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# What Do Case-Control Studies Estimate? Survey of Methods and Assumptions in Published Case-Control Research

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To evaluate strategies used to select cases and controls and how reported odds ratios are interpreted, the authors examined 150 case-control studies published in leading general medicine, epidemiology, and clinical specialist journals from 2001 to 2007. Most of the studies (125/150; 83%) were based on incident cases; among these, the source population was mostly dynamic (102/125; 82%). A minority (23/125; 18%) sampled from a fixed cohort. Among studies with incident cases, 105 (84%) could interpret the odds ratio as a rate ratio. Fifty-seven (46% of 125) required the source population to be stable for such interpretation, while the remaining 48 (38% of 125) did not need any assumptions because of matching on time or concurrent sampling. Another 17 (14% of 125) studies with incident cases could interpret the odds ratio as a risk ratio, with 16 of them requiring the rare disease assumption for this interpretation. The rare disease assumption was discussed in 4 studies but was not relevant to any of them. No investigators mentioned the need for a stable population. The authors conclude that in current case-control research, a stable exposure distribution is much more frequently needed to interpret odds ratios than the rare disease assumption. At present, investigators conducting case-control studies rarely discuss what their odds ratios estimate.

case-control studies; epidemiologic methods; odds ratio

Abbreviation: STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

The case-control study is an important type of study in observational research. Given its advantages in speed and efficiency, the case-control study is often the first design choice in studies on the etiology of disease (1). The case-control design is indispensable if the disease is rare or assessment of the exposure is expensive, and in situations where results are needed quickly to inform public health policy (2).

A crucial issue in case-control studies is the approach used to identify cases and controls. A first consideration is whether cases are incident or prevalent. If cases are incident, a second consideration is whether cases and controls are from a fixed cohort or a dynamic population. In these circumstances, the meaning of the odds ratio depends on the way in which controls were selected (from the population at risk at the beginning of follow-up, from the population that was free of disease at the end of follow-up, or from the person-time at risk) and on the underlying assumptions (3–7). For example, much emphasis is often placed on the need for a disease to be rare in order for the odds ratio to estimate the risk ratio if controls are sampled at the end of the follow-up period from a fixed cohort. Depending on the nature of the cases, the type of source population, the sampling strategy, and the underlying assumptions, the odds ratio obtained in a case-control study can be interpreted as a risk ratio, rate ratio, or prevalence odds ratio, or it can remain an odds ratio without such interpretation if assumptions are not met.

We performed a survey of case-control studies recently published in leading general medicine, epidemiology, and clinical specialist journals. We examined the methods used and types of populations studied and assessed what was estimated by the odds ratio and whether the rare disease assumption or other assumptions were important in this context.

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## MATERIALS AND METHODS

### Selection of articles

We examined case-control studies published in 5 general medicine journals (*Annals of Internal Medicine, BMJ, JAMA, Lancet, New England Journal of Medicine*), 5 general epidemiology journals (*American Journal of Epidemiology, Epidemiology, International Journal of Epidemiology, Journal of Clinical Epidemiology, Journal of Epidemiology and Community Health*), and 10 clinical specialist journals (*American Journal of Respiratory and Critical Care Medicine, Archives of General Psychiatry, Arthritis and Rheumatism, Blood, Circulation, Clinical Infectious Diseases, Diabetes Care, Journal of the American Geriatrics Society, Journal of the National Cancer Institute, Pediatrics*). We identified eligible studies in a PubMed (National Library of Medicine) literature search combining the journal names with the Medical Subject Heading ''case-control studies.'' We selected 50 case-control studies from each of the 3 types of journals—10 from each general medicine and epidemiology journal and 5 from each clinical specialist journal. We started in March 2007 with the most recently indexed items and went backwards in time until we identified 150 eligible studies. Articles that were published electronically ahead of print were included. We included original articles and short reports but excluded letters and other editorial material. Articles that did not report any measure of association and case-crossover studies were also excluded. The decision to include 150 studies was based on pragmatic considerations rather than formal sample-size calculations.

