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Study Designs and Potential Biases in Sports Injury Research

The Case-Control Study

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Summary

Several different epidemiological study designs can be used for aetiological investigations of potential risk factors for the occurrence of sports injuries. The case-control study is an example of a retrospective design in which the investigator starts with the classification of injury status (case or control) and obtains information regarding prior exposure to risk factors. Several decisions need to be made when designing case-control studies. Firstly, the source of the study participants needs to be considered. Cases and controls need to be identified from the same source, i.e. same sport or clinic. Secondly, the same eligibility criteria need to be applied to potential cases and controls. Thirdly, when an injury occurred

must be established. The fourth issue concerns the status of cases (incident or prevalent cases). Finally, the number and size of the control groups needs to be determined.

Strengths of the case-control study design are the high level of information obtained, the relatively low cost and its usefulness for studying rare sports injuries. The higher susceptibility to bias is one of the limitations of case-control studies. Bias in a case-control study can lead to over or underestimation of the true association between an alleged risk factor and the occurrence of sports injuries. Three types of bias have been distinguished: (i) selection bias; (ii) information bias; and (iii) confounding. Furthermore, the applicability of this type of design is limited to risk factors that remain relatively stable after the occurrence of an injury. The effect of changeable risk factors, such as quadriceps strength and range of motion, is difficult to assess since in many cases data at the time of injury are unavailable.

Sports injuries do not occur randomly. It is hypothesised that certain factors predispose individual sports participants to sustain injuries.[1,2] In sports injury epidemiology, information on groups of players is used to determine which factors predispose players to the occurrence of their injuries. Epidemiological research regarding predisposing factors for sports injuries has received little attention in the literature.[3] Most of the studies are descriptive and have focused on the frequency and rate of injury in various sports. The most frequently used study design in sports injury research is the case series.[4] By using this study design, data about demographic variables and factors potentially associated with injury occurrence (risk factors) are collected only on those who sustained sports injuries. This study design cannot be used to determine the association between risk factors and the occurrence of specific types of injuries since information on the uninjured population is unavailable.[3]

Several different epidemiological study designs can be used for the aetiological investigation of potential risk factors for sports injuries. Epidemiologists can classify the design of studies according to the observation and control of the study factor under investigation to either experimental or observational studies.[5]

In experimental studies, risk factors are controlled by the investigators, ideally, by randomising 2 or more groups according to the value of the study factor. These studies are conducted prospectively. The effect of an intervention aimed at reducing the incidence of injuries can be measured by using this design. Ekstrand and Gilquist[6] used this type of study design to determine the effect of a prophylactic programme (e.g. equipment change, ankle taping, controlled rehabilitation, information about rules) on the incidence of soccer injuries. 12 teams were randomly allocated to either the experimental group, which received the prophylactic programme, or the control group. Theoretically, randomisation distributes factors, potentially influencing the results, equally among both groups thereby eliminating their effect.

In observational studies, the investigator observes the presence or absence of the study factor and outcome without controlling the factor. Since the investigators do not manipulate the study factor, observational studies are easier to conduct. As a result, they are the most frequently used type of study design in epidemiology.[5]

Several different observational study designs can be distinguished according to the direction of the temporal relationship between the observation of the study factor and injury occurrence, such as cohort, cross-sectional and case-control studies.[7] In a cohort study data are collected prospectively. The investigator starts with a group of players with exposure to a certain risk factor and another group without such exposure. Both groups are then followed for a predetermined length of time during which the players either become injured, sustain no

injury or are removed from the population at risk. This type of forward study design was used by Lysens,[8] who examined physical education students at the beginning of the academic year. The objective of the study was to investigate the predictability of sports injuries by risk factors such as age, physical fitness, and muscle tightness. The students were followed to determine the occurrence of injuries during a period of 4 years.

In a nondirectional design, such as a cross-sectional study, the investigator collects information regarding study factors and injury occurrences at one point in time. This type of study design was used by Marti[9] in a study on the risks associated with regular running in young and middle-aged women. Ten days before the start of the road race, a questionnaire was mailed to the participants. In this self-administered questionnaire, the runners were asked about injuries during the previous 12 months, and potential aetiological factors such as characteristics of running shoes and usual running terrain.

A third type of observational study design is the case-control study. This design is one in which the investigator starts with the classification of injury status and obtains information regarding prior exposure to risk factors after the injury was sustained. This type of design was used by Johnson et al.,[10] who obtained information from injured skiers who were examined at an injury clinic. A population of uninjured skiers was requested to provide the same information. Despite its great potential, the case-control study has been the least frequently used design to study the association between risk factors and sports injury occurrence.[4] In a sample from 4 journals published in 1988, only 7% of all original research articles with an epidemiological approach used the case-control study design.

