

REVIEW ARTICLE

WHEN IS A CASE-CONTROL STUDY NOT A CASE-CONTROL STUDY?

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**Objective:** There is confusion in the rehabilitation literature about case-control studies because terms such as “cases” and “controls”, used to refer to the subjects in the study, are confused with the design of the study. The aim of this study was to estimate the extent to which the label “case-control study” is misused in the rehabilitation literature and in the literature of other health disciplines.

**Design:** A structured review revealed 7 rehabilitation journals, which, during the period 2000–2006, published 86 research articles in which the key word “case-control” or “case control” appeared in the title or abstract. For comparison purposes, other English language journals whose titles began with “Archives of” were also searched.

**Results:** The proportion of mislabeled case-control studies in rehabilitation journals was 97% (83 of 86 studies were mislabeled). In contrast, 34% (76 of 221) of case-control studies published in the sample of non-rehabilitation journals were found to be mislabeled. The most frequent type of rehabilitation study misclassified as case-control was a cross-sectional study (56/86) followed by intervention studies (13/86).

**Discussion:** The extent of mislabeling indicates that the case-control design is poorly understood by the rehabilitation community. This is not solely an issue of semantics; mislabeling led to misinterpretation of findings.

**Conclusion:** In rehabilitation, the research questions answered by case-control studies, regarding the etiology of health events, are rarely posed. Rehabilitation researchers must be attentive to issues of design and report correctly on design in publications.

**Key words:** methodology, case-control studies, cohort studies, cross-sectional studies, rehabilitation, research design, epidemiologic research design.

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INTRODUCTION

Research designs are tools to help the researcher arrive at the correct answer to their research question. The questions commonly asked in clinical rehabilitation lend themselves more naturally to some research designs than others. Table I provides

Table I. Taxonomy of designs to answer questions in health sciences

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*I. Longitudinal*

A. Studies of deliberate interventions

1. Sequential
  - i. Cross-over*
  - ii. Self-controlled (single subject)*
2. Parallel
3. Externally controlled

B. Studies of factors

1. Causal factors
  - i. Cohort study (prospective or historical)*
  - ii. Case-control study*
2. Natural experiments
3. Time (natural history, prognosis, incidence)

*II. Cross-sectional studies*

A. Descriptive studies of health states, diseases (*prevalence*)

B. Diagnosis, detection or classification of health states or diseases

1. Normal values
2. Disease severity

C. Processes behind health states or diseases

1. Exploratory (investigator driven experiments of mechanisms, *qualitative studies*)
2. Observational (determinants)
3. Case-reports

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Words in italics were added to apply to research questions in the rehabilitation field.  
From reference (1).

a taxonomy developed by John C. Bailar III, in which designs are classified according to the intent of the study (1).

Research in clinical rehabilitation is replete with examples of experimental and quasi-experimental designs to answer questions about the impact of deliberate interventions. Also common in rehabilitation research are cross-sectional studies to answer questions about the prevalence of health outcomes and about relationships between variables. Longitudinal studies ask questions about prognostic factors, natural history, and incidence of health outcomes. However, rehabilitation researchers rarely ask questions about etiology, which has been the main realm of epidemiologic research. Two designs are used for etiologic research: (i) cohort studies; and (ii) case-control studies. Confusion may arise because of the large number of study designs available to answer questions pertinent to rehabilitation research. Confusion may also arise because different disciplines use different terms to label the variables under study. In studies of causal factors, the variable hypothesized as being the cause of the effect can have different names (see

Table II); likewise the effect variable has different names. In this article we will adopt the epidemiologic terminology of exposure and outcome.

The classical definition of a case-control study (2) is a study in which "individuals with a particular condition or disease (the cases) are selected for comparison with a series of individuals in whom the condition or disease is absent (the controls). Cases and controls are compared with respect to existing or past attributes or exposures thought to be relevant to the development of the condition or disease under study".

Use of "cases" and "controls" to refer to the subjects in the study can be a source of confusion for study designers and readers. In clinical rehabilitation research, a common design is to compare people *with* a condition to people *without* a condition on current abilities or on development of future outcomes. Researchers often use the expressions "cases" to refer to people with health conditions and "controls" to refer to healthy people who are recruited into studies to provide comparative data. Through use of the labels "case" and "control" to refer to these two different types of study subjects, investigators may inadvertently mislabel studies that compare outcomes of healthy controls with outcomes among people with conditions, such as stroke, spinal cord injury, multiple sclerosis, or back pain, as "case-control" studies. The issue is not simply one of semantics, as such mislabeling is likely to cause confusion in conducting and analyzing the study and, consequently, in interpreting the findings.