### Definitions

Cases and controls can be selected from *fixed* cohorts (e.g., a birth cohort of people born in 1 calendar year) or from a *dynamic* population affected by births and deaths, immigration, and emigration (for example, the population of a city) (8). These 2 types of populations are also known as *closed* and *open* populations (7). A *stable* population denotes a population in which the composition of the population, including the exposure distribution, does not change over time. A fixed population is by definition not stable. Dynamic populations may be stable and are likely to be stable over short time periods and for certain exposures—for example, genetic factors.

Within fixed cohorts, we distinguished 3 approaches to sampling controls. First, controls can be selected from persons who remain free of disease at the *end* of follow-up. This traditional case-control sampling design is also called the *exclusive design* (6), the *cumulative design* (3, 7), or *cumulative incidence sampling* (3). Second, controls can be selected at the *beginning* of follow-up from the total study population at risk; this is also called the *inclusive design* (6), the *case-cohort study* (9), or the *case-base study* (10). Third, controls can be sampled concurrently with the cases; that is, each time a new case is diagnosed, a control is selected from the population at risk at that point in time. This means that controls are selected from the person-time at risk and controls are matched on time to the cases.

Within dynamic populations, controls are often selected from the person-time at risk; this is also called *incidence density sampling* (3, 11) or just *density sampling* (7). This can be done by matching the controls on time (e.g., a case was diagnosed on June 5, 2006, and the corresponding control was randomly selected from the population that was at risk of becoming a case on the same day) or by assessing exposure in the control and case at the same point in time (e.g., controls were assigned index dates similar to the dates of diagnosis of their cases and exposure was assessed in a specified time window, such as 6 months before the index date). Another approach to sampling controls from a dynamic population is to select controls at some point in time, either at the end, at the beginning, or during the period in which the cases are diagnosed (e.g., the cases were diagnosed between January 2003 and December 2005 and the controls were sampled from the population that was at risk of becoming a case in December 2005).

### Interpretation of odds ratios

We developed a decision tree (Figure 1) to identify what is estimated by the odds ratio calculated from case-control studies, depending on the nature of the cases, the type of source population, the strategy used to select controls, and the underlying assumptions. If the cases are incident and controls are sampled at the end of the follow-up period from a fixed cohort, the odds ratio estimates the risk ratio when the assumption of a rare disease is met (4, 6). When sampling controls at the beginning of the follow-up period in a fixed cohort, the odds ratio also estimates a risk ratio, assuming that censoring is unrelated to exposure (4) (this assumption also applies to sampling at the end of follow-up (3), but for simplicity we focus on the rare disease assumption in that sampling scheme). The odds ratio from a case-control study that sampled controls concurrently with the cases in a fixed cohort reflects the rate ratio if matching on time is taken into account in the analysis (4, 6). If the controls are sampled from a dynamic population and are matched on time (sampled either at the same time or by using an index date), the odds ratio from a matched analysis estimates the rate ratio irrespective of whether the population is stable (3, 4). Of note, the impact of ignoring the matching in the analysis tends to be small unless exposures change substantially during the study period (3). Conversely, if controls from a dynamic population are sampled at some point in time during case accrual, the source population needs to be stable in its exposure distribution in order for the odds ratio to estimate a rate ratio (11).

If cases are prevalent, the odds ratio always equals the prevalence odds ratio. Its interpretation is a rate ratio if the duration of disease does not depend on exposure status and a prevalence ratio if the disease is rare (11). We have not pursued these distinctions or assessed them in the papers: Studies based on prevalent cases were rare in our sample, and the first assumption relies on subject matter knowledge and is difficult to check.

