Observational Studies: Uses and Limitations

31

Aaron S. Hess and Alaa Abd-Elsayed

Introduction

Observational studies analyze subjects without any experimental intervention by the investigator. Observational studies can be either *retrospective*, e.g., using an existing clinical, administrative, or public data base to define a group of subjects, or *prospective*, defining the group in advance, recruiting them, and following them forward in time [1]. In either case, subject exposures and outcomes are defined by their own circumstances, care, choices and are not under the control of the investigator. Observational studies are generally far cheaper, easier, and less ethically complex than analogous experimental studies, and they are the most popular and common method of clinical research. The validity and interpretation of observational studies is less clear than experimental studies, however, lack of randomization and investigator control increase opportunity for bias, confounding, and reduces the validity of many statistical tests. Common forms of observational studies in clinical research include *cross-sectional* studies, *ecologic* studies, *case-control* studies, and *cohort* studies. Cohort studies and cross-sectional studies are discussed in detail in separate chapters. For example, a retrospective study of the association between neurocognitive function and chronic pain may be confounded by the association of age with both factors, a phenomenon that might be adjusted for with a multivariable statistical model.

Topic

Observational study design begins with definition and selection of the population of interest, as well as the exposures and outcomes to be recorded. Observational research is *nonexperimental*, or *non-interventional*, although the investigators may take active and even invasive measures to recruit, maintain, and collect data from study participants [1]. *Bias*, or unmeasurable distortions in the characteristics of selected patients compared to the theoretical study population, is a major threat to the validity of all observational studies. By definition, bias cannot be measured or controlled for, but its sources can be anticipated and limited by careful study design and sampling technique [2]. For example, studies of inpatient chronic pain patients drawn from Medicare databases may be biased toward patients with lower socioeconomic status compared to hospital registries. *Confounding*, or the presence of factors associated with both exposure and outcome that distorts their apparent relationship in the data, is a common phenomenon that can be managed with careful study design and statistical adjustment.

A. S. Hess (✉) · A. Abd-Elsayed
Department of Anesthesiology, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
e-mail: aaron.hess@wisc.edu

© Springer Nature Switzerland AG 2019
A. Abd-Elsayed (ed.), *Pain*, https://doi.org/10.1007/978-3-319-99124-5_31

The most common study designs in observational clinical research are *cohort*, *case-control*, *cross-sectional* and *ecologic*. Observational studies are defined by whether patients are selected based on their exposure or outcome, and when the outcome is measured relative to the exposure. In cohort studies, patients are selected based on their exposures and then observed for a subsequent outcome of interest. Cohort studies can be conducted *retrospectively*, when longitudinal patient information already exists in a database, or *prospectively*, by identifying patients and following them forward until the outcome occurs. Case-control studies start with identification of the patients with the outcome of interest (cases) or without (controls) and then looking backwards in time for the exposure of interest. Case-control studies can only be performed retrospectively. Cohort studies and case-control studies are discussed in more detail in separate chapters. Cross-sectional studies look for the presence of co-existing exposures and outcomes at a single point in time, e.g., using a survey or census, and therefore cannot draw any conclusions about their temporal relationship. Ecologic studies are similar to cross-sectional studies but look at exposures and outcomes among whole groups or populations, without individual data.

Observational studies are considered a lower standard of evidence than experimental studies, particularly randomized, controlled clinical trials. When patient exposures are not under the control of the investigator, which they are not in observational studies, the relationship between exposure and outcome may be biased or confounded by unmeasurable or uncontrollable factors, significantly reducing study validity. Cohort and case-control studies have greater validity in establishing associations between exposures and outcomes compared to cross-sectional and ecologic studies, but they can only establish a temporal, not a causal relationship. Observational studies are still a major tool in clinical research for hypothesis generation and evaluation, and for many questions they are the only economically viable or ethically sound option.

High Yield Points

- Observational studies are non-experimental clinical research.
- Common types of observational studies in clinical research include cohort, case-control, cross-sectional, and ecologic studies.
- Observational studies are typically cheaper, easier, and ethically less complex than clinical trials or other experimental studies.
- Observational studies are a lower standard of evidence than experimental studies, are more prone to bias and confounding, and cannot be used to demonstrate causality.
- Observational studies can be either retrospective (using existing data) or prospective (collecting new data).

Questions

In 2015, Hauser and colleagues published a study of 2508 German citizens. Each participant answered a one-time survey that included questions on presence of chronic pain, chronic pain stages, and disease load [3].

1. This study design is best described as:
   A. Cohort
   B. Case-control
   C. Cross-sectional
   D. Ecologic
   Answer: C
2. In the Hauser study, the odds of chronic, disabling pain was significantly higher among obese survey respondents (odds ratio [OR] = 3.6, 95% CI 2.2–5.8). Based only on this study, what might have caused this result?
   A. Obesity contributing chronic, disabling pain
   B. Chronic, disabling pain contributing to obesity
   C. Selection bias
   D. All of the above
   Answer: D

In 2017, Shah and colleagues published a retrospective cohort study of 1,352,902 previously opioid-naïve patients in an insurance claims database in which they found that initial opioid prescription dose in morphine equivalents and in days' supply were each significantly associated with the probability of long-term opioid use [4].

3. Which of the following likely did *not* have contributed to the observed association?
   A. Selection bias from studying insured patients
   B. Confounding caused by more severe injuries leading to longer-term pain
   C. Long-term opioid use leading to large initial doses (reverse causation)
   D. None of the above

   Answer: C

References

1. Rothman K. Modern epidemiology, vol. 93. 3rd ed. Philadelphia: LWW; 2008. p. 100.
2. Woodward M. Epidemiology study design and data analysis. 3rd ed. Boca Raton: CRC Press; 2013. p. 19.
3. Häuser W, Schmutzer G, Hilbert A, Brähler E, Henningsen P. Prevalence of chronic disabling noncancer pain and associated demographic and medical variables: a cross-sectional survey in the general German population. Clin J Pain. 2015;31(10):886–92.
4. Shah A, Hayes C, Martin B. Factors influencing long-term opioid use among opioid naïve patients: an examination of initial prescription characteristics and pain etiologies. J Pain. 2017;18(11):1374–83.