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Matched case-control studies: a review of reported statistical methodology

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Daniel J Niven[1]
Luc R Berthiaume[1]
Gordon H Fick[2]
Kevin B Laupland[1]

[1]Department of Critical Care Medicine, Peter Lougheed Centre, Calgary, [2]Department of Community Health Sciences, University of Calgary, Calgary, Alberta, Canada

Background: Case-control studies are a common and efficient means of studying rare diseases or illnesses with long latency periods. Matching of cases and controls is frequently employed to control the effects of known potential confounding variables. The analysis of matched data requires specific statistical methods.

Methods: The objective of this study was to determine the proportion of published, peer-reviewed matched case-control studies that used statistical methods appropriate for matched data. Using a comprehensive set of search criteria we identified 37 matched case-control studies for detailed analysis.

Results: Among these 37 articles, only 16 studies were analyzed with proper statistical techniques (43%). Studies that were properly analyzed were more likely to have included case patients with cancer and cardiovascular disease compared to those that did not use proper statistics (10/16 or 63%, versus 5/21 or 24%, $P = 0.02$). They were also more likely to have matched multiple controls for each case (14/16 or 88%, versus 13/21 or 62%, $P = 0.08$). In addition, studies with properly analyzed data were more likely to have been published in a journal with an impact factor listed in the top 100 according to the Journal Citation Reports index (12/16 or 69%, versus 1/21 or 5%, $P \leq 0.0001$).

Conclusion: The findings of this study raise concern that the majority of matched case-control studies report results that are derived from improper statistical analyses. This may lead to errors in estimating the relationship between a disease and exposure, as well as the incorrect adaptation of emerging medical literature.

Keywords: case-control, matched, dependent data, statistics

Introduction

Case-control studies provide a quick and efficient means of studying diseases with long latency periods or with low incidence in the population.[1] Given their utility, it is not surprising that a Medline search of the English language literature with the words "case-control" in the title revealed more than 1000 articles published in 2010. Although they are convenient and common, there are several important considerations in the design of case-control studies.[1,2] One consideration is the decision to match cases to controls and the subsequent selection of statistical techniques that are appropriate for the matched data. The analysis of matched (dependent) data is different from unmatched (independent) data and is described in detail by Breslow and Day.[3] In their text on the analysis of case-control studies, they describe the use of paired *t*-tests for measured outcomes with 1:1 matching and with a symmetrical distribution, the Wilcoxon signed ranks test for measured outcomes with 1:1 matching as a non-parametric alternative,

Correspondence: Daniel J Niven
Critical Care Medicine, Peter Lougheed Centre, 3500 26th Ave NE, Calgary, Alberta, Canada, T1Y 6J4
Tel +1 403 943 5791
Fax +1 403 291 1491
Email daniel.niven@albertahealthservices.ca

model-based options such as the appropriate linear regression to handle modification and additional potential confounding, and matched sets other than 1:1 matching. For dichotomous outcomes, they describe McNemar's test, a Mantel–Haenszel matched-pairs analysis, and additional methods to handle matched sets other than 1:1 matching. They also describe conditional logistic regression to handle all forms of matching as well as the consideration of modification and other potential confounding.[3]

We recently published a study wherein matching was employed to control for known potential confounding variables.[4] During the analysis, we noticed that many of the peer-reviewed publications that describe the use of matched data, employ inconsistent statistical methods of analysis. Data analyses that employ incorrect statistical methods will commonly result in inappropriate conclusions. Therefore, the current study was designed to evaluate the statistical methodology in a collection of matched case-control studies.

Methods

A literature review was conducted using PubMed from January 1, 2010 to December 1, 2010 with the goal of identifying articles that employed a matched case-control design. The search-term was "case-control" (found in the article title only) and the search was limited to human studies published in the English language literature in PubMed's defined subset of "core clinical journals" (see Appendix 1 for a list of these core clinical journals). This search strategy was chosen to yield a representative sample of case-control studies in a variety of subject areas, published in peer-reviewed, mainstream journals. One of the authors screened all the abstracts for relevance and appropriate full-length articles were subsequently retrieved for appraisal. To maintain relative homogeneity among the final collection of articles, it was decided, a priori, to exclude articles that focused on subjects in the pediatric age group (under 18 years of age). We also excluded studies that used matching methods other than simple, individual criteria-based matching, ie, frequency-matching, and propensity-matching, as this type of data is analyzed with different statistical methods.[5]

Each full length article was independently reviewed in detail by two of the authors. The goal of this review was to evaluate the appropriateness of the statistical methodology. Disagreements between the reviewers were resolved by the independent evaluation of a senior biostatistician. Inter-observer agreement was quantified using the kappa statistic, wherein a kappa value of 0.61 to 1.0 indicates substantial agreement.[6] Statistical methods were appropriate for matched data if they were consistent with those described by Breslow and Day.[3] Each article was appraised using the following analysis scoring system: (1) continuous outcomes analyzed using the paired *t*-test, or Wilcoxon signed ranks test, or others, as described above and dichotomous outcomes analyzed using McNemar's test, a Mantel–Haenszel matched-pairs analysis, conditional logistic regression, or other, as described above; (2) investigators failed to analyze continuous outcomes with a paired *t*-test or the Wilcoxon signed ranks test, or did not use McNemar's test, a Mantel–Haenszel matched-pairs analysis, or conditional logistic regression for dichotomous outcomes; and (3) the authors did not use any of the aforementioned statistical methods for continuous and dichotomous outcomes.