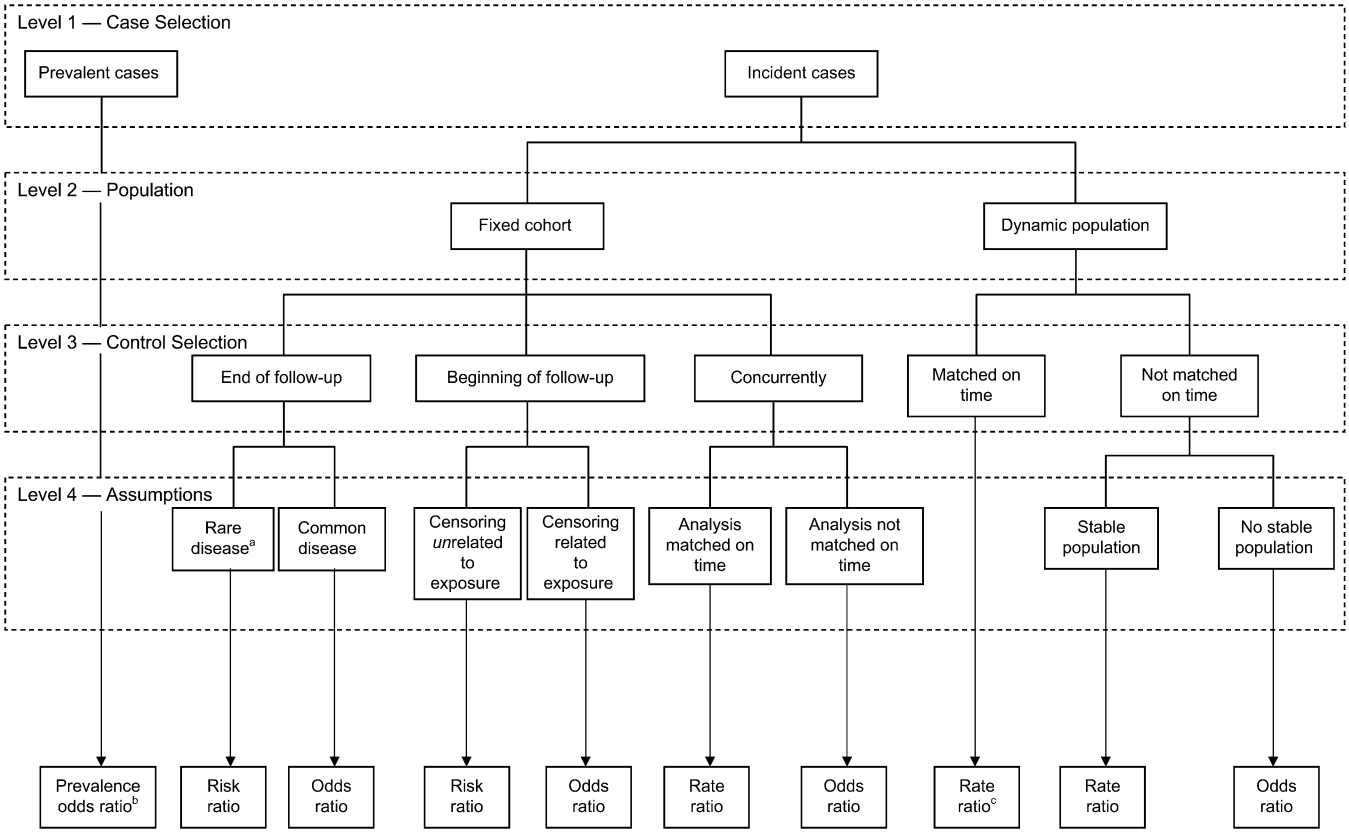


**Figure 1.** Decision tree for identifying what is being estimated by the odds ratio calculated from case-control studies, depending on the nature of the cases (prevalent or incident; level 1), the type of source population (fixed cohort or dynamic population; level 2), the sampling design used to select controls (level 3), and the underlying assumptions (level 4). [a] The assumption that censoring is unrelated to exposure is also required when sampling controls at the end of the follow-up period (see Materials and Methods). [b] The prevalence odds ratio can be interpreted as a rate ratio or a prevalence ratio, depending on assumptions (see Materials and Methods). [c] The odds ratio derived when controls are sampled from a dynamic population and matched on time can only be interpreted as a rate ratio if the analysis takes matching on time into account, although the impact of ignoring the matching tends to be small unless exposure trends are large.

