

Retrospective Studies and Chart Reviews

Dean R Hess PhD RRT FAARC

Introduction
Case Series
Case-Control Study
Matched Case-Control Study
Summary

A retrospective study uses existing data that have been recorded for reasons other than research. A retrospective case series is the description of a group of cases with a new or unusual disease or treatment. With a case-control study, cases with and without the condition of interest are identified, and the degree of exposure to a possible risk factor is then retrospectively compared between the 2 groups. With a matched case-control study, control subjects are selected such that they resemble (match) the cases with regards to certain characteristics (eg, age, comorbidity, severity of disease). Retrospective study designs are generally considered inferior to prospective study designs. Therefore, a retrospective study design should never be used when a prospective design is feasible. *Key words: research, respiratory care, research methodology, study design, retrospective, case control.* [Respir Care 2004;49(10):1171–1174. © 2004 Daedalus Enterprises]

Introduction

A retrospective study uses existing data that have been recorded for reasons other than research. In health care these are often called “chart reviews” because the data source is the medical record. Figure 1 contrasts retrospective and prospective studies. There are 3 general types of retrospective study: case report, case series, and case-control study. A retrospective study contains many of the same study-design elements as a prospective study (Table 1). Many times investigators view retrospective studies as

“quick and dirty” because the data are quickly gleaned from existing records to answer a question. However, a well done retrospective study may not be quick and is definitely not “dirty.” Although a retrospective design is usually discouraged when a prospective study is feasible, a retrospective study can serve a useful purpose. A particularly useful application of a retrospective study is as a pilot study that is completed in anticipation of a prospective study. The retrospective study can help to focus the study question, clarify the hypothesis, determine an appropriate sample size, and identify feasibility issues for a prospective study.

Case Series

A *case report* is a report of one unusual and/or instructive case (eg, symptoms not previously observed with a given medical condition, or an unexpected or new combination of medical conditions in one case), whereas a *case series* is a report of multiple similar unusual or instructive cases. A retrospective case series can be used to study a disease that occurs infrequently or to generate a hypothesis that can be tested more rigorously in a prospective study.

Dean R Hess PhD RRT FAARC is affiliated with the Department of Respiratory Care, Massachusetts General Hospital, and Harvard Medical School, Boston, Massachusetts.

Dean R Hess PhD RRT FAARC presented a version of this article at the RESPIRATORY CARE Journal symposium, “The ABCs of Research,” at the 49th International Respiratory Congress, held December 8–11, 2003, in Las Vegas, Nevada.

Correspondence: Dean R Hess PhD RRT FAARC, Respiratory Care, Ellison 401, Massachusetts General Hospital, 55 Fruit Street, Boston MA 02114. E-mail: dhess@partners.org.

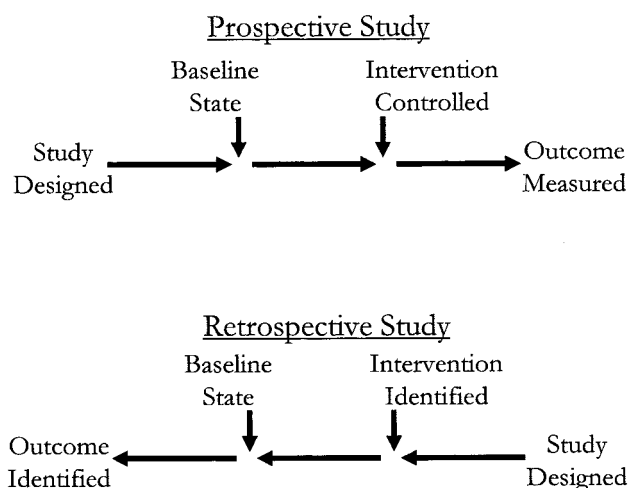


Fig. 1. Prospective versus retrospective study design. In a prospective study, the baseline state of the subjects is determined, the controlled intervention is applied, and then the outcome is measured. In a retrospective study, the intervention, baseline state, and outcome are obtained from existing information that was recorded for reasons other than the study.

There are several important disadvantages of a case series. First, as with any retrospective study, the investigator depends on the availability and accuracy of the medical record. Second, a case series is subject to selection bias because the investigator self-selects the cases. Third, a case series is uncontrolled.