The topic of this research paper arose out of a course assignment in a research design course for graduate students in Rehabilitation Science. A student on the 2006 course chose to review an article labeled as a "case-control study" (3). On examination, this article was not a case-control study but a prognostic longitudinal study of the impact of visual spatial neglect on outcomes of stroke rehabilitation. Labeling the persons with neglect as "cases" and the persons without neglect as "controls" likely contributed to the author mislabeling the design. Presence or absence of neglect was not the outcome of this study, as it would be in a true case-control study, but it was the exposure. The outcomes were length of stay, discharge destination, function at discharge, and change in function from admission to discharge. This study should have been classified as a longitudinal prognostic study, as the intent of the study was to identify whether neglect was a factor associated with poor functional recovery after rehabilitation. The conclusion of the study was that neglect was a prognostic factor negatively affecting outcome. In this study, the mislabeling of the design affected the study conclusions because the sample selected was not representative of all persons with neglect or without neglect, but was a selected sample meeting certain criteria for

admission to rehabilitation. Excluding persons not admitted to rehabilitation means that no inferences can be made about neglect and function in the wider population. If persons with neglect who were admitted to rehabilitation differed substantially from persons with neglect who were not admitted, it would not be possible to draw conclusions about neglect by studying such a select subgroup.

One author (NM) has encountered other studies in the rehabilitation literature that were misclassified as case-control studies. Thus, we decided to estimate the extent to which the label "case-control study" was misused in the rehabilitation literature and to contrast the proportion of misuse in the rehabilitation literature to the proportion of misuse in the literature of selected other health disciplines. The overall aim of the exercise is to educate clinical rehabilitation colleagues about the fundamental principles of this powerful epidemiologic design. This paper is one of 2 dealing with case-control studies in rehabilitation; the second paper in this issue illustrates the methodological and statistical features of case-control designs (4).

## METHODS

As the article described above (3), which incorrectly identified the study design as case-control, was published in the *Archives of Physical Medicine and Rehabilitation (APMR)*, this journal was selected as the starting point for the examination of mislabeling. We consulted the Web of Science impact factor listings and obtained a list of rehabilitation journals that were indexed in 2005. Of the 25 journals rated, 18 were excluded because they were specialty rehabilitation journals or were published in a language other than English. The remaining 7 journals were all searched. For comparison purposes with disciplines outside rehabilitation, also searched were English language journals starting with "Archives of" dealing with adult health conditions for which it is not unusual for rehabilitation professionals to be part of the healthcare team.

The database PubMed was searched directly from Reference Manager, using the key word "case-control" or "case control" in the title or abstract, as the design used by the authors would be expected to be indicated there. The search was restricted to the targeted journals, the time-frame 2000 through 2006, and research articles on human subjects. The abstracts of all articles were obtained and read by NM, who classified the studies into case-control or other. Four criteria were used to make the decision: (i) intent of study was etiological; (ii) sampling was based on outcome status; (iii) controls were sampled using standard statistical methods for sampling subgroups from larger populations; and (iv) status on etiological factors was ascertained for a time period prior to the onset of the outcome. (See the second article for more details on the design and analysis of proper case-control studies (4)). All abstracts that NM identified as potentially meeting these criteria were read by MG and a final decision reached after discussion. If a decision as to the study design could not be made from the abstract, the full article was obtained and read by both authors and a joint decision reached. The mislabeled articles from the rehabilitation literature were further scrutinized by NM to identify the most appropriate study design label. Non-interventional studies with data collected at one time-point were classified as cross-sectional, those with data collected at more than one time-point were classified as longitudinal. Studies with an intervention and where the study objective indicated an evaluative intent were classified as studies of deliberate interventions.