### Data extraction

We used a standardized data extraction form to assess the articles. Data items extracted included general items, such as journal name, year of publication, number of cases, number of controls, main exposure, and condition studied, and also specific items about the nature of the cases (incident or prevalent), the type of source population, the sampling method, and the time period in which cases and controls were sampled. The extraction form was pilot-tested on 6 articles (2 articles from each journal type) that were not included in the study, and the form was modified where necessary. Two reviewers (M. J. K. and P. S.) independently assessed all 150 articles. If authors referred to a previous paper for a full description of the methods, information from this previous paper was used.

We defined rules on how to assess specific situations. Congenital diseases were always classified as prevalent. If incident and prevalent cases were included in 1 analysis, we classified the nature of cases as prevalent. If cases and controls were sampled from a fixed cohort and the controls were sampled among persons who had follow-up equal to or longer than that of the cases, we considered this equivalent to sampling at the end of follow-up of cases. For sampling from a dynamic population, we distinguished 2 categories of "unclear": "unclear regarding time," meaning that investigators did not explicitly state when controls were sampled in time (at the beginning, at the end, or during the period of case selection), and "unclear regarding source population," meaning that it was not clear whether the controls had been sampled from the same population as the cases.

### Survey of textbooks

After assessing the published case-control studies, we wondered how widely used textbooks described the interpretation of the odds ratio in case-control studies. We therefore examined a convenience sample of 26 English-language textbooks of epidemiology from the medical school library

in Utrecht, the Netherlands, and from our personal and institutional libraries (2, 7, 12–35).

### Data analysis

For key items, we computed the percentage of agreement between the 2 reviewers extracting data (M. J. K. and P. S.) and the kappa statistic (36). Frequencies and summary statistics for key study features were calculated for the 3 journal types. Differences between journal types were tested with Fisher's exact test in the case of proportions and the Kruskal-Wallis test for non-normally distributed continuous variables. We used the decision tree shown in Figure 1 to assess what was estimated by the odds ratio.

## RESULTS

Our search produced 4,647, 3,351, and 6,508 "hits" in the general medicine journals, the epidemiology journals, and the clinical specialist journals, respectively. On the basis of this search, we identified the 50 most recent eligible case-control studies for each journal type. The publication dates of the selected articles ranged from May 2001 to March 2007 for studies published in general medicine journals (median, November 2005), from October 2002 to March 2007 for studies published in general epidemiology journals (median, April 2006), and from August 2004 to April 2007 for studies published in clinical specialist journals (median, December 2006). Eleven (7%) of the 150 articles were short reports; 5 were published in general medicine journals, 3 in general epidemiology journals, and 3 in clinical specialist journals. References for the 150 included articles are available from the authors upon request.

The initial observed agreement between the 2 data extractors and the kappa values ranged from substantial to fair (36): For origin of cases, 76.7% agreement, $\kappa = 0.60$; for origin of controls, 83.3% agreement, $\kappa = 0.68$; for nature of cases, 80.5% agreement, $\kappa = 0.37$; for type of source population, 81.9% agreement, $\kappa = 0.60$; and for sampling design, 70.7% agreement, $\kappa = 0.54$. The low agreement for nature of the cases was due to disagreements on whether cases could be classified as prevalent cases or whether this was unclear, not due to disagreements on incident cases. Most discrepancies were resolved in discussions with the senior authors (J. P. V. and M. E.).

Table 1 shows the characteristics of the case-control studies by type of journal. The numbers of cases and controls were highest in articles published in epidemiology journals and lowest in reports from clinical specialist journals. Medications were the most commonly studied exposure in studies published in general medicine journals. Precursor disease states were most common in epidemiology and clinical specialist articles, while environmental factors were most common in epidemiology articles. Cardiovascular disease outcomes were mainly studied in general medicine journals, while cancer outcomes were common in epidemiology journals.