Following the review of their statistical methodology, the collection of matched case-control articles were reviewed a second time for factors that may be associated with the use of statistical methods appropriate for matched data. These factors included items that form common issues in the design of matched case-control studies, namely the case population definition, the number of matching variables, and the control-to-case ratio. In addition, we used the 2010 Journal Citation Reports (JCR) index to determine whether the appropriateness of the statistical methodology was associated with the impact factor of the publishing journal. Using the JCR index, we determined that an impact factor of at least 12.245 was required for a journal to be listed in the top 100 major journals. Data was analyzed using Stata (v11.0; Stata Corp, College Station, TX) and statistical significance was set at $P \leq 0.05$.

Results

The initial search strategy yielded 74 articles (Figure 1). Upon review of these abstracts, 36 articles were excluded for reasons outlined in Figure 1. The remaining 38 articles were reviewed in detail.[7–44] After reviewing the articles, two of the authors identified one study that employed frequency-matching rather than individual patient-matching.[21] Exclusion of this study from further statistical evaluation left 37 studies for the overall analysis. Table 1 provides a summary of these 37 studies. The two authors reviewing the studies agreed on the appropriateness of the statistical methods in 36 of the 37 studies (97%) and the inter-observer agreement, as measured by the kappa statistic, was 0.94. Sixteen of the selected studies were analyzed with correct statistical methods (analysis score of 1, 43%), and 21 were analyzed with at least one incorrect statistical method (sum of analysis score 2 and 3, 57%).

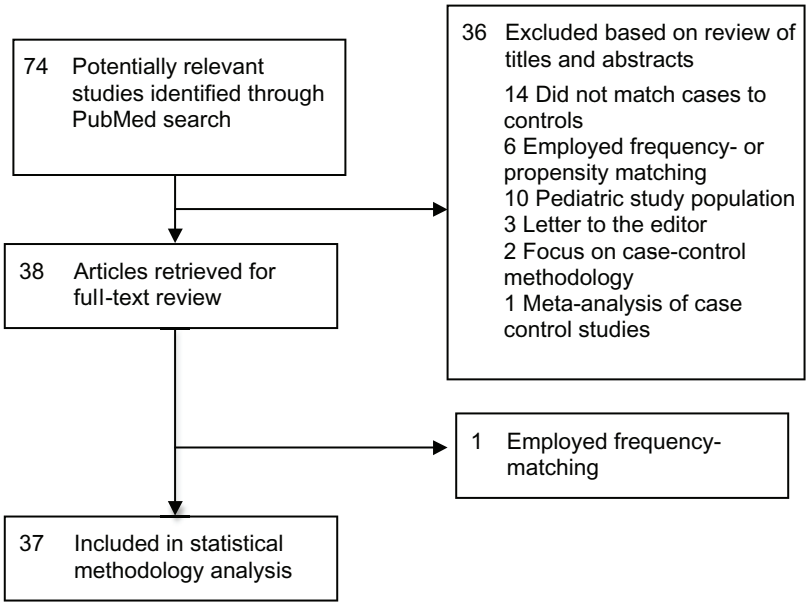

Figure 1 Search strategy flow.

Given the low number of studies with correctly analyzed data, each of the 37 articles was reviewed for factors that may be associated with the use of correct statistical tests (Table 2). Studies that were properly analyzed were more likely to have included case patients with cancer and cardiovascular disease compared to those that did not use proper statistics (10/16 or 63%, versus 5/21 or 24%, $P = 0.02$). Furthermore, properly analyzed studies were more likely to have matched multiple controls for each case (14/16 or 88%, versus 13/21 or 62%, $P = 0.1$).

Table 3 presents the data on each publishing journal's impact factor, in addition to the association between the previously described study design characteristics and correct statistical methodology. From this table, it is clear that matched case-control articles published in the *British Medical Journal* (BMJ) were consistently analyzed with correct statistical techniques. Furthermore, the BMJ was responsible for publishing the greatest number of articles in this series of matched case-control studies (7/37 or 19%). This is in contrast to articles published in *Archives of Otolaryngology-Head and Neck Surgery, Journal of Clinical Endocrinology and Metabolism,* and *Neurology* wherein the data was frequently analyzed incorrectly. Moreover, matched case-control studies published in *Lancet* were notably inconsistent in their statistical methodology. From this table, it is also evident that more studies in the correctly analyzed collection were published in a journal with an impact factor within the top 100 listing on JCR (11/16 or 69%, versus 1/21 or 5%, $P \leq 0.0001$). The median (interquartile range [IQR]) impact factor among studies that were correctly analyzed was 13.471 (8.516–13.950), compared to 6.495 (4.231–8.017) for those with incorrect statistical methodology (Wilcoxon rank sum test, $P = 0.0009$).

Discussion

To our knowledge, this is the first study to assess the appropriateness of the statistical methodology used in a published series of matched case-control studies. From this structured review of studies published in a number of diverse mainstream, peer-reviewed journals it is clear that matched case-control studies are not consistently analyzed using appropriate statistical methods. More than 50% of the articles reviewed in this study present data that was analyzed with improper statistics. For many of these studies, this may simply change the strength of the association between the disease and exposure of interest; however, for studies with small numbers of discordant sets, the use of appropriate statistical methods may alter the significance of the findings. Unfortunately, none of the articles reviewed in this study with incorrect statistical methodology provided the data in a format whereby the magnitude of the difference between a proper and improper analysis could be assessed. This is important, as it is clear from recent reviews of the literature that the use of statistics in medical literature is increasing over time.[45,46] However, if the analyses are being performed incorrectly, this increased use of statistics does not equate to an improvement in study quality and may lead to the adoption of incorrect medical literature.