The objective of this review is to determine the applicability of the case-control design to the study of sports injury occurrence. This design will be described in detail in conjunction with its strengths and limitations.

1. Definition and Description

The case-control study, also known as a retrospective study, compares a group of cases (injured players) with 1 or more control groups with respect to 1 or more previous exposures (fig. 1). Usually cases enter the study as they are diagnosed. Controls enter the study as they are identified from non-cases, which is dictated by the study design. Case-control studies are the most frequently used type of analytical design for studying diseases.[11] This may be due to the relatively low cost, timeliness of results and prevalence of disease.

The objective of a case-control study is to provide a valid, and reasonably precise, estimate of the strength of at least 1 hypothesised cause-effect relationship.[12] To achieve this objective, several issues need to be considered regarding the design and conduct of a case-control study.

1.1 Statistical Analysis

A measure of association between a risk factor and the occurrence of sports injuries to be used in case-control studies is the odds ratio (OR). Table I symbolically represents the number of cases and controls with and without exposure to the risk factor under consideration, and is based on fig. 1.

The estimated OR is given by: $a \times d/(b \times c)$, which is the ratio of the odds of disease in exposed individuals relative to unexposed individuals. This measure ranges from zero to infinity. ORs greater

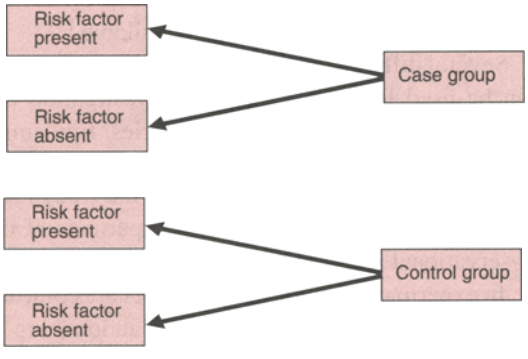

Fig. 1. The direction of data collection in case-control studies, showing the retrospective nature of such studies.

Table I. Number of cases and controls in a target population with and without exposure to a risk factor. The estimated odds ratio is given by: $a \times d/(b \times c)$; m_1, m_2, n_1, n_2 and n are used in the Mantel-Haenszel χ^2 test

Exposure	No. of cases	No. of controls	**Total**
Yes	a	b	m_1
No	c	d	m_1
Total	n_1	n_2	n

than unity denote an increased likelihood of developing injuries when exposed. If an OR of 1.6 was observed in a hypothetical study of the effect of preventive knee braces on the occurrence of medial collateral ligament (MCL) sprains, players wearing braces are 1.6 times more likely to develop this type of injury as those who did not wear braces. ORs less than unity indicate a preventive effect of exposure to the risk factor. For example, if an OR of 0.4 was found for the relationship between preventive knee braces and MCL injuries, those who wore braces are 0.4 times more likely to develop injuries compared with players who did not wear braces. An OR of unity means no increased or decreased likelihood of injury occurrence is associated with the alleged risk factor.

A 95% confidence interval (CI) for the estimated OR can be constructed that describes the sampling range for the estimated OR.[7] The 95% CI for the estimated OR equals:

$$OR_{est} \times \exp\left(\pm 1.96 \times \sqrt{\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}}\right) \quad \text{(Eq. 1)}$$

By using the Mantel-Haenszel χ^2 test, it can be determined if the hypothesis of no association between the exposure and injury occurrence can be accepted. If the data provide evidence against the null hypothesis, then this hypothesis can be rejected in favour of the alternative hypothesis.

$$\chi^2 = \frac{(n-1) \times (ad-bc)^2}{n_1 \times n_2 \times m_1 \times m_2} \quad \text{(Eq. 2)}$$

If the value for this test statistic is greater than 3.84, a statistically significant association at $p < 0.05$ (2-sided) exists between the risk factor and the occurrence of injuries.

A hypothetical association between the use of preventive knee braces and occurrence of MCL injuries is provided in table II. The estimated OR is calculated as $90 \times 145/(128 \times 189)$ and equals 0.54. This means that players who used preventive knee braces were 0.54 times more likely to sustain MCL injuries compared with players not using braces. The 95% CI is $0.54 \times 2.718^{(1.96 \times 0.03)} = (0.38, 0.76)$. Note that the value of 1 is not included in this 95% CI. The Mantel-Haenszel χ^2 value equals:

$$\chi^2 = \frac{(552-1) \times (145 \times 90 - 128 \times 189)^2}{334 \times 218 \times 273 \times 279}$$

$$= \frac{6.84 \times 10^{10}}{5.55 \times 10^9} = 12.3 \quad \text{(Eq. 3)}$$

This is statistically significant at $p < 0.05$ (2-sided). Thus, hypothetically there is a statistical association between the use of preventive knee braces and the occurrence of MCL injuries.