Table 2 presents information on the nature of the cases included in these studies and the source populations and sampling methods used to select controls. On the basis of this information, we also list the effect measure estimated by the odds ratio, conditional on assumptions. Studies based on incident cases and a dynamic source population were most common; they were particularly common among studies published in epidemiology journals. Among the 125 studies with incident cases, a rate ratio was estimable in 105 (84%). This was true without any assumption for 48 of the studies (38%) and under the assumption of a stable dynamic source population for 57 studies (46%). The stable population assumption might be more likely to be met for the studies with a shorter duration of case accrual. Accrual was 1 year or less in 9 of the 57 studies (16%), 1–≤5 years in 29 studies (51%), 5–≤10 years in 10 studies (18%), more than 10 years in 3 studies (5%), and unclear in 6 studies (11%). Of the 125 studies that sampled incident cases, a minority (18%) sampled from a fixed cohort. In 17 (14%) of the 125 studies, the estimated odds ratio reflected the risk ratio, with 16 requiring the rare disease assumption. In 12 (8%) of all 150 studies, investigators estimated a prevalence odds ratio, which can be interpreted as a rate ratio or prevalence ratio depending on assumptions not further considered here. In 16 studies (11%), it was unclear what the odds ratio estimated. Ten of these studies were published in clinical specialist journals.

Table 3 compares the interpretation of the odds ratio and the assumptions required as determined in this study with the measure(s) of association reported and the assumptions discussed by each article's authors. Almost all studies ($n = 135$; 90%) presented results as an odds ratio. In 18 of those studies, the investigators stated that the odds ratio was an approximation of the relative risk, and in 2 the investigators stated that their odds ratio was an unbiased estimate of the incidence rate ratio (see footnotes to Table 3). Investigators in 2 studies inappropriately reported a rate ratio, and in 1 study they inappropriately reported a risk ratio. In 4 studies, investigators discussed the rare disease assumption, but in none of these studies was the rare disease assumption required in order to interpret the odds ratio. In none of the studies that needed a stable population in order for the odds ratio to estimate the rate ratio did investigators discuss this assumption.

In our survey of 26 textbooks (2, 7, 12–35), we found that 8 (31%) did not mention any assumption regarding interpretation of the odds ratio in case-control studies and a further 8 (31%) mentioned only the rare disease assumption. Eight (31%) textbooks discussed the different sampling methods in fixed cohorts and dynamic populations in some detail, with another 2 vaguely referring to different modes of sampling.

## DISCUSSION

This survey of 150 published case-control studies found that in most studies, the odds ratio estimated the rate ratio; however, in a substantial proportion of these studies, the assumption of a stable population was required in order to interpret the odds ratio as a rate ratio. In contrast, the rare disease assumption was needed only in relatively few studies in order for the odds ratio to estimate the risk ratio. In

**Table 1.** Characteristics of 150 Published Case-Control Studies Included in an Evaluation of Strategies Used for Case and Control Selection and Interpretation of Reported Odds Ratios, by Type of Journal