Table 1 Details of studies included in statistical methodology analysis

Study	Case population	Cases (n)	Controls (n)	Matching variables	Analysis score[a]
Ances et al[7]	Patients with human immunodeficiency virus (HIV)	10	20	Gender, education	3
Antonelli et al[8]	Patients with systemic lupus erythematosus	153	918	Gender, age	3
Carnaby-Mann et al[9]	Patients with dysphagia who entered the McNeill Dysphagia Therapy Program	8	16	Age, gender, primary medical diagnosis	2
Dubois et al[10]	Patients with previous thoracic radiation therapy undergoing coronary stenting	41	82	Gender, stented vessel, drug-eluting stent use, available duration of follow-up, unstable coronary disease, renal insufficiency, diabetes mellitus, bifurcation disease, stent length and size, ejection fraction	1[b]
Etminan et al[11]	Patients who had a coronary revascularization procedure between 1995–2004 with a discharge diagnosis of epilepsy	217	2170	Age, cohort entry day	1
Friedland et al[12]	Patients with cochlear implants	28	28	Pre-cochlear implant score on Hearing In Noise Test–Quiet, duration of deafness	3
Garg et al[13]	Patients 18–65 years old with migraine headaches onset before age 50	144	144	Age, gender	1
Green et al[14]	Patients $\geq$ 40 years old with incident esophageal, gastric, or colorectal cancer	15 613	77 750	Age, gender, general practice, observation time	1
Jenab et al[15]	Patients with incident colorectal cancer	1248	1248	Age, gender, study center, time of day at blood collection, duration of fasting at blood collection; women were further matched by menopausal status, phase of menstrual cycle at time of blood collection, use of hormone replacement therapy	1
Kermani et al[16]	Incident cases with giant cell arteritis	204	407	Age, gender, length of medical history	3
Koscieiny et al[17]	Patients with claudication or critical ischemia undergoing surgery for occlusion of the superficial femoral artery (SFA)	28	28	Occluded SFA, patent popliteal artery not amenable to endovascular intervention, patent profunda femoris artery with less than 50% stenosis before the first branch, $\geq$1 patent crural outflow artery, American Society of Anesthesiologists Class I, II, or III, patient mobile before surgery, or expected to have postoperative mobility, on aspirin and a statin	3
Lang et al[18]	Patients with HIV found to have an incident myocardial infarction	289	884	Age, gender, clinical center	2[c]
Marshall et al[19]	Patients with HIV and Kaposi's sarcoma	21	14	Unclear	3
Martinez et al[20]	Patients with sudden cardiac death, or near death on antidepressants	568	14 812	Date of incident antidepressant prescription, year of birth, gender, indication for antidepressant prescription	1
Nickel et al[22]	Females with interstitial cystitis/painful bladder syndrome	207	117	Age, partner status, education	3
O'donnell et al[23]	Patients with first acute stroke	3000	3000	Age, gender, $\pm$ ethnic origin	3[d]
Parker et al[24]	Patients with incident venous thromboembolism	25, 532	89, 491	Age, calendar time, gender, family practice	1
Persoon et al[25]	Patients with limb shaking associated with internal carotid artery occlusion	34	68	Age, gender	3
Pouwels et al[26]	Patients with incident admission for a hip fracture	6,763	26,341	Year of birth, gender, geographic location, index admission date	1
Renoux et al[27]	Patients with incident diagnosis of stroke and on hormone replacement therapy	15,710	59,958	Age, general practice attended, year of joining the practice	1
Ripatti et al[28]	Patients with coronary artery disease	2,101	3,914	Gender, birth year	1[e]

Roder et al[29]	Patients with total hip arthroplasty and signs of cup failure	809	3,986	Hospital site of total hip arthroplasty, date of surgery; a follow-up exam within 6 months of the follow-up interval of the case; cup design, size, and material	1
Schaer et al[30]	Patients with atrial fibrillation	4661	18 642	Age, gender, general practice, calendar time	1
Schillaci et al[31]	Patients aged 18–50 years with migraine headaches	60	60	Age, gender, blood pressure	2
Siriwardena et al[32]	Patients with incident myocardial infarction	16, 012	62, 694	Age, gender, general practice, calendar time	1
Talving et al[33]	Patients with severe traumatic brain injury receiving erythropoiesis stimulating agent	89	178	Age, gender, mechanism, Glasgow Coma Scale, hypotension, injury severity score, abbreviated injury scale, presence of anemia	3
Tammemagi et al[34]	Never smokers or former smokers with adult-onset chronic rhinosinusitis	306	306	Age, gender, race/ethnicity	2
Taran et al[35]	Women with a diagnosis of cellular meiomyomas	99	198	Surgeon, surgical procedure, year of surgery	2
Telem et al[36]	Patients with anastamotic leak following colorectal surgery	90	180	Procedure, surgeon	3
Trifiro et al[37]	Elderly patients receiving an anti-psychotic drug prescription with an incident episode of community-acquired pneumonia	258	1689	Year of birth, gender, index date	1
Vickers et al[38]	Patients with prostate cancer	126	373	Date of birth, date of baseline blood tests	1
Vlaar et al[39]	Patients with transfusion-associated lung injury admitted to an intensive care unit	109	327[f]	Age, gender, admission diagnosis	3
Warensjö et al[40]	Consecutive patients with incident myocardial infarction	444	556	Gender, age, date of health survey, and geographic region	2
Wassenaar et al[41]	Patients with acromegaly undergoing screening colonoscopy	107	214	Age, gender	3
White et al[42]	Patients who discontinued zonisamide due to psychiatric or cognitive adverse events	59	118	Zonisamide initiation date	2
Wohl et al[43]	Patients older than 20 years of age with a diagnosis of pemphigus	255	509	Age, gender	3
Yates and James[44]	Physicians with a finding of serious professional misconduct	59	236	Year of graduation from medical school	1