2. Definition of Cases

2.1 Source

Case-control studies are best suited for the study of injuries for which medical care is sought or when they can be identified by medical surveillance systems. Implementation of large scale and expensive community surveys to identify cases negates one of the principal advantages of case-control studies – their relatively low cost.

Depending on the objective of a study, cases (injured players) can be identified from a variety of sources, e.g. medical records, hospital emergency departments, athletic trainers, (private) sports medicine clinics or contacting the player directly. Potential biases (see section 4) and limitations of each method must be considered before committing the study to a particular case finding method. For example, many injured players will not be admitted

Table II. Hypothetical example of a case-control study of the association between the use of preventive knee braces (pkb) and occurrence of medial collateral ligament injuries. The estimated odds ratio is 0.54 and the 95% confidence interval is (0.38, 0.76)

Use of pkb	Cases	Controls	**Total**
Yes	145	128	**273**
No	189	90	**279**
Total	**334**	**218**	**552**

to the hospital and therefore will not be found in hospital discharge records. Those who are admitted to the hospital will most likely be more severely injured than those treated and released from emergency rooms. Injuries treated on inpatient and outpatient basis may have different risk factors associated with their occurrence. Furthermore, access to the medical system may affect the number and types of injuries seen at a medical facility, for example, people living in rural areas generally have less access to the medical system than those living in urban or suburban areas. It is likely that athletic trainers and coaches will see most of the injuries sustained by participation in organised sports. The selected case finding method and study objective are closely related and need to be treated as such.

2.2 Eligibility Criteria

Exclusion criteria for potential study participants need to be established to achieve a homogeneous group of injured players. The use of a non-homogeneous group of cases in a study will result in a distortion of the association under investigation. It is not recommended, for example, to include players with MCL and anterior cruciate ligament (ACL) injuries in the case group when studying the effect of preventive knee braces, as braces are not expected to protect the knee against ACL injuries.[13] It is easier to perceive one association at a time.

Criteria for exclusion also depend on the definition of exposure to the risk factor. Cases should have had the potential for exposure to the risk factor under consideration to be eligible to be included in the study.[7] American football players should not be included in the case group in an hypothetical study about game-related meniscus injuries if they do not have the potential for exposure under game-related conditions. That is, if they do not have any menisci.

Eligibility criteria can be applied in the selection phase or in the analysis phase of a study. An advantage of restricting the type of cases in the selection phase is that it avoids collection of unnecessary information on those players later to be found ineligible. The pre-established eligibility criteria have to be uniformly applied to all potential cases to avoid bias.

Following are 2 examples of case definitions used to define a case group. Haddon et al.[14] looked for associations between ski bindings and injuries. Cases were skiers purchasing tickets to ski on 4 consecutive weekends, who were subsequently injured while skiing and came to the resort's medical facility on the day of injury. This means that skiers have to fulfil all of the these criteria to be included in the study as part of the case group. All injured skiers regardless of gender, age and skiing experience were included in the study.

Messier and Pittala,[15] in a study of running injuries, collected data on injured runners who had been running a minimum of 10 miles/week (16km) for at least 1 year. Those individuals running less than 10 miles/week, those running less than 1 year, or both, met at least 1 of the exclusion criteria and were subsequently not included in the study.

2.3 Diagnosis and Classification of Injury

Objective criteria for determining the occurrence and classification of injuries need to be established. These criteria are to be applied to all potential cases in a uniform and standardised manner. Some of the criteria that can be used to determine if a player sustained an injury are the player's use of medical treatment,[16] time loss from participation[1] or death.[17] Different injury rates and types of injuries will be observed depending on the criteria used. As a result, potentially different risk factors will be associated with the occurrence of these injuries.

The injury classification can be determined by medical professionals such as orthopaedic surgeons and athletic trainers or by the actual individuals participating in the study. Medical professionals use standardised and valid techniques to classify individuals according to their injury status. The diagnosis of the injuries by trained medical professionals has the potential to be most scientifically valid and reliable but is also the most costly to obtain.

Self-administered questionnaires can also be used to identify cases. Criteria have to be established to determine if an injury actually occurred and the respondent subjectively determines its presence or absence. This method is inferior to the diagnosis by medical professionals but is considerably quicker and less costly. It is necessary for self-treated injuries. For example, Walter et al.[18] presented all runners with criteria for having sustained running-related injuries. An injury was defined as being severe enough to reduce the distance trained, to take medicine, or to see a health professional. Study participants were considered having sustained running-related injuries when at least 1 of the above criteria was met.