| | General Medicine Articles ($n$ = 50) | | General Epidemiology Articles ($n$ = 50) | | Clinical Specialist Articles ($n$ = 50) | | $P$ Value[a] |
|---|---|---|---|---|---|---|---|
| | No. | % or Range | No. | % or Range | No. | % or Range | |
| Country of study participants | | | | | | | |
| United States | 17 | 34 | 15 | 30 | 18 | 36 | 0.974 |
| Europe, except United Kingdom | 11 | 22 | 14 | 28 | 13 | 26 | |
| United Kingdom | 8 | 16 | 7 | 14 | 5 | 10 | |
| Several countries (including United States, Europe, or United Kingdom) | 5 | 10 | 3 | 6 | 5 | 10 | |
| Other | 9 | 18 | 11 | 22 | 9 | 18 | |
| Median no. (and range) of cases | 494 | 26–13,556 | 611 | 42–22,225 | 282 | 18–21,169 | 0.031 |
| Median no. (and range) of controls | 846 | 27–135,386 | 1,204 | 85–180,220 | 585 | 20–423,128 | 0.032 |
| Source of cases | | | | | | | |
| Population-based | 34 | 68 | 34 | 68 | 28 | 56 | 0.526 |
| Hospital-based | 14 | 28 | 15 | 30 | 21 | 42 | |
| Both | 1 | 2 | 1 | 2 | 0 | 0 | |
| Unclear | 1 | 2 | 0 | 0 | 1 | 2 | |
| Source of controls | | | | | | | |
| Population-based | 38 | 76 | 37 | 74 | 32 | 64 | 0.521 |
| Hospital-based | 9 | 18 | 8 | 16 | 10 | 20 | |
| Both | 2 | 4 | 3 | 6 | 2 | 4 | |
| Unclear | 1 | 2 | 2 | 4 | 6 | 12 | |
| Exposure | | | | | | | |
| Medications | 20 | 40 | 5 | 10 | 6 | 12 | <0.001 |
| Precursor disease states | 3 | 6 | 11 | 22 | 11 | 22 | |
| Genetic factors | 5 | 10 | 1 | 2 | 12 | 24 | |
| Environmental factors | 0 | 0 | 10 | 20 | 4 | 8 | |
| Other[b] | 22 | 44 | 23 | 46 | 17 | 34 | |
| Outcome category | | | | | | | |
| Cardiovascular disease | 18 | 36 | 9 | 18 | 11 | 22 | 0.001 |
| Cancer | 5 | 10 | 23 | 46 | 8 | 16 | |
| Infectious disease | 12 | 24 | 4 | 8 | 12 | 24 | |
| Other[c] | 15 | 30 | 14 | 28 | 19 | 38 | |

[a] $P$ value from Fisher's exact test or the Kruskal-Wallis test.
[b] Includes 2 studies with 2 exposures (genetic factor and precursor disease state; genetic factor and other).
[c] Includes 2 studies with 2 outcome categories (cardiovascular disease and cancer for both studies).

most studies, investigators reported odds ratios, and very few interpreted them as estimates of the risk or rate ratio or discussed the assumptions that may be required in this context.

The different sampling designs used in case-control studies and their implications in terms of what is estimated by the odds ratio have been described in detail in the methodological literature (2–7, 11, 37), but we are not aware of any other survey that has examined the approaches actually used to select controls in published case-control research. A survey of epidemiologic studies identified several issues of concern regarding the design, analysis, and reporting of epidemiologic research (38), but it did not address what the odds ratios estimated in case-control studies. Several assumptions need to be considered in this context. We found that the well-known and extensively discussed rare disease assumption was needed in relatively few studies (16 of 125; 13%) for the odds ratio to estimate a risk ratio, whereas assuming that the exposure distribution was stable in the population over time was required in 57 studies (46% of 125) for the odds ratio to estimate a rate ratio. The underlying reason was that only relatively few studies sampled

**Table 2.** Distribution of 150 Published Case-Control Studies According to Type of Journal, Nature of the Cases, Type of Source Population, Sampling Method Used to Select Controls, and Interpretation of the Odds Ratio