Notes: [a]See Methods section for an outline of the statistical scoring system; [b]Categorical variables assessed using the Cochran–Mantel–Haenszel test with the matched pair as a stratification variable; [c]Used univariate conditional logistic regression to perform hypothesis test on baseline continuous variables; [d]Authors mentioned deliberately analyzing the data as if it were not matched; [e]Based on analysis of the nested COROGENE matched case-control sample; [f]three separate control groups of 109 patients each.

Table 2 Study design and publication characteristics

Factor	Correct analysis[a] (n = 16)	Incorrect analysis[b] (n = 21)	P[c]
Case population, n (%)			
Cancer or cardiovascular disease[d]	10 (63)	5 (24)	0.02
HIV	0 (0)	3 (14)	0.1
Other	6 (38)	13 (62)	0.1
Basic science topic, n (%)	1 (6)	1 (5)	0.8
Medical topic, n (%)	13 (81)	15 (71)	0.5
Surgical topic, n (%)	2 (13)	5 (24)	0.4
>2 matching variables, n (%)	11 (63)	12 (57)	0.5
>1:1 control-to-case ratio, n (%)	14 (88)	13 (62)	0.1
Publishing journal in top 100 according to JCR, n (%)	11 (69)	1 (5)	<0.0001

Notes: [a]Correct statistical analysis: received a statistical analysis score of "1"; [b]Incorrect statistical analysis: received a statistical analysis score of "2" or "3"; [c]Proportions compared via Fisher's exact test; [d]cardiovascular disease was defined as any disease of the coronary vascular, peripheral vascular, cerebrovascular, and cardiac electrical system.

Abbreviations: HIV, human immunodeficiency virus; JCR, journal citation reports.

Although this study appears to be the first to evaluate the quality of the statistical methods employed in a series of matched case-control studies, it is not the first study to review the quality of statistical methods in medical journals. A number of these studies were published in the 1980's and 1990's at a time that coincided with a rapid rise in the use of statistics in medical research. They consistently found that a minority of studies reported unacceptable methods of data analysis and concluded that this is likely due to the fact that individuals leading these medical publications may not have a solid grasp on basic statistical concepts.[45,47] This may not be any different in today's medical literature and is likely further compounded by the fact that statisticians are not consistently involved in the peer review process,[48] a step that often improves the quality of the statistical methodology of accepted articles.[49] Furthermore, the advent of sophisticated statistical software has allowed the novice researcher to perform complex statistical analyses in a matter of seconds, whereas these complicated analyses were previously performed solely by statisticians as they required careful thought and complex mathematical formulae.

The study design characteristics and their relation to the proper analysis of matched data as shown in Table 2, generate a few interesting hypotheses. First, studies involving case populations with cancer or cardiovascular disease were more likely to employ statistical techniques that account for dependent data than studies involving other case definitions. The reason for this is not clear but it may be a reflection of the rigor with which these studies were designed. Second, a greater number of studies in the incorrectly analyzed collection focused on a surgical topic, compared to studies in the correctly analyzed collection. Although the reasons for this finding are unclear, one potential explanation might be that the use of inferential statistics in surgical studies is a more recent development when compared to studies focusing on other medical topics. Older surgical research involved smaller sample sizes and very few of these studies employed inferential statistics.[46] The observation that studies with multiple controls matched to each case were more likely to use statistics that were appropriate for matched data was not surprising. The decision to match more than one control per case may increase the power of case-control studies,[1] which, in turn, increases the strength of the study and reflects a thoughtful, systematic approach to the study design. This same thought was likely extended to the analysis phase and resulted in the correct application of statistical methodology.

Furthermore, the observations made with regard to the publishing journal's impact factor were also not surprising. Recent studies have shown that there is a correlation with the strength of study design (including the use of recommended statistical reporting) and journal publication characteristics including the journal's impact factor.[50,51] Lee and colleagues reviewed 243 randomly selected articles from the general internal medicine literature published between January 1, 1999 and December 31, 1999 to determine if there was a link between methodological quality and journal characteristics.[50] The authors found significant associations between quality scores and higher citation rates, higher impact factors, higher circulation, and lower manuscript acceptance rates. Similarly, Kuroki et al investigated the potential link between research methodology and statistical reporting in medical journals with a high impact factor compared to moderate-impact-factor obstetrics and gynecology journals.[51] The high-impact-factor medical journals included: *Journal of the American Medical Association*, *The Lancet*, and the *New England Journal of Medicine*; whereas the moderate-impact-factor group included *American Journal of Obstetrics and Gynecology*, *British Journal of Obstetrics and Gynecology*, and *Obstetrics and Gynecology*. The authors found that the majority of studies included in the high-impact-factor group were randomized controlled trials (35%) and had high compliance with recommended statistical reporting (84% compared to 65%, $P = 0.002$). Therefore, our finding of an increased impact factor in the correct statistical analysis group aligns with trends observed in similar studies.