2.4 Status of Cases

As a final step in the selection of injured players, it must be decided if prevalent or incident cases are used to study the relationship between a risk factor and a particular type of sports injury. Prevalent cases include players who previously sustained a sports injury and are still injured at the time of data collection, such as during rehabilitation. Incident cases are players who are enrolled in the study as soon as they sustained injuries and are, after giving informed consent, requested to provide information about potential risk factors. The difference between prevalent and incident cases is that the latter group is contacted as soon as they become injured. The time between injury occurrence and data collection is longer when using prevalent cases.

Several issues need to be considered in the choice between incident and prevalent cases. It can be expected that incident cases will recall information more accurately than prevalent cases and likely with less bias based on the shorter time period between time of injury and data collection. Also, when using incident cases, it is more likely that a certain precipitating risk factor preceded the injury occurrence. When using prevalent cases, a risk factor can change as a result of the injury occurrence and a spurious association may be found. An example, is the relationship between level of quadriceps strength and the occurrence of MCL sprains. As a result of inactivity after sustaining the injury, the players' quadriceps strength may decrease thereby making it impossible to determine the predisposing effect of the level of quadriceps strength on injury occurrence.

With prevalent cases, the injury may be more severe compared with incident cases. Different risk factors are potentially associated with more severe injuries so prevalent cases are a select group of players not necessarily representative of all injured players.

Also, players whose injuries required them to be sidelined longer, are more likely to be selected to be in the study when using prevalent cases. For example, players with multiple injuries may have a longer recovery period. These players may have both a different risk of injury and exposure to the risk factor under consideration, thereby introducing bias.

Finally, the usual objective of an aetiological investigation is to determine risk factors for the occurrence of sports injuries and not for the prevalence of injuries. Based on the advantages of using incident over prevalent cases, it is recommended that the former type instead of the latter type of cases be used in studying risk factors for sports injury occurrence.

3. Definition of Control Groups

3.1 Source

One of the most critical parts of conducting a case-control study is the selection of 1 or more control groups. A control group is used to compare the history of exposure to risk factors with that in the case group. There are many ways of selecting a control group all with implications for the association between the alleged risk factor and injury occurrence. Theoretically, cases and controls need to be derived from the same population to reduce potential biases.[5,19] Controls should be comparable with cases in the sense that both groups should have had the potential for exposure to the risk factor during the time period under consideration.

Controls should be individuals who could have been brought to the investigator's attention had they been cases. Therefore, it is essential that cases and controls participate in the same sport.

Selection mechanisms will have selected these players to participate in a sport which may potentially be related to the injury occurrence.[20] For example, when conducting a case-control study about skiing injuries, Haddon et al.[14] interviewed injured skiers from a ski clinic. The investigators interviewed every fiftieth skier buying a ticket for consideration in the control group. This control group is appropriate since it is expected to be similar in theory to those who sustained a skiing injury in that they had the potential of sustaining an injury which would have resulted in a visit to the ski clinic.

One or more controls can be matched on correlates of exposure. Matching refers to the pairing of 1 or more controls to each case on the basis of their similarity with selected variables.[21] The difference in disease occurrence will not be the result of the variables on which the study participants are matched since cases and controls are similar with respect to these variables. If a case and matched control are subsequently both exposed or unexposed, they will not contribute to the matched analysis and information is lost. This is called overmatching, and will result in a reduction in efficiency. One example of overmatching is when the matching factor is associated with the exposure but not with the occurrence of a particular type of injury. For example, it is expected that the availability of preventive knee braces in American football is a correlate of their use during games and practices. It is not associated with the occurrence of MCL injuries. When matching on the availability of the braces, it is expected that overmatching is introduced, resulting in a loss of information and efficiency.

A control group can be selected from either uninjured players participating in the same sport or from players with different types of injury than the injury being studied. The first group is referred to as a population-based control group, while the second group is referred to as an injury-based control group. The population-based approach can select uninjured players from the same sport as the cases. An injury-based control group is a control group identified at a certain point during the players' treatment process. Examples of injury-based control groups are injured players seen by athletic trainers and patients seen at emergency departments.

