23%). On multivariate analysis, students who performed research prior to (odds ratio [OR], 4.8; 95% confidence interval [95% CI], 1.4 to 16.7; P = .01) or during medical school (OR, 2.4; 95% CI, 1.1 to 5.6; P = .03) and students satisfied with advising from all sources at UCSF (OR, 1.8; 95% CI, 1.4 to 2.4; P < .001) were more likely to have mentors.
Example: Cross-sectional Study of Mentoring Relationships

<table>
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<tr>
<th>METHODS</th>
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<tbody>
<tr>
<td>We performed a cross-sectional descriptive and analytic study of all third- and fourth-year medical students attending UCSF in Spring, 1999. We asked students to complete an anonymous questionnaire during courses in which attendance was required so that all students would be accessible for study entrance. Students not present at class and those who chose not to respond were excluded.</td>
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<td>The survey included questions about demographics, perceived class rank, research experience, and career goals. Students were asked if they had developed a mentoring relationship, and if so, to describe it, including the functions performed by the mentor. Students without mentors were asked about perceived barriers to mentoring.</td>
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Questions:

1. What makes this study design cross-sectional?
2. What is the outcome of interest in this study?
3. What associated characteristics were investigated?

When designing a cross-sectional study, one must ensure that the sample is representative of the population of interest. The best way to prevent bias is to ensure that random sampling methods are used. Also, one should keep the following advantages and disadvantages of using this type of study in mind.

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<th>Cross-Sectional Study</th>
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<td><strong>Advantages</strong></td>
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<td>• Relatively inexpensive and can be completed quickly</td>
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<td>• Allows for estimation of the prevalence of the outcome of interest</td>
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<td>• Allows for the assessment of many outcomes and risk factors</td>
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<td>• There is no loss to follow-up</td>
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Like the cross-sectional study, the next type of study can also be carried out fairly quickly; however, it involves data that has been recalled or collected from the past.
Case-control (Retrospective) Study

In a case-control study, two groups of individuals are initially identified: (1) a group that has the disease under study (the cases) and (2) a group that does not have the disease under study but is as similar as possible to the cases (the controls). Cases are then compared to controls to assess whether they differ on explanatory variables of interest (e.g., their prior health habits or exposure to risk factors). This is also called a retrospective study because it involves data that was recalled from or collected in the past.

Example: Case-Control Study Investigating Mobile Phone Use and Cancer


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Mobile phone use and risk of glioma in adults: case-control study

Sarah J Hepworth, medical statistician,1 Minouk J Schoemaker, medical statistician,2 Kenneth R Mull, professor of epidemiology,3 Anthony J Swerdlow, professor of epidemiology,2 Martie J A van Tongeren, senior lecturer in occupational and environmental health,4 and Patricia A McKinney, professor of paediatric epidemiology1

Abstract

Objective To investigate the risk of glioma in adults in relation to mobile phone use.

Design Population based case-control study with collection of personal interview data.

Setting Five areas of the United Kingdom.

Participants 966 people aged 18 to 69 years diagnosed with a glioma from 1 December 2000 to 29 February 2004 and 1716 controls randomly selected from general practitioner lists.

Main outcome measures Odds ratios for risk of glioma in relation to mobile phone use.

Results The overall odds ratio for regular phone use was 0.94 (95% confidence interval 0.78 to 1.13). There was no relation for risk of glioma and time since first use, lifetime years of use, and cumulative number of calls and hours of use. A significant excess risk for reported phone use ipsilateral to the tumour (1.24, 1.02 to 1.52) was paralleled by a significant reduction in risk (0.75, 0.61 to 0.93) for contralateral use.

Conclusions Use of a mobile phone, either in the short or medium term, is not associated with an increased risk of glioma. This is consistent with most but not all published studies. The complementary positive and negative risks associated with ipsilateral and contralateral use of the phone in relation to the side of the tumour might be due to recall bias.
Example: Case-Control Study Investigating Mobile Phone Use and Cancer

From the methods section:

In the most recent year we have published data for (1992) an estimated 98% of the UK population was registered with a general practitioner. Controls were randomly selected from general practitioners' lists by a preset algorithm. In the south east the controls were frequency matched to reflect the age, sex, and geographical distribution of cases. In the northern centres one control per case was individually matched on age, sex, and general practice after the patient with glioma was interviewed. Nonparticipating controls were replaced. Parallel case-control studies of meningioma, acoustic neuroma, and other brain tumours were carried out with identical methods and questionnaires; the controls for these cases were included in the present analyses.