Table 3 A list of the publishing journals and impact factors among the collection of articles reviewed in this study

Journal	Study(s)	Impact factor[a]
Analyzed correctly		
Journal of Bone and Joint Surgery, American Volume	Roder et al[29]	2.967
Heart	Dubois et al[10]	4.706
Journal of Clinical Endocrinology and Metabolism	Pouwels et al[26]	6.495
Neurology	Etminan et al[11]	8.017
Canadian Medical Association Journal	Siriwardena et al[32]	9.015
British Medical Journal	Green et al,[14] Jenab et al,[15] Martinez et al,[20] Parker et al,[24] Renoux et al,[27] Vickers et al,[38] Yates and James[44]	13.471
Circulation	[b]Garg et al[13]	14.429
Annals of Internal Medicine	Schaer et al,[30] Trifiro et al[37]	16.729
The Lancet	Ripatti et al[28]	33.633
Analyzed incorrectly		
Archives of Otolaryngology, Head and Neck Surgery	Friedland et al,[12] Tammemagi et al[34]	1.571
Archives of Physical Medicine and Rehabilitation	Carnaby-Mann et al[9]	2.254
American Journal of Obstetrics and Gynecology	Taran et al[35]	3.313
Journal of Urology	Nickel et al[22]	3.862
Archives of Dermatology	Wohl et al[43]	4.231
British Journal of Surgery	Koscieiny et al[17]	4.444
Archives of Surgery	Telem et al[36]	4.500
Critical Care Medicine	Vlaar et al[39]	6.254
Journal of Infectious Diseases	Marshall et al[19]	6.288
Journal of Clinical Endocrinology and Metabolism	Antonelli et al,[8] Wassenaar et al[41]	6.495
American Journal of Clinical Nutrition	Warensjö et al[40]	6.606
Annals of Surgery	Talving et al[33]	7.474
Neurology	Ances et al,[7] Schillaci et al,[31] White et al[42]	8.017
Arthritis and Rheumatism	Kermani et al[16]	8.435
Brain	Persoon et al[25]	9.230
Archives of Internal Medicine	Lang et al[18]	10.639
The Lancet	O'donnell et al[23]	33.633

Notes: [a]Impact factor as listed on Journal Citation Reports for 2010; [b]Excellent example of the analysis of matched data.

This study has a number of pertinent strengths and limitations that warrant discussion. First, this study is novel; as to our knowledge, this is the first review of the appropriateness of the statistical methodology employed in a collection of matched case-control studies. Second, the studies selected for review focused on a broad range of topics in a number of different peer-reviewed journals, so, although we reviewed only 37 studies, this sample is representative of the much larger population of available articles. Furthermore, many of these articles were published in mainstream journals read by individuals from a variety of backgrounds such as the *British Medical Journal*, the *Canadian Medical Association Journal*, and the *Lancet*. The major limitation of this study is that the methodology of the articles was not assessed with a validated scoring system. To our knowledge, such a scoring system does not exist for matched case-control studies, and other validated scoring systems were not applicable to the current study's objectives.[52] In spite of this limitation, the inter-observer agreement between the authors reviewing the studies was high. This suggests that the scoring system used in this study was applied in a consistent manner, and our conclusion regarding inconsistent use of proper statistical methods in matched case-control studies is valid. Another important limitation is the inability to determine whether the use of proper statistics would change the conclusions presented by studies that used improper statistical methods. This is due to the fact that very few case-control studies presented tables outlining the number of discordant sets. This limitation notwithstanding, it is possible that the use of proper statistical methods will at least decrease the strength of the association between the outcome and exposure variables when compared to that obtained from improper statistical methodology.

Conclusion

The majority of matched case-control studies reviewed in this investigation used improper statistical methods. Although matching cases to controls provides a means of controlling for known potential confounding variables, it is a complicated process that requires a great deal of thought in order to be effective. Improper application of this methodology can distort a study's power and possibly lead to the reporting of

incorrect disease-exposure associations. The acceptance of invalid conclusions and subsequent adaptation into medical practice may lead to the inappropriate use of resources and even worse, harm to individuals. This is why guidelines such as CONSORT (Consolidated Standards of Reporting Trials) and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) were created.[53,54] These documents contain templates that are designed to create homogeneity in the reporting of randomized clinical trials and observational studies, respectively. The results of the current study suggest that although the STROBE checklist includes recommendations for outlining the matching methodology when reporting a matched case-control study, these comprehensive epidemiologic guidelines may require an additional section that outlines the proper statistical techniques to be employed when conducting a matched case-control study.