Three reasons can be given for the use of injured players as controls,[22,23] including minimising of recall bias, minimisation of interviewer bias and practicality. It can be hypothesised that players who sustained the type of injury under consideration (cases) are more likely to ruminate about mechanisms resulting in their injuries than uninjured players. This means that injured players (cases) are more likely to recall exposure to different risk factors than uninjured controls, possibly resulting in recall bias. The use of information from controls with other types of injuries will enable the investigators to control for recall bias depending on the type of injuries selected to make up the control group. A second advantage of using injured players as the control group is that interviewer bias is minimised. This type of bias is possible when an interviewer is collecting different or more information from cases than controls. Bias caused by the interviewer is expected to be less when controls are made up of injured players. Thirdly, the cost of studing injured players because they are readily available, may be lower than when using uninjured players as the control group.

There are limitations with using injured players as the control group.[22] Unless the control group is made up of players with injuries unassociated with the risk factor under consideration, exposure to this risk factor does not refer to the risk of injury relative to the uninjured players. If the control group includes injuries (expected to be) associated with the study factor, the OR will be biased. The control group should consist of players with a variety of different types of injuries that are unassociated with the risk factor under consideration.

When selecting the appropriate types of injuries to be included in the control group, various questions arise.[7] Should injured controls be excluded if their diagnosis is weakly associated with

the risk factor? What about speculative associations frequently found in sports injury epidemiology? An advantage of using a population-based control group (uninjured players) is that the effect of a risk factor is compared with the uninjured population and the likelihood of becoming injured is determined. A further limitation of using an injury-based control group over a population-based control group is that the results cannot be generalised to the population as a whole since no representative sample of the uninjured players was selected.

An example of using injury-based controls is the selection of players with a variety of different types of injuries from the same clinic from which cases (players with the type of injury under investigation) were selected. This is an appropriate control group since it is expected that cases and controls are selected from the same population when no difference in referral patterns exists between cases and controls. Players with injuries which are (potentially) associated with the risk factor under consideration should be excluded from the control group to obtain an unbiased estimate of risk.

To illustrate the difference between using injured and uninjured controls, suppose a hypothetical study to determine the effectiveness of shin guards in reducing tibial fractures among college soccer players. Cases in this study may be identified by athletic trainers as they occur over the course of a season. A possible control group may consist of a sample of uninjured players participating in the same game or practice in which a tibial fracture occurred. Another control group may consist of players having sustained different types of injuries in the same season as cases occurred. An advantage of selecting uninjured soccer players from the same game or practice as players who sustained a tibial fracture is that factors potentially associated with the injury occurrence that are beyond the investigator's control and difficult to quantify, such as the intensity of the game or practice and weather conditions, are controlled. Players with different types of injuries being used as the control group will most likely not have sustained the injury in the same game or practice as the injury of interest. Generally, it is difficult to identify the most appropriate control group to determine the association between the alleged risk factor and the occurrence of a particular type of sports injury.

3.2 Eligibility Criteria

The requirement that controls be similar to cases for the past potential of injury exposure during the time period of risk under consideration implies that certain players will not be eligible for participation in the study. For example, when studying the effect of certain preventive measures on the occurrence of ACL injuries, players without this ligament will not be at risk for such injury and need to be excluded from the control group. The same exclusion criteria should be applied to cases and controls.

In a study about risk factors for downhill skiing, Bouter et al.[24] selected injured skiers (cases) from insurance files. Controls were skiers who filed an insurance claim with the same company for reasons other than injury. The controls are only eligible when they skied during the same period as cases and filed an insurance claim with the same company. The same eligibility criteria are applied to both cases and controls.

If, based on their history, players are excluded from the case group but not from the control group or vice versa, the association between the alleged risk factor and injury occurrence may be artificially decreased or increased.[25] This highlights the importance of applying eligibility criteria similarly to potential cases and controls. For example, in the study about the efficacy of preventive knee braces in American football, injured players are included as cases whether or not they sustained a previous injury. If, the control group has been restricted to players who have never sustained an MCL injury, the association of interest will be distorted based on the difference in the applicability of eligibility criteria between cases and controls when it is expected that having sustained a previous injury predisposes players to sustain a subsequent injury.

3.3 Number of Control Groups

In many cases it is difficult to determine the most appropriate control group so more than 1 control group can be used. An association will have a much greater likelihood of being accepted when different types of control groups are used all demonstrating the same findings. Reasons for using more than 1 control group, e.g. in cancer research, are to permit comparisons with studies that used controls with different types of cancer than the one under investigation, to address potential inadequacies of other control groups in the study, or to evaluate potential biases.[22] Cole[26] has recommended always using more than 1 control group. However, this may add considerably to the cost of the study. Furthermore, what if the association is not consistent across control groups? To resolve the issues surrounding the number of control groups necessary to discern a particular association, it is recommended to use more than 1 control group only if an additional group can add something unique that is important to control.[7]

3.4 Size of the Control Group

The size of the control group depends on many aspects of the study design: the estimated proportion exposed among controls (p_0), the magnitude of effect of interest (R) such as the OR, the level of statistical significance (α), and the probability of missing a real effect (β).[21] The sample size for each group is calculated by:

$$n = \frac{2pq\,(Z_\alpha + Z_\beta)^2}{(p_1 - p_0)^2} \qquad \text{(Eq. 4)}$$

where $p_1 = p_0R/[1 + p_0(R - 1)]$, $p = 0.5(p_1 + p_0)$, $q = 1 - p$, $q_1 = 1 - p_1$ and $q_0 = 1 - p_0$.