A few examples will illustrate the case series design. In the mid-1990s, inhaled nitric oxide (INO) was used in relatively few hospitals worldwide. One of the largest experiences with INO was at the Massachusetts General Hospital. Manktelow et al¹ reviewed that experience, which included 88 patients with acute respiratory distress syndrome. They reported a clinically important response to INO (improvement in oxygenation) in 58% of the patients,

consistent with what was subsequently reported in prospective controlled trials. They also used a multivariate logistic regression model to analyze the effect of multiple variables on the responsiveness to INO, which showed that only septic shock remained a significant discriminant for responsiveness to INO. Because the majority of patients with acute respiratory distress syndrome demonstrate a clinically useful physiologic response to INO, the logical next hypothesis to be tested was whether INO improves survival in those patients. Unfortunately, subsequent prospective randomized, controlled trials showed no survival benefit for INO with patients with acute respiratory distress syndrome.^{2,3}

Another example of a retrospective case series comes from Wijkstra et al.⁴ They summarized the outcomes of all the patients admitted to an in-patient, long-term, assisted-ventilation unit between 1986 and 2001. They concluded that such a unit can provide a safe environment for severely impaired, ventilator-dependent patients. About a third of the patients eventually left for a more independent community-based care setting. Better outcomes were seen among patients with spinal cord injury and neuromuscular disease than among patients with chronic obstructive pulmonary disease and thoracic restriction. This was an appropriate topic for a retrospective study because there are few of these patients (only 50 patients in 15 years) and there are few hospitals that have specialized units for these patients.

Case-Control Study

A case-control study, although retrospective, is superior to a case series because of the presence of a control group. Cases with and without the condition of interest are identified. The degree of exposure to a possible risk factor is then compared between the 2 groups. The case-control study design assumes that (1) cases differ from controls only in having the disease, (2) exposure should be equally distributed between cases and controls if the exposure does not cause the disease, and (3) greater exposure among cases would indicate that exposure increases the risk of the disease. The exposure is determined retrospectively. Ideally, the data collectors are unaware of whether a subject is a case or a control, and the data collectors should be unaware of the study hypothesis. The cases and the controls must be assessed for exposure in the same way. Figure 2 illustrates the case-control study design. Figure 3 compares a case-control study to a prospective randomized trial.

Certain types of study bias are unique to case-control studies. For hospital-based case-control studies the study population is the collection of clinical records of the participating hospital. However, the cases and the controls may have had different hospital admission rates; this is called Berkson's bias. For example, many patients with

Table 1. Important Elements in a Retrospective Study Design*

1. Write the study question
2. Develop the hypothesis
3. Search the literature
4. Consider the statistical issues, such as sample size and how the results will be analyzed
5. Write the protocol: where the data will be found, what data will be needed, how data will be collected, how data will be analyzed
6. Obtain permission: institutional review board (patient?), data source (eg, medical records department)
7. Collect the data
8. Analyze the data
9. Explain the results
10. Write the report

*Note that these are by and large the same as the elements of a prospective study design.

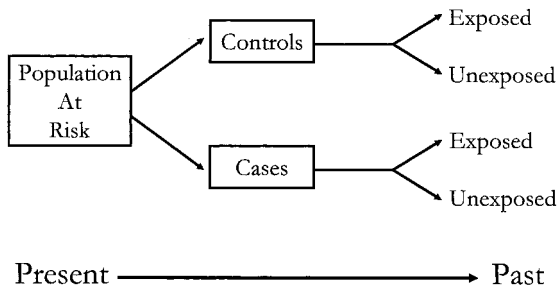


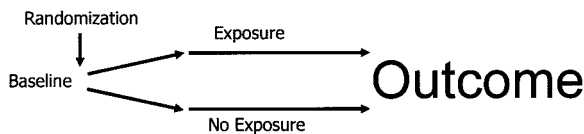
Fig. 2. Case-control study design. Cases and controls are selected from the population at risk. The degree of exposure to a possible risk factor is identified in the cases and in the controls.

asthma are not admitted to the hospital. A case-control study of asthma using hospital records would select only the most severe cases. For population-based case-control studies the study population is the collection of subjects who would become cases if they developed disease. This can result in cases that are not representative of the intended population; this is called Neyman's bias.

A commonly used statistic for case-control studies is the *odds ratio*, defined as the ratio of the odds of an outcome in an exposed group to the odds of the same outcome in a group that was not exposed. An odds ratio of 1 means that the odds of a given outcome are equal for those who were exposed and those who were not exposed to a possible risk factor. An odds ratio < 1 means that the given outcome is less likely among those who were exposed than among those who were not. An odds ratio > 1 means that the given outcome is more likely among those who were exposed than among those who were not.

There are both strengths and weaknesses to case-control studies. The strengths include: fewer constraints by the frequency of the disease; shorter waiting time than a prospective cohort study; case-control studies are sometimes feasible when randomized controlled trial are not; and case-control studies cost less and have fewer practical restrictions. The weaknesses include: a less well defined target

Randomized Controlled Trial:



Case-Control Study:

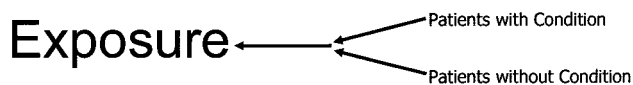


Fig. 3. Comparison of a randomized controlled trial and a case-control study.