| Nature of Cases, Type of Source Population, and Control Sampling Method | General Medicine Articles ($n$ = 50) | | General Epidemiology Articles ($n$ = 50) | | Clinical Specialist Articles ($n$ = 50) | | Total ($n$ = 150) | | Interpretation of Odds Ratio | |
|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | Effect Measure | Assumption To Be Met |
| Incident cases | 44 | 88 | 46 | 92 | 35 | 70 | 125 | 83 | | |
| Fixed cohort | 9 | 18 | 3 | 6 | 11 | 22 | 23 | 15 | | |
| Sampling at end of follow-up | 6 | | 1 | | 9 | | 16 | | Risk ratio | Rare disease |
| Sampling at beginning of follow-up | 0 | | 0 | | 1 | | 1 | | Risk ratio | Censoring unrelated to exposure |
| Sampling concurrently | 3 | | 1 | | 1 | | 5[a] | | Rate ratio | None |
| Unclear sampling | 0 | | 1 | | 0 | | 1 | | Unclear | |
| Dynamic population | 35 | 70 | 43 | 86 | 24 | 48 | 102 | 68 | | |
| Matched on time | 17 | | 17 | | 9 | | 43[b] | | Rate ratio | None |
| Not matched on time | 11 | | 8 | | 6 | | 25 | | Rate ratio | Stable population |
| Unclear regarding time | 7 | | 17 | | 8 | | 32 | | Rate ratio | Stable population |
| Unclear regarding source population | 0 | | 1 | | 1 | | 2 | | Unclear | |
| Prevalent cases | 5 | 10 | 1 | 2 | 6 | 12 | 12 | 8 | Prevalence odds ratio | None |
| Unclear nature of cases | 1 | 2 | 3 | 6 | 9 | 18 | 13 | 9 | Unclear | |

[a] Investigators in all studies used an analysis matched on time.
[b] In 32 studies, investigators used an analysis matched on time.

from fixed cohorts, while approximately two-thirds sampled from dynamic populations. Our results thus support the notion that the rare disease assumption is less important in case-control research than is generally assumed. Greenland and Thomas (3) pointed out that the bias associated with a more frequent disease becomes substantial only when the cumulative incidence over the study period is greater than approximately 10% percent, which is uncommon in practice (although other figures have been reported in this context, ranging from 5% (6) to 20% (7)). In contrast, Greenland and

**Table 3.** Distribution of 150 Published Case-Control Studies According to Interpretation of the Odds Ratio and Assumptions Required as Determined in the Current Survey Versus Measure of Association Reported and Assumptions Discussed by the Authors of the Original Studies

| Interpretation of Odds Ratio | Assumption Required | Total No. of Studies | Measure of Association Reported by Authors | | | | | | Assumption Discussed by Authors | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Odds Ratio | | Risk Ratio | Rate Ratio[a] | Relative Risk | Likelihood Ratio | Rare Disease | Stable Population | None | |
| | | | No. | % | | | | | | | No. | % |
| Rate ratio | Population stable | 57 | 56 | 98[b] | 0 | 1 | 0 | 0 | 1 | 0 | 56 | 98 |
| Rate ratio | None | 48 | 38 | 79[b,c] | 1 | 6 | 3 | 0 | 2 | 0 | 46 | 96 |
| Risk ratio | Disease rare | 16 | 13 | 81[d] | 0 | 1 | 1 | 1 | 0 | 0 | 16 | 100 |
| Risk ratio | Censoring unrelated to exposure | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 100 |
| Prevalence odds ratio | None | 12 | 12 | 100[d] | 0 | 0 | 0 | 0 | 1 | 0 | 11 | 92 |
| Unclear | Unclear | 16 | 16 | 100[d] | 0 | 0 | 0 | 0 | 0 | 0 | 16 | 100 |
| Total | | 150 | 135 | 90 | 1 | 9 | 4 | 1 | 4 | 0 | 146 | 97 |

[a] Includes incidence rate ratio and hazard ratio.
[b] In 6 studies, authors primarily reported an odds ratio but indicated that this could be interpreted as a relative risk.
[c] In 2 studies, authors primarily reported an odds ratio but indicated that this could be interpreted as a rate ratio.
[d] In 2 studies, authors primarily reported an odds ratio but indicated that this could be interpreted as a relative risk.

Thomas showed that changes in the proportion of a dynamic population that is exposed can lead to biased estimates (3). We did not check whether relevant assumptions had in fact been met for each study included in our survey—that is, that the disease was sufficiently rare, the population was stable, or censoring was unrelated to exposure. We considered this to be infeasible because too little information was reported in the articles to reliably check these assumptions.