For example, if the estimated proportion of uninjured American football players wearing preventive knee braces is 0.25 (p_0), the magnitude of effect of interest is 2.0 (R), $\alpha = 0.05$, and $\beta = 0.10$, then the calculations to determine the sample size are:

$$p_1 = 0.25 \times 2.0/[1 + 0.25(2 - 1)] = 0.40 \qquad \text{(Eq. 5)}$$

$$p = 0.5(0.40 + 0.25) = 0.325, \quad q = 0.675 \qquad \text{(Eq. 6)}$$

$$n = \frac{2 \times 0.325 \times 0.675\,(1.96 + 1.28)^2}{(0.40 - 0.25)^2} = 122.7 = 123 \qquad \text{(Eq. 7)}$$

In total, 246 study participants need to be enrolled in the study not taking into account a less than perfect response rate and other factors affecting the attrition of study participants.

When the number of available controls is large and the cost of collecting information about exposure from controls is lower than for cases, the ratio of controls to cases should be greater than 1.[21] In general, the increase in statistical power (the probability of finding an effect when there is an effect) will be limited if the ratio of controls to cases exceeds 4. It is not recommended to have more than 4 controls for each case unless there is no additional cost associated with the collection of information from more controls.

4. Types and Presence of Bias

Schlesselman[21] defines bias as any systematic error in the design, conduct or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of injury. The presence of bias is evaluated by comparing an estimate of a risk factor's effect from a study with the 'true' measure of effect. The direction of bias can be away or towards the null. If bias is away from the null an association between a risk factor and the occurrence of injury was found in the study but in reality the association is weaker. The true association is overestimated by the study. In a hypothetical study, an OR of 2.0 (95% confidence interval 1.9 to 2.1) was found for the use of alcohol on the occurrence of ski injuries. If the true association is 1.4, bias is away from the null thereby overestimating the true effect of alcohol consumption. Bias can also be towards the null. This means that the observed OR by conducting the study underestimated the true association. Suppose that the true association between alcohol use and skiing injuries is 1.4. If the study found an OR of 1.1 (95% confidence interval 0.9 to 1.2), bias is towards the null.

Many different types of bias can distort the findings of a study.[27] Three different categories of

biases are identified by Kleinbaum et al.:[5] selection bias, information bias and confounding.

4.1 Selection Bias

Selection bias refers to a distortion in the OR resulting from the manner in which study participants (cases and controls) are selected into the study population.[28] Selection bias occurs if cases or controls are likely to be selected based on their exposure to the risk factor under consideration. The OR can be over or underestimated by the study depending on which of the cells in the four-fold table (table I) is overrepresented relative to the population from which they were accumulated.

Schlesselman[21] lists several types of selection bias. Characteristics associated with differing surveillance, diagnosis, referral or selection of players can all lead to ORs biased towards or away from the null. The potential association between participation of American football players on artificial and natural surfaces and the occurrence of turf-toes (metatarsophalangeal joint sprains) will be used to illustrate the presence and direction of various types of selection biases.

The true association between the type of surface (artificial or natural grass) and occurrence of metatarsophalangeal sprains is shown in table III. Players participating on artificial surface are 2.67 times more likely to sustain turf-toes as players on natural grass. Selection bias as a result of differing surveillance between cases and controls may occur if players who sustained an injury to the metatarsophalangeal joint while playing on artificial turf are more likely to be detected during data collection than the same type of injury sustained on grass. If only 85% of the injuries sustained on artificial turf and 65% of those sustained on grass are detected, the OR will have overestimated the true OR (table IV).

Table III. The true association between type of surface and the occurrence of turf-toes (metatarsophalangeal sprains)[a] in American football players

Type of surface	Cases	Controls	**Total**
Artificial	40	20	**60**
Natural grass	60	80	**140**
Total	**100**	**100**	**200**

a Odds ratio = 2.67; 95% confidence interval = (1.42, 5.03).