Contributors

Kevin B Laupland conceived the research question and Daniel J Niven and Kevin B Laupland designed the study. Daniel J Niven carried out the literature search, screened all relevant abstracts, and independently evaluated each study selected for the detailed review of the reported statistical methodology. Daniel J Niven also analyzed the data, and drafted the manuscript. Luc R Berthiaume independently evaluated the statistical methodology of the included studies, and contributed to manuscript revision. Gordon H Fick is a senior biostatistician and settled discrepancies between Daniel J Niven and Luc R Berthiaume during the review of the selected studies. Kevin B Laupland contributed to manuscript revision. All authors approved the final manuscript for publication.

Ethics

As this study did not involve collecting data from patients, formal approval from the regional ethics board was not required.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Hennekens CH, Buring JE. Case-control Studies. In: Mayrent SL, editor. *Epidemiology in Medicine*. Philadelphia: Lippincott Williams & Wilkins; 1987:132–152.
2. Schulz KF, Grimes DA. Case-control studies: research in reverse. *Lancet.* 2002;359(9304):431–434.
3. Breslow NE, Day NE. *Statistical Methods in Cancer Research; Volume 1 – The Analysis of Case-Control Studies*. Lyon, France: International Agency for Research on Cancer; 1980.
4. Niven DJ, Fick GH, Kirkpatrick AW, Grant V, Laupland KB. Cost and outcomes of nosocomial bloodstream infections complicating major traumatic injury. *J Hosp Infect*. 2010;76(4):296–299.
5. Jewell NP. Matched Studies. In: *Statistics for Epidemiology*. Boca Raton, Florida: Chapman and Hall/CRC; 2009:270–298.
6. Rosner B. Hypothesis Testing: Categorical Data. In: Crockett CD, Ann, Purrington, Linda, editors. *Fundamentals of Biostatistics*, 6th ed. Belmont: Thomson Brooks/Cole; 2006:385–446.
7. Ances BM, Christensen JJ, Teshome M, et al. Cognitively unimpaired HIV-positive subjects do not have increased 11C-PiB: a case-control study. *Neurology*. 2010;75(2):111–115.
8. Antonelli A, Mosca M, Fallahi P, et al. Thyroid cancer in systemic lupus erythematosus: a case-control study. *J Clin Endocrinol Metab*. 2010;95(1):314–318.
9. Carnaby-Mann GD, Crary MA. McNeill dysphagia therapy program: a case-control study. *Archives of Physical Medicine and Rehabilitation*. 2010;91(5):743–749.
10. Dubois CL, Pappas C, Belmans A, et al. Clinical outcome of coronary stenting after thoracic radiotherapy: a case-control study. *Heart*. 2010;96(9):678–682.
11. Etminan M, Samii A, Brophy JM. Statin use and risk of epilepsy: a nested case-control study. *Neurology*. 2010;75(17):1496–1500.
12. Friedland DR, Runge-Samuelson C, Baig H, Jensen J. Case-control analysis of cochlear implant performance in elderly patients. *Arch Otolaryngol Head Neck Surg*. 2010;136(5):432–438.
13. Garg P, Servoss SJ, Wu JC, et al. Lack of association between migraine headache and patent foramen ovale: results of a case-control study. *Circulation*. 2010;121(12):1406–1412.
14. Green J, Czanner G, Reeves G, Watson J, Wise L, Beral V. Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort. *BMJ*. 2010;341:c4444.
15. Jenab M, Bueno-de-Mesquita HB, Ferrari P, et al. Association between pre-diagnostic circulating vitamin D concentration and risk of colorectal cancer in European populations:a nested case-control study. *BMJ*. 2010;340:b5500.
16. Kermani TA, Schäfer VS, Crowson CS, et al. Cancer preceding giant cell arteritis: a case-control study. *Arthritis Rheum*. 2010;62(6):1763–1769.
17. Koscielny A, Pütz U, Willinek W, Hirner A, Mommertz G. Case-control comparison of profundaplasty and femoropopliteal supragenicular bypass for peripheral arterial disease. *Br J Surg*. 2010;97(3):344–348.
18. Lang S, Mary-Krause M, Cotte L, et al. Impact of individual antiretroviral drugs on the risk of myocardial infarction in human immunodeficiency virus-infected patients: a case-control study nested within the French Hospital Database on HIV ANRS cohort CO4. *Arch Intern Med*. 2010;170(14):1228–1238.
19. Marshall V, Martró E, Labo N, et al. Kaposi sarcoma (KS)-associated herpesvirus microRNA sequence analysis and KS risk in a European AIDS-KS case control study. *J Infect Dis*. 2010;202(7):1126–1135.
20. Martinez C, Assimes TL, Mines D, Dell'aniello S, Suissa S. Use of venlafaxine compared with other antidepressants and the risk of sudden cardiac death or near death: a nested case-control study. *BMJ*. 2010;340:c249.
21. Mente A, Yusuf S, Islam S, et al. Metabolic syndrome and risk of acute myocardial infarction a case-control study of 26,903 subjects from 52 countries. *J Am Coll Cardiol*. 2010;55(21):2390–2398.
22. Nickel JC, Tripp DA, Pontari M, et al. Psychosocial phenotyping in women with interstitial cystitis/painful bladder syndrome: a case control study. *J Urol*. 2010;183(1):167–172.
23. O'Donnell MJ, Xavier D, Liu L, et al. Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): a case-control study. *Lancet*. 2010;376(9735):112–123.
24. Parker C, Coupland C, Hippisley-Cox J. Antipsychotic drugs and risk of venous thromboembolism: nested case-control study. *BMJ*. 2010;341:c4245.