The most widely used case-control design involves sampling of controls from a dynamic population, which often requires the assumption of a stable population for the odds ratio to estimate a rate ratio. A stable population means that the exposure distribution of the controls does not change over time in this dynamic population. For example, genetic exposures tend to be more stable in populations than lifestyle exposures. For many exposures, the shorter the period over which cases are accrued the more likely it is that the population will be stable. However, some environmental or lifestyle exposures may not be stable even over short periods of time, and matching on time is advisable in these situations. In our survey, the interpretation of the odds ratio as a rate ratio required the stable population assumption in many studies, but this was not discussed in any of the articles.

Our survey had some limitations. In 13 (9%) of the 150 studies, the nature of the cases remained unclear, and it was not possible to determine what the odds ratio estimated or whether certain assumptions were required in order to interpret the odds ratio. There may have been additional studies in this group requiring the rare disease assumption. Furthermore, initial agreement between the 2 observers who extracted data was low for the nature of the cases, although consensus was generally reached after discussion or consultation with a third reviewer. Our experience confirms the results of previous analyses, which found that reporting on important methodological aspects of the research is often wanting in epidemiologic studies (7, 38–41). For example, to decide whether cases were incident or prevalent, we often had to rely on a single word, such as ''consecutive,'' which indicates incident cases. We sometimes also needed tacit knowledge about health care systems—for example, when the databases of health maintenance organizations were used to identify cases and controls. However, we refrained from second-guessing and coded items as ''unclear'' if the information provided was clearly insufficient.

We acknowledge that some case-control studies may have been missed by our search, which was exclusively based on the term ''case-control studies.'' For example, we probably missed case-control studies that were not described as such by the authors and not indexed as case-control studies. These studies might well have differed in relevant aspects from those included in our survey. In addition, case-cohort studies may have been underrepresented in our study population, although an additional, specific search for case-cohort studies in the journals and time periods selected revealed that we may have missed only 3 such studies. We included only journals with high impact factors, and our results cannot be applied to all journals that publish results of case-control research. We selected 50 recent studies from each of the 3 groups of journals. However, the rate of publication of case-control studies differed across these groups. Compared with epidemiology journals, fewer case-control studies were published in general medicine and specialist journals, and thus case-control studies from the latter types of journals were overrepresented in our sample. This will have influenced the combined results. For example, the rare disease assumption was less often needed in studies published in epidemiology journals, so our study overestimated the relevance of this assumption. By the same token, the combined results will have underestimated the importance of assuming a stable population.

Our survey has implications for the reporting of case-control study results. The STROBE initiative (Strengthening the Reporting of Observational Studies in Epidemiology) recently published a checklist of items that should be addressed in reports of observational studies, including items that are specific to case-control studies (42, 43). Although the appropriate use and potential of the STROBE initiative is a matter of debate (44–47), we believe these recommendations can help researchers report more transparently on the nature of the cases, the source population, and the methods used to select controls. In addition, we and others (5) believe that investigators should report and discuss what measure of association is being estimated by the odds ratio calculated in their case-control study. Our survey also has important implications for teaching on case-control studies. In our sample of widely used English-language textbooks, we found that the need for the rare disease assumption tends to be emphasized in sections covering case-control studies. However, this only concerns studies that sample controls at the end of the follow-up period in fixed cohorts, and our survey of published papers shows that this situation is rare in practice. In more advanced textbooks, the sampling of controls at the beginning of the follow-up period and concurrent sampling in fixed cohorts are sometimes also covered in detail, but in actual practice these situations are even less common.

In conclusion, since the majority of case-control studies sample from a dynamic population and since most studies seem to rely on the assumption of a stable population, this type of sampling and the importance of the stability assumption should be emphasized in the teaching of epidemiology. In addition, we hope that our survey will alert investigators conducting case-control studies to the need for complete and transparent reporting of the strategies used to select cases and controls, as well as the need to discuss what measure of association is being estimated by the odds ratio.

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