Table IV. Overestimation of the true odds ratio for injury to the metatarsophalangeal joint among American football players, due to the presence of selection bias as a result of differing surveillance[a]

Type of surface	Cases	Controls	**Total**
Artificial	34	20	**54**
Natural grass	39	80	**119**
Total	**73**	**100**	**173**

a Estimated odds ratio = 3.49; 95% confidence interval = (1.78, 6.83).

Another type of selection bias occurs when differential diagnostic procedures for cases and controls are used. Selection bias will distort the findings if knowledge of exposure to a risk factor alters the diagnosis between cases and controls. For example, if athletic trainers are aware that American football players sustained foot injuries on artificial turf, they may be more likely to make the diagnosis of turf-toe than when they know a player sustained the same type of injury while playing on grass. This will overestimate the true OR.

Another type of selection bias is due to differential response rates for cases and controls associated with exposure status. The direction of this bias depends on which of the response rates is higher. If, in a case-control study, cases who sustained turf-toes on artificial turf are less likely to respond to a questionnaire than cases who sustained their injuries on natural grass, the true OR will be underestimated by the study. If the latter group of cases is less likely to respond, the true OR will have been overestimated.

Avoiding selection bias is dependent upon the extent to which the researchers are aware of its occurrence. Selecting the most appropriate case and control group depends on the *a priori* knowledge about the possibility for selection bias. One way to assess the presence of selection bias is the use of more than 1 control group. If the ORs do not differ when using 2 different control groups, this suggests no selection bias. However, both ORs may have been biased to the same extent. If the ORs differ between control groups, selection bias may have played a role. Correcting selection bias in the

analysis stage of the study can be done if reliable estimates of the underlying selection or loss probabilities can be determined.[28]

4.2 Information or Measurement Bias

Information bias[5] refers to a distortion in the OR because of measurement error or misclassification of study participants on 1 or more variables. Information bias, just as selection bias, can distort the study findings towards or away from the null. A distortion in the estimated OR as a result of information bias results when measurement of either exposure to the risk factor under consideration or the injury status is systematically inaccurate. When the injury status is misclassified, players are classified as having sustained an injury while they did not and *vice versa.* It is expected that exposure status will be more likely misclassified than injury status since in most case-control studies the presence or absence of an injury is determined by medical professionals using relatively valid and reliable diagnostic procedures.

Case-control studies are also more likely to suffer from exposure misclassification than injury misclassification as a result of the retrospective nature of this type of study design. Recall bias is one type of information bias in which exposure status is misclassified. This bias only occurs when faulty or incomplete information about exposure to a risk factor depends on injury status.[29] Recall bias does not occur when faulty or incomplete information is recalled to the same degree by cases and controls. The magnitude of recall bias is expected to increase for most injuries as time between the occurrence of the injury and data collection increases.

Recall bias may occur for several reasons. One possibility is that cases and controls differ in their reply for data collection because of memory loss or confusion. For example, when studying risk factors for the occurrence of head injuries in a particular sport, cases may provide faulty information when they are interviewed shortly after their injury. When using players without head injuries as the controls group, the estimate of the risk factor under consideration may be flawed because of the presence of recall bias.

Table V shows the presence of recall bias by using an hypothetical example of metatarsophalangeal sprains and its relationship to participation on artificial surfaces. Had there been no bias in the study, the true association is 2.67 (see table III). If 90% of the players who sustained their injury on natural grass think they actually did, 46 players are classified as having sustained their injury on this surface. All players who indicated they had sustained their injury on artificial surfaces actually did. This means that the true OR is overestimated by the study and bias is said to be present.

The extent of recall bias can be assessed when actual exposure status can be verified through unbiased records. In most studies only biased records are available. When no unbiased exposure records exist, the presence of recall bias can be evaluated by constructing a validity scale.[29] This includes the researcher's identification of a number of previously evaluated exposures which have been ruled out as risk factors for the injury under consideration. When injured players stated to have been exposed to a large number of validity scale items in comparison to controls, it is likely that recall bias is present.

4.3 Confounding

A confounder is a risk factor for the injury under investigation whose control in some appropriate way will reduce or completely correct bias when estimating the true risk factor-injury relationship.[5] Confounding refers to the effect of an extraneous variable that wholly or partially accounts for the apparent effect of the risk factor under consideration,

Table V. Overestimation of the true odds ratio for occurence of metatarsophalangeal sprains among American football players, as a result of differential recall of exposure among cases and controls[a]

Type of surface	Cases	Controls	**Total**
Artificial	46	20	**66**
Natural grass	54	80	**134**
Total	**100**	**100**	**200**

a Estimated odds ratio = 3.41; 95% confidence interval = (1.82, 6.39).

or that masks an underlying true association.[5] A potential loss in efficiency or power maybe present when controlling for confounders. This may lead to an increase in the width of the confidence intervals. A confounder is an extraneous variable which satisfies 3 conditions: (i) it is a risk factor for the injury under consideration; (ii) it is associated with the risk factor under investigation; and (iii) it is not an intermediate step between the exposure and injury occurrence.