25. Persoon S, Kappelle LJ, Klijn CJM. Limb-shaking transient ischaemic attacks in patients with internal carotid artery occlusion: a case-control study. *Brain*. 2010;133(3):915–922.
26. Pouwels S, Lalmohamed A, van Staa T, et al. Use of organic nitrates and the risk of hip fracture: a population-based case-control study. *J Clin Endocrinol Metab*. 2010;95(4):1924–1931.
27. Renoux C, Dell'aniello S, Garbe E, Suissa S. Transdermal and oral hormone replacement therapy and the risk of stroke: a nested case-control study. *BMJ*. 2010;340:c2519.
28. Ripatti S, Tikkanen E, Orho-Melander M, et al. A multilocus genetic risk score for coronary heart disease: case-control and prospective cohort analyses. *Lancet*. 2010;376(9750):1393–1400.
29. Röder C, Bach B, Berry DJ, Eggli S, Langenhahn R, Busato A. Obesity, age, sex, diagnosis, and fixation mode differently affect early cup failure in total hip arthroplasty: a matched case-control study of 4420 patients. *J Bone Joint Surg Am*. 2010;92(10):1954–1963.
30. Schaer BA, Schneider C, Jick SS, Conen D, Osswald S, Meier CR. Risk for incident atrial fibrillation in patients who receive antihypertensive drugs: a nested case-control study. *Ann Intern Med*. 2010; 152(2):78–84.
31. Schillaci G, Sarchielli P, Corbelli I, et al. Aortic stiffness and pulse wave reflection in young subjects with migraine: A case-control study. *Neurology*. 2010;75(11):960–966.
32. Siriwardena AN, Gwini SM, Coupland CAC. Influenza vaccination, pneumococcal vaccination and risk of acute myocardial infarction: matched case-control study. *CMAJ*. 2010;182(15):1617–1623.
33. Talving P, Lustenberger T, Kobayashi L, et al. Erythropoiesis stimulating agent administration improves survival after severe traumatic brain injury: a matched case control study. *Annals of Surgery*. 2010;251(1):1–4.
34. Tammemagi CM, Davis RM, Benninger MS, Holm AL, Krajenta R. Secondhand smoke as a potential cause of chronic rhinosinusitis: a case-control study. *Arch Otolaryngol Head Neck Surg*. 2010;136(4): 327–334.
35. Taran FA, Weaver AL, Gostout BS, Stewart EA. Understanding cellular leiomyomas: a case-control study. *Am J Obstet Gynecol*. 2010;203(2):109.e1–e6.
36. Telem DA, Chin EH, Nguyen SQ, Divino CM. Risk factors for anastomotic leak following colorectal surgery: a case-control study. *Archives of Surgery*. 2010;145(4):371–376.
37. Trifirò G, Gambassi G, Sen EF, et al. Association of community-acquired pneumonia with antipsychotic drug use in elderly patients: a nested case-control study. *Ann Intern Med*. 2010;152(7):418–425.
38. Vickers AJ, Cronin AM, Björk T, et al. Prostate specific antigen concentration at age 60 and death or metastasis from prostate cancer: case-control study. *BMJ*. 2010;341:c4521.
39. Vlaar APJ, Binnekade JM, Prins D, et al. Risk factors and outcome of transfusion-related acute lung injury in the critically ill: a nested case-control study. *Crit Care Med*. 2010;38(3):771–778.
40. Warensjö E, Jansson J-H, Cederholm T, et al. Biomarkers of milk fat and the risk of myocardial infarction in men and women: a prospective, matched case-control study. *Am J Clin Nutr*. 2010;92(1):194–202.
41. Wassenaar MJE, Cazemier M, Biermasz NR, et al. Acromegaly is associated with an increased prevalence of colonic diverticula: a case-control study. *J Clin Endocrinol Metab*. 2010;95(5):2073–2079.
42. White JR, Walczak TS, Marino SE, Beniak TE, Leppik IE, Birnbaum AK. Zonisamide discontinuation due to psychiatric and cognitive adverse events: a case-control study. *Neurology*. 2010;75(6):513–518.
43. Wohl Y, Dreiher J, Cohen AD. Pemphigus and osteoporosis: a case-control study. *Arch Dermatol*. 2010;146(10):1126–1131.
44. Yates J, James D. Risk factors at medical school for subsequent professional misconduct: multicentre retrospective case-control study. *BMJ*. 2010;340:c2040.
45. Altman DG. Statistical reviewing for medical journals. *Stat Med*. 1998;17(23):2661–2674.
46. Kurichi JE, Sonnad SS. Statistical methods in the surgical literature. *J Am Coll Surg*. 2006;202(3):476–484.
47. Wulff HR, Andersen B, Brandenhoff P, Guttler F. What do doctors know about statistics? *Stat Med*. 1987;6(1):3–10.
48. Goodman SN, Altman DG, George SL. Statistical reviewing policies of medical journals: caveat lector? *J Gen Intern Med*. 1998;13(11): 753–756.
49. Gardner MJ, Bond J. An exploratory study of statistical assessment of papers published in the British Medical Journal. *JAMA*. 1990;263(10):1355–1357.
50. Lee KP, Schotland M, Bacchetti P, Bero LA. Association of journal quality indicators with methodological quality of clinical research articles. *JAMA*. 2002;287(21):2805–2808.
51. Kuroki LM, Allsworth JE, Peipert JF. Methodology and analytic techniques used in clinical research: associations with journal impact factor. *Obstet Gynecol*. 2009;114(4):877–884.
52. Cho MK, Bero LA. Instruments for assessing the quality of drug studies published in the medical literature. *JAMA*. 1994;272(2):101–104.
53. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med*. 2010;152(11):726–732.
54. Vandenbroucke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Epidemiology*. 2007;18(6):805–835.