Calculation of odds ratio:

	Cases	Controls	
Exposed	a	b	a + b
Not Exposed	c	d	c + d
	a + c	b + d	N

Odds ratio = ad/bc

Males:

	Cases (lung cancer)	Controls (no lung cancer)	
Smokers	647	622	1269
Non-smokers	2	27	29
	649	649	1298

Odds ratio = 14.1

Females:

	Cases (lung cancer)	Controls (no lung cancer)	
Smokers	41	28	69
Non-smokers	19	32	51
	60	60	120

Odds ratio = 2.5

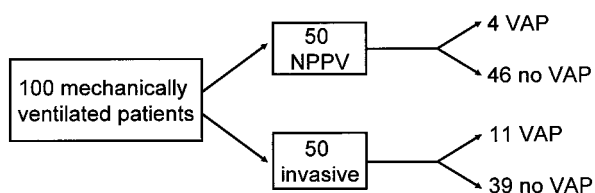
Fig. 4. Calculation of the odds ratio in a case-control study. The upper panel shows the general principle of calculating the odds ratio. The lower 2 panels show an example from the study by Doll and Hill.⁵

population; risk of selection bias; and it is difficult or impossible to ascertain cause-and-effect, because of confounding factors.

A classic case-control study relevant to respiratory disease was published by Doll and Hill⁵ in 1950. They studied the relationship between lung cancer and cigarette smoking. Patients with lung cancer were identified in 20 London hospitals; those were the cases. An equal number of controls were identified among hospitalized patients of the same age group with diagnoses other than lung cancer. Figure 4 summarizes the study's results. For men the odds ratio was 14.1, meaning that male smokers had a 14.1 times greater chance of lung cancer than male nonsmokers.

Matched Case-Control Study

With a matched case-control study design, the control subjects are selected so they resemble (match) the cases



	Noninvasive ventilation	Invasive ventilation	
Pneumonia	4	11	15
No Pneumonia	46	39	85
	50	50	100

Odds ratio = 0.31

Fig. 5. Results of a matched case-control study to examine the risk of ventilator-associated pneumonia (VAP) among patients who did or did not receive noninvasive ventilation (NPPV). (Adapted from Reference 6).

with regard to certain characteristics (eg, age, comorbidity, severity of disease). The goal is to compare case and control patients who have similar characteristics and thereby to adjust for potential confounders and increase the precision of the comparison.

Girou et al⁶ did a matched case-control study to determine whether noninvasive ventilation was associated with a lower risk of nosocomial pneumonia. A sample of 50 patients who received noninvasive ventilation (the cases) was matched to 50 patients who received invasive ventilation (the controls). The controls were matched to cases based on the same diagnosis at admission, and age ± 5 years, Simplified Acute Physiology Score II ± 6 points, Logistic Organ Dysfunction score ± 3 points, and no contraindications to noninvasive ventilation. Figure 5 summarizes the results. The odds ratio is 0.31, meaning that the odds of nosocomial pneumonia were lower among the patients who received noninvasive ventilation.

Summary

There are advantages and disadvantages to retrospective study designs (Table 2). With few exceptions, retrospec-

Table 2. Advantages and Disadvantages of Retrospective Studies

Advantages

- Inexpensive
- Uses existing records
- Allows study of rare occurrences
- Easier to assess conditions where there is a long latency between exposure and disease
- Can generate hypothesis that is then tested prospectively (quality improvement initiatives)

Disadvantages

- Relies on accuracy of written record or recall of individuals (recall bias): garbage in → garbage out
- Important data may not be available: nothing in → nothing out
- Difficult to control bias and confounders: no randomization, no blinding
- May be impossible to access important information (restricted by statute or institutional regulations)
- Difficult to establish cause and effect
- Results are, at best, hypothesis-generating

tive study designs are inferior to prospective study designs. A retrospective study design should never be used when a prospective design is feasible.

REFERENCES

1. Manktelow C, Bigatello LM, Hess D, Hurford WE. Physiologic determinants of the response to inhaled nitric oxide in patients with acute respiratory distress syndrome. *Anesthesiology* 1997;87(2):297-307.
2. Taylor RW, Zimmerman JL, Dellinger RP, Straube RC, Criner GJ, Davis K Jr, et al. Inhaled Nitric Oxide in ARDS Study Group. Low-dose inhaled nitric oxide in patients with acute lung injury: a randomized controlled trial. *JAMA* 2004;291(13):1603-1609.
3. Lundin S, Mang H, Smithies M, Stenqvist O, Frostell C. Inhalation of nitric oxide in acute lung injury: results of a European multicentre study. The European Study Group of Inhaled Nitric Oxide. *Intensive Care Med* 1999;25(9):911-919.
4. Wijkstra PJ, Avendano MA, Goldstein RS. Inpatient chronic assisted ventilatory care: a 15-year experience. *Chest* 2003;124(3):850-856.
5. Doll R, Hill AB. Smoking and carcinoma of the lung. *Br Med J* 1950;3(2):739-748.
6. Girou E, Schortgen F, Delclaux C, Brun-Buisson C, Blot F, Lefort Y, et al. Association of noninvasive ventilation with nosocomial infections and survival in critically ill patients. *JAMA* 2000;284(18):2361-2367.