## RESULTS

A total of 307 articles from 16 journals were identified with "case-control" in the title or abstract. Seven abstracts (5-11)

Table II. Terminology used by different disciplines to label variables in studies of causal factors

Field of science	"Cause"	"Effect"
Epidemiological	Exposure or predictor	Outcome
Psychological	Independent	Dependent
Medical	Risk factor or determinant	Disease or event
Statistical	X variable (Explanatory)	Y variable (Response)

were selected for review by both authors and only 2 articles could not be classified based on the abstract and were reviewed by the second rater (8, 10). Table III shows that the proportion of studies mislabeled ranged from 0% to 100% for both types of journals. *Archives of Internal Medicine* had only 4 of 75 studies (5%) mislabeled; *APMR* had the highest number of studies labeled "case-control"; 68 in all, and all but one were incorrectly labeled studies (99%). The other 4 rehabilitation journals published far fewer articles labeled as case-control; 18 in all, and 16 of these (89%) were mislabeled. Impact factor did not appear to be associated in any consistent way with incorrect labeling. Table IV gives the revised classification of the designs that were labeled incorrectly as case-control in the rehabilitation literature. Because we were concerned that the design given in the abstract was not the design indicated in the body of the text, the methods section of a random selection of articles were reviewed to ascertain the design label used in the text. For the rehabilitation series, 52 articles were reviewed, but only 2 (<4%) identified a design in the body of the text and in both of these the design name matched that in the abstract. For the series of other medical/surgical journals, 56 articles were reviewed and 27 (48%) of these gave the study design in the article, which matched the design in the abstract. In the medical series of journals, the convention of naming the design in the article varied by journal, with a much higher proportion in *Archives of Internal Medicine* (18 of 20 articles had a design label) but only 25% of articles in the other journals (9/36).

#### Mislabeled cross-sectional studies

The most frequent type of study misclassified as a case-control study in the rehabilitation literature was a cross-sectional study (55/86). A cross-sectional study is one in which subjects are

selected at one point in time and attributes of the subjects are then assessed. Cross-sectional studies of health can serve 3 intents: (i) to describe the characteristics or impact of a health state or estimate prevalence; (ii) to refine methods for diagnosis, detection or classification; or (iii) to explore processes and mechanisms behind health states.

The term case-control study was used frequently to describe studies of the impact of the condition under study, and people with the specific health condition were ambiguously labeled as "cases" and, for comparison purposes, people without the condition were ambiguously labeled "controls". The intent of these studies was to quantify the differences between the groups on key variables, showing the impact of the condition, most commonly, on function. Thus, a group with the condition under study and another group without the condition were compared on variables reflecting impact measured at one point in time.

To illustrate some of the problems that arise when a study is misclassified, consider the study by Lee et al. (12) in which persons with and without lymphoma were compared on tests of functional capacity. The intent appeared to be to highlight the disabilities associated with cancer. Labeling those with lymphoma as "cases" and those without as "controls" was probably a reason for choosing the wrong label for this cross-sectional study describing physical function. This cross-sectional study did not present the sampling strategy; hence, it is impossible to know the denominator and the characteristics of the people not participating. Were non-participants doing reasonably well or very poorly? When in the course of the disease or its treatment was the testing done? Were only persons newly diagnosed with lymphoma included? Was the testing done on the day of chemotherapy or between cycles? The authors point out that the differences between the lymphoma

Table III. Proportion of studies labeled as case-control studies that were incorrectly and correctly classified according to journal type

	Impact factor*	Studies, n	Mislabeled studies, n (%)	Correctly labeled studies, n (%)
<i>Medical/surgical journals</i> †				
Archives of Gerontology and Geriatrics	0.73	3	0 (0)	3 (100)
Archives of Internal Medicine	8.02	75	4 (5)	71 (95)
Archives of Gynecology and Obstetrics	n.a.	23	10 (43)	13 (57)
Archives of Neurology	4.90	53	23 (43)	30 (57)
Archives of General Psychiatry	12.62	39	17 (44)	22 (56)
Archives of Surgery	3.05	25	19 (76)	6 (24)
Archives of Orthopaedic and Trauma Surgery	0.68	3	3 (100)	0 (0)
Sub-total		221	76 (34)	145 (66)
<i>Rehabilitation journals</i> †				
Disability and Rehabilitation	0.99	1	0 (0)	1 (100)
American Journal of Physical Medicine and Rehabilitation	1.14	6	5 (83)	1 (17)
Archives of Physical Medicine and Rehabilitation	1.73	68	67 (99)	1 (1)
Clinical Rehabilitation	1.45	7	7 (100)	0 (0)
Journal of Rehabilitation Medicine	1.80	4	4 (100)	0 (0)
Sub-total		86	83 (97)	3 (3)

\*For 2005 from Web of Science.