Questions:

1. Who are the cases?

2. Who are the controls?

3. Were the cases matched with controls on an individual basis? If so, what characteristics were used as matching criteria?

4. How is matching cases and controls similar to a matched-pair experimental design? How is it different?

<table>
<thead>
<tr>
<th>Case-Control Study</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<td></td>
<td>• Relatively inexpensive and can be completed quickly&lt;br&gt;• Controls can be chosen to reduce the effect of potential confounding variables&lt;br&gt;• Allows for the investigation of rare diseases or diseases with a long induction period</td>
<td>• Doesn’t allow for causal inference&lt;br&gt;• Doesn’t ensure that the exposure preceded the disease&lt;br&gt;• It is difficult to select both cases and controls who are representative of their respective populations&lt;br&gt;• People may not remember past events accurately&lt;br&gt;• Doesn’t allow us to estimate the prevalence of a disease</td>
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</table>
Finally, the third type of observational study involves following participants into the future rather than analyzing data from the past.

**Cohort (Prospective) Study**

In a cohort study (also called a longitudinal study), a group of disease-free individuals (the cohort) is identified at one point in time, and information is obtained to determine which members of the cohort are exposed to the factor of interest. The subjects are then followed over a period of time until some of them develop the disease, and the incidence of the disease in the exposed individuals is compared with the incidence in those not exposed. This is also called a prospective study because it involves following participants into the future.

![Cohort Study Diagram]

**Example: Cohort Study Investigating Methamphetamine Use and Schizophrenia**

*The American Journal of Psychiatry, VOL. 169, No. 4*

**Methamphetamine Use and Schizophrenia: A Population-Based Cohort Study in California**


**Abstract**

**Objective:** Clinical investigators in Japan have long suggested that exposure to methamphetamine might cause a persistent schizophrenia-like psychosis. This possibility is discounted in the Western literature. To investigate the relationship between drug use and later schizophrenia, the authors conducted a large-scale cohort study of drug users initially free of persistent psychosis.

**Method:** A population-based cohort study was conducted using data from California inpatient hospital discharge records from 1990 through 2000. Patients with methamphetamine-related conditions (N=42,412) and those with other drug use disorders (cannabis, cocaine, alcohol, and opioids) were propensity score-matched to individuals with primary appendicitis who served as a population proxy comparison group; the methamphetamine cohort was also matched to the other drug cohorts. Cox modeling was used to estimate differences between matched groups in the rates of subsequent admission with schizophrenia diagnoses.
Example: Cohort Study Investigating Methamphetamine Use and Schizophrenia

**Results:** The methamphetamine cohort had a significantly higher risk of schizophrenia than the appendicitis group (hazard ratio=9.37) and the cocaine, opioid, and alcohol groups (hazard ratios ranging from 1.46 to 2.81), but not significantly different from that of the cannabis group. The risk of schizophrenia was higher in all drug cohorts than in the appendicitis group.

**Conclusions:** Study limitations include difficulty in confirming schizophrenia diagnoses independent of drug intoxication and the possibility of undetected schizophrenia predating drug exposure. The study’s findings suggest that individuals with methamphetamine-related disorders have a higher risk of schizophrenia than those with other drug use disorders, with the exception of cannabis use disorders. The elevated risk in methamphetamine users may be explained by shared etiological mechanisms involved in the development of schizophrenia.

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<tr>
<th>Cohort Study</th>
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<tr>
<td><strong>Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
<td></td>
</tr>
<tr>
<td>• Ensures that exposure precedes the disease</td>
<td>• Doesn’t allow for causal inference</td>
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<td>• Can be used to study more than one outcome</td>
<td>• Can be costly and may take a long time</td>
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<td>• Good for the study of rare exposures</td>
<td>• When studying rare outcomes, a very large sample size is required</td>
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<td>• Allows for the incidence of the outcome to be measured</td>
<td>• Prone to dropout</td>
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**FINAL COMMENT ON REPRESENTATIVE SAMPLES**

When interpreting both randomized experiments and observational studies, keep in mind that the data collected can be used to make inferences about the larger population if the sample can be considered representative of the population. In the next chapter, we’ll discuss in detail strategies for obtaining samples.

When observational studies are based on random samples, it is reasonable to assume those samples are representative of the population from which they were drawn. Similarly, when the subjects in a designed experiment are first randomly selected from a population and then randomly assigned to treatment groups, it is reasonable to assume the subjects under study are representative of the population of interest.

When observational studies or designed experiments use volunteers, however, one should think carefully about whether the results should be extended to a specific population.