Appendix 1 List of "core clinical journal" subset of PubMed journals

Academic Medicine: journal of the Association of American Medical Colleges
AJR: American Journal of Roentgenology
American Family Physician
American Heart Journal
The American Journal of Cardiology
The American Journal of Clinical Nutrition
American Journal of Clinical Pathology
The American Journal of Medicine
The American Journal of Nursing
American Journal of Obstetrics and Gynecology
American Journal of Ophthalmology
American Journal of Pathology
American Journal of Physical Medicine and Rehabilitation/Association of Academic Physiatrists
The American Journal of Psychiatry
American Journal of Public Health
American Journal of Respiratory and Critical Care Medicine
American Journal of Surgery
The American Journal of the Medical Sciences
The American Journal of Tropical Medicine and Hygiene
Anaesthesia
Anesthesia and Analgesia
Anesthesiology
Annals of Emergency Medicine
Annals of Internal Medicine
The Annals of Otology, Rhinology, and Laryngology
Annals of surgery
The Annals of Thoracic Surgery
Archives of Dermatology
Archives of Disease in Childhood
Archives of Disease in Childhood, fetal and neonatal edition
Archives of Environmental and Occupational Health [continues Archives of environmental health]
Archives of General Psychiatry
Archives of Internal Medicine
Archives of Neurology
Archives of Ophthalmology
Archives of Otolaryngology, head and neck surgery
Archives of Pathology and Laboratory Medicine
Archives of Pediatrics and Adolescent Medicine
Archives of Physical Medicine and Rehabilitation
Archives of Surgery (Chicago, Ill : 1960)
Arthritis and Rheumatism
BJOG : an international journal of obstetrics and gynaecology [continues British journal of obstetrics and gynaecology]
Blood
BMJ (Clinical research ed)
Brain: a journal of neurology
The British Journal of Radiology
The British Journal of Surgery
CA: A cancer Journal for Clinicians
Cancer
Chest
Circulation
Clinical Orthopedics and Related Research
Clinical Pediatrics
Clinical Toxicology: the official journal of the American Academy of Clinical Toxicology and European Association of Poisons Centers and Clinical Toxicologists [continues Journal of toxicology. Clinical toxicology]
Clinical Pharmacology and Therapeutics
CMAJ: Canadian Medical Association Journal/Journal de l'Association Medicale Canadienne
Critical Care Medicine

(*Continued*)

Appendix 1 (*Continued*)

Current Problems in Surgery
Diabetes
Digestive Diseases and Sciences
DM: Disease-a-month
Endocrinology
Gastroenterology
Gut
Heart and Lung: the journal of critical care
Heart (British Cardiac Society)
Hospital Practice (1995) [Formed by the union of: Hospital practice (Family practice ed.); Hospital practice (Hospital ed.); and Hospital practice (Office ed). No issues published between 2001 Sep 15;36(9) and 2009 Dec;37(1)]
Hospitals and Health Networks/AHA
JAMA: Journal of the American Medical Association
The Journal of Allergy and Clinical Immunology
The Journal of Bone and Joint Surgery, American volume
The Journal of Bone and Joint Surgery, British volume
The Journal of Clinical Endocrinology and Metabolism
The Journal of Clinical Investigation
Journal of Clinical Pathology
The Journal of Family Practice
Journal of Immunology (Baltimore, Md : 1950)
The Journal of Infectious Diseases
The Journal of Laryngology and Otology
The Journal of Nervous and Mental Disease
Journal of Neurosurgery
The Journal of Nursing Administration
Journal of Oral and Maxillofacial Surgery: official journal of the American Association of Oral and Maxillofacial Surgeons
The Journal of Pediatrics
Journal of the American College of Cardiology
Journal of the American College of Surgeons
Journal of the American Dietetic Association
The Journal of Thoracic and Cardiovascular Surgery
The Journal of Trauma
The Journal of Urology
The Journals of Gerontology. Series A, Biological sciences and medical sciences
The Journals of Gerontology. Series B, Psychological sciences and social sciences
Lancet
Mayo Clinic Proceedings
The Medical Clinics of North America
The Medical Letter on Drugs and Therapeutics
Medicine
Neurology
The New England Journal of Medicine
The Nursing Clinics of North America
Nursing Outlook
Nursing Research
Obstetrics and Gynecology
The Orthopedic Clinics of North America
Pediatric Clinics of North America
Pediatrics
Physical Therapy
Plastic and Reconstructive Surgery
Postgraduate Medicine
Progress in Cardiovascular Diseases
Public Health Reports (Washington, DC : 1974)
Radiologic Clinics of North America
Radiology
Rheumatology (Oxford, England) [continues British Journal of Rheumatology]

(*Continued*)

Appendix 1 (*Continued*)

Southern Medical Journal
Surgery
The Surgical Clinics of North America
Translational Research: the journal of laboratory and clinical medicine [continues The Journal of Laboratory and Clinical Medicine]
The Urologic Clinics of North America