†Two additional medical journals, *Archives of Clinical Neuropsychology* and *Archives of Psychiatric Nursing*, and 2 additional rehabilitation journals, *Physical Therapy*, and *Journal of Rehabilitation*, were searched, but no titles/abstracts using the term case-control were identified (and therefore the journals are not listed in the table).

n.a.: not available.

Table IV. Study design designation for case-control studies in rehabilitation series of journals (n = 86)

Actual study design	n	Reference numbers
Longitudinal		
Deliberate interventions	13	17, 18, 24, 36, 38, 47–54
Prognosis	12	3, 6, 39, 46, 55–62
Cohort studies of factors	2	8, 27
Cross-sectional		
Descriptive studies of health states, diseases including prevalence studies	22	5, 7, 12–14, 16, 23, 26, 27, 63–75
Diagnosis, detection or classification of health states or diseases (studies of measurement properties)	10	15, 22, 28–35
Investigator driven experiments of mechanisms	24	19–21, 25, 76–95
Correctly labeled as case-control	3	9–11

Rehabilitation series as listed in Table III.

group and the non-lymphoma group could have been due to chemotherapy rather than lymphoma. This is a highly likely explanation. Had the authors desired to answer the question “Does lymphoma cause a decrease in motor function?” a true cohort study would have been more appropriate, selecting persons at time of diagnosis and following them over time to see fluctuations in function with respect to fluctuations in other symptoms and treatment, and, in parallel, following an age- and sex- comparable cohort of persons without lymphoma. If the authors were interested in the effects of and recovery from chemotherapy, not an uninteresting question, a repeated measures study would be appropriate. Without consideration of sampling from an underlying cohort, this study has a strong potential for selection bias.

Some authors recognized the cross-sectional nature of their study design and used the term “cross-sectional case-control study” (13, 14) as an attempt to convey this message; a better label would have been a cross-sectional study of the impact of spinal cord injury (13) or of epicondylitis (14). Other designs mislabeled as case-control used qualifiers such as: “prospective or follow-up case-control study” (15–17), “randomized case-control study” (18), “non-randomized case-control study” (19, 20), “repeated measures case-control study” (21, 22), “descriptive case-control study” (23), and “cross-sectional and longitudinal randomized case-control study” (24).

The intent of other mislabeled cross-sectional studies was to define relationships between variables in order to develop hypotheses about mechanisms underlying impairments or disease processes. For example, Lange et al. (25) studied persons in the post-acute phase of stroke with different types of lesions: 20 right hemispheric vs 15 left hemispheric and 11 cortical vs 19 subcortical. In comparing performance on tests of organizational strategy and recall, they concluded that visual memory impairments after stroke may be “caused” by a lack of organizational strategy rather than an impairment of memory. The intent of this cross-sectional study was to identify possible mechanisms underlying memory impairments in persons with stroke and a better design label would have been a cross-sectional study of mechanism. However, this study has several flaws. A prevalent sample of persons with stroke and different types of lesions was chosen. The denominator for this sample is unknown. This group was sampled at a secondary care centre and hence was missing persons who would have had similar lesions but did not go to this centre. This missing

group may have had a different pattern of performance on the memory tests. In addition, there is no historical portrait of the evolution of these memory deficits. Is it possible that some memory deficits resolved and, had testing been done earlier, there may have not been differences between groups? A cohort study is the optimal design for the research question and would have required enumerating all persons with acute stroke and following them forward in time to identify the evolution of memory deficits. A case-control study would not have been the optimal design; neither would a cross-sectional study for the reasons pointed out above.

Three studies (5, 26, 27) correctly identified persons with and without the outcome of interest as cases and controls and intended to identify etiological factors, but their study design was cross-sectional in nature and, hence, could not untangle the temporal sequence of the variables under study.

#### *Mislabeled cross-sectional diagnostic or measurement studies*

Another group of mislabeled rehabilitation studies were those designed to assess methods for the diagnosis, detection or classification of health states or diseases (15, 22, 28–35). These mislabeled “case-control” studies were cross-sectional studies as both the new test and the standard test or multiple administrations of the same test were administered at the same time on people whose status on the outcome was known at the time (prevalent sample), usually a group with the outcome and “controls”, hence perhaps the confusion. For example, Sunnerhagen et al. (34) conducted a test of inter- and intra-rater reliability of a sit-to-stand test in 19 persons with prior stroke, incorrectly labeled “cases”, and 12 “controls”.

#### *Mislabeled intervention studies*

Twenty-seven of the rehabilitation studies were longitudinal in nature with data collection over at least 2 time-points and 13 of these studies were of interventions. Table I indicates that several designs can provide information about the effects of interventions, including randomized clinical trials (RCT). Aruin (36) used a cross-over design, in which 6 persons with hemiparesis and 6 subjects without neurological damage participated in an experiment to transport an object under 3 different conditions: no support, a skateboard, and touch. All subjects improved their ability to regulate grip force using light touch, and the authors concluded that these findings may have implications for therapy. Clearly, the intent of this study was to evaluate different strategies

to improve hand function and it would have been better labeled a cross-over study. Had the authors identified their study as a cross-over design, it is likely they would have tested for carry-over effects and included a term for order which may have altered the results of the statistical testing (1, 37). It would also have potentially stimulated a power calculation.

Kurabayashi et al. (38) used an experimental design to determine if immersion in acidic mineral water vs plain water reduced the bacterial flora on the hands of persons with hemiplegia with 2 degrees of severity, incorrectly labeled "cases", in comparison to several other groups including persons with diabetes, dementia and healthy individuals, incorrectly labeled "controls". The question could have been answered by using only one sample drawn from the target population, persons with hemiplegia, and conducting the cross-over design as described. Having multiple samples, essentially introduced multiple research questions pertaining to the impact of the acidic mineral bath in each of the 5 populations and another question relating to whether the impact differed between these populations, which is a question of statistical interaction. This study would best be labeled a cross-over study in multiple populations, and the study needed to be powered to detect the interaction.

#### *Mislabeled longitudinal prognostic studies*

Twelve rehabilitation studies were reclassified as longitudinal prognostic studies. For example, the study by Cully et al. (39) found that the extent of depressive symptomatology measured at admission to rehabilitation was associated with functional ability at discharge from rehabilitation. Information on depression was obtained from the medical chart (historical data) so the study can be classified as an historical longitudinal study to identify prognostic factors for functional ability. Persons with depressive symptomatology were labeled incorrectly as "cases" and those without as "controls". This study would have been difficult to design as a case-control study as there would have to be a standardized method for determining functional ability and then turning it into a dichotomous variable. A cohort study would have been a better option, but, as the setting itself introduces a selection bias, the base population would have to be all persons with stroke divided by level of depressive symptomatology before admission to rehabilitation. In other words, it is likely that the people admitted to rehabilitation with depression were those who had other factors positively predisposing them to benefit from rehabilitation. The effect of this would be to underestimate the effect of depression on functional outcome. The authors were correct in identifying that their study could not identify whether depression was a cause of poor functional recovery, rather they concluded both are inter-related. Without enumerating a well-defined cohort, it is not possible to know how depression and recovery are related because of the exclusion of two important groups, namely depressed and non-depressed individuals not admitted to rehabilitation.

#### *Mislabeled cohort studies*

Gregory et al. (8) used an existing survey database originally assembled in 1981 to identify persons who were disability-free

at the start of the study (1981) and had developed disability by the time of follow-up in 1993 (cases,  $n=45$ ). A control group of 126 persons were disability-free at both study start and follow-up. Factors present in 1981 were studied for their impact on the development of disability. The mislabeling was somewhat understandable because 3 of the 4 criteria for a true case-control study were satisfied: etiological intent, sampling based on outcome, and exposure status ascertained prior to the outcome. The criterion that was not met was the sampling of controls. In fact, all persons in a select sub-group of the total cohort (174/3481) were studied and there was no sampling strategy at all. To be a "case", the person had to meet 2 criteria, develop a disability by 1993 and survive with this disability to 1993. In a true case-control study, anyone developing disability in the follow-up period would be a case and controls would be sampled from among those who were disability-free when the case became a case. The study by Gregory et al. (8) is closer to a cohort study, but with several limitations because of the restricted nature of the cohort studied. The associations found were with surviving and remaining in the study with a disability to 1993 rather than associations with developing disability, which was the actual intent of the study.

#### *Correctly labeled case-control studies*

Three rehabilitation studies were correctly labeled (9–11). Chen et al. (9) identified, from a consecutively assembled database of spinal cord patients with urological problems, 41 persons with urinary stones (cases) and 171 controls. Fluid intake in the 12 months preceding onset of urinary stones was the exposure of interest. Richardson & Jamieson (10) used a database of persons referred for electrodiagnosis to identify cases of mononeuropathy and unmatched controls; the exposure of interest was smoking history, which was associated with conduction velocity. Ydreborg & Ekberg (11) identified from a disability pension database for the period 1999–2000, 99 cases who were rejected for a full disability pension and 198 controls who had been granted a full disability pension. Determinants of rejection were unemployment, living in an urban environment, and age below 50 years.

## DISCUSSION

There was a high degree of mislabeling of case-control studies by rehabilitation researchers, indicating a poor understanding of this design. The observation that many of these mislabeled studies had serious problems with analysis and interpretation of findings illustrates that this mislabeling is not just an issue of semantics. The misunderstanding of fundamental principles of research design introduces a strong potential for bias. The fact that these mislabeled studies were published with the wrong label is surprising given that in one of the journals, *APMR*, the Instructions for Authors clearly and correctly outline the features of case-control studies (40).

Researchers, reviewers, and editors in rehabilitation sciences need to be more rigorous in their use of design terminology in order that our science keeps pace with research in other

fields. We suggest that editors be more vigilant in verifying the labeling of research designs.

Rehabilitation researchers also need to be more careful in labeling their study designs and should consult textbooks and articles on research design before starting a study (1, 2, 37, 41–43). Educators of rehabilitation researchers also have a responsibility to ensure their graduates are familiar with all research designs applied in the health field, including case-control studies. Although rare in rehabilitation research, there are examples of case-control studies in rehabilitation that could be used for teaching purposes (9–11, 44, 45).

### Limitations

A systematic review was not conducted; however, the review was structured. The choice of medical/surgical journals was unbiased, but not random. Data were presented for the medical/surgical journals and rehabilitation journals, but no hypotheses were posed or tested and no statistical testing was carried out. Selection of comparator journals was based on the objective of supplying an unbiased view from outside the rehabilitation field. The rehabilitation journals were chosen based on the listing from the Web of Science in 2005; we restricted the selection to general rather than specialty rehabilitation journals and those published in English. The Web of Science does not list all general publications dealing with the field of rehabilitation.

The original study designation was based only on a review of the titles and abstracts, unless there was ambiguity in the abstract. To ensure that the design identified in the abstract matched the design labeling in the text of the paper we randomly selected articles from both the rehabilitation series and the medical journal series and reviewed the methods sections. To our dismay, rehabilitation journals rarely indicated in the text what design had been used. As the abstracts were structured, a design had to be identified; this convention did not carry over into the body of the text. In contrast, almost all of the articles in *Archives of Internal Medicine* (18/20 reviewed) had a design section in the article text. The convention of having a design section in a research article has not been adopted by all journals.

The re-classification of the mislabeled studies was done by only one author (NM) based on the data collected and the research objective. There may be some error in the assignment, particularly for cross-sectional studies, as the intent of the study was not always clear. Often the focus of the research papers was on the data collected rather than on the intent of the study or the research question. As an example, consider this objective: “The first aim was to report gait characteristics of community-residing nondisabled nonagenarians and compare them with young-old subjects (age range 70–85 years).” (46). It is not clear from the objective what the authors wanted to know from the data they were going to collect; results indicated that elderly people who walked faster lived longer.

Thus, some studies could have been classified into more than one type depending on the interpretation of the research question. Rehabilitation researchers need to focus more on making sure the research question is correct and clearly reflects

what the authors wish to know. This will facilitate choosing the correct design and designing the study to get the correct answer. We also did not critique the studies that we judged were labeled correctly (9–11) and there may have been some design flaws in these studies. We restricted the search to the years 2000–2006 to reflect modern research methods.

In conclusion, in answer to the question posed in the title: When is a case-control study not a case-control study? When it is a cross-sectional study of impact, diagnostic accuracy, or mechanisms or when it is a study of deliberate interventions, prognostic factors or a cohort study. In rehabilitation, the research questions answered by case-control studies are rarely posed. Even when used appropriately, case-control studies are methodologically complex to design and analyze to ensure an unbiased answer (43).

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