Type of session (game or practice), for example, may be a confounder for the association between the occurrence of MCL sprains and the use of preventive knee braces in American football.[30] It is generally accepted that the knee injury rate during games is substantially higher compared with training when controlling for the number and duration of both types of sessions.[31] This satisfies the first requirement of a variable being a confounder. If American football players wear preventive knee braces more often during games than during training (second requirement), then the type of session is considered a confounder for the relationship between preventive knee braces and the occurrence of knee injuries in American football. This will bias the study findings.

The criterion for establishing the presence of confounding involves the comparison of a crude with an adjusted measure of effect. A crude measure is an estimate of the OR displaying the relationship between a risk factor and injury occurrence without controlling for the effect of extraneous variables. An adjusted measure is an estimate of the same relationship but controlling for the effect of 1 or more extraneous variables. Confounding is present when the crude and adjusted measure of effect differ substantially in value.

An example is a case-control study for assessing the effect of wearing preventive knee braces on the occurrence of MCL sprains with type of session (game or practice) as potential confounder.[30] Suppose, players having worn a preventive knee brace are 0.4 times more likely to sustain MCL injuries than players who did not wear braces at the time of injury (i.e. $OR_{est} = 0.4$) without controlling for the effect of type of session on this relationship. This is an estimate of a crude measure of effect. Suppose also that the OR was found to be 0.7 when controlling for type of session. This is an estimate of the adjusted OR. In this example, the crude and adjusted ORs differ substantially and confounding is said to be present when not controlling for type of session.

Importantly, the crude and adjusted ORs must not be statistically tested to determine if they differ substantially from each other.[7] Confounding is a validity issue that concerns whether or not there is a distortion of the exposure-injury relationship after controlling for 1 or more extraneous variables. In the example concerning the relationship between MCL injuries and the use of preventive knee braces, the crude and adjusted ORs were subjectively compared with each other and not statistically tested. After the investigators decide which of the extraneous variables need to be controlled and an appropriate adjusted measure of effect has been chosen, he or she can use statistical testing to determine if the effect measure is significantly different from 1 by using various statistical tests available in multivariate analyses.

Confounding may have been present in a recently conducted case-control study of the association between range of motion (ROM) of the hip and occurrence of running-related injuries.[32] Runners were matched on age and weekly running distance. In this study it was found that the ROM of injured runners was significantly lower than ROM of the uninjured runners. These findings may be partially explained by a difference between cases and controls in other potentially running-related risk factors such as performance of warming-up or flexibility exercises.[2] Performing flexibility exercises may be related to both ROM and injury occurrence and thus be a confounder.

More than one risk factor should be studied in the multivariate approach.[33] When more than one risk factor is included in a study, more comparisons between adjusted and crude estimates of the OR need to be made. Statistical techniques that can be used to accomplish this are stratified analysis[5]

and logistic regression.[34] Stratification is a technique by which four-fold tables are created based on the value of variables the investigator wishes to control.[35] Stratification reduces or eliminates the effect of confounders by evaluating the effect of an exposure on injury occurrence within strata of the confounding variables. For example, the association between the use of preventive knee braces and the occurrence of MCL injuries can be stratified, i.e. determined separately, for games and practices. When the stratified ORs do not differ substantially from each other, an adjusted OR can be calculated based on the stratification.[36]

A limitation with using stratified analysis is that many cases and controls are necessary when several variables are considered simultaneously since information on only a few study participants makes the findings difficult to interpret. One of the advantages of logistic regression is that many more variables can be considered simultaneously in comparison with stratification. Logistic regression calculates adjusted ORs based on the effect of variables included in the aetiological model. Logistic regression is used more often to account for the complex nature of the aetiology of diseases and sports injuries.

5. Applicability to Sports Injury Research

5.1 Internal and External Risk Factors

Risk factors for injury occurrence can be classified into internal (personal) and external (environmental) factors.[1] Internal risk factors are characteristics of the player, some of which are impossible to change (such as age and gender). Other internal risk factors are player characteristics that can be changed to a certain extent, such as a player's quadriceps strength, hamstring flexibility, and overall agility. External risk factors, the counterpart to internal risk factors, are characteristics of the environment in which the player participates, such as game or practice-related circumstances. In many instances they are difficult to change. The possibility of change of internal or external risk factors after the injury occurred has implications for the utility of case-control studies.

Since case-control studies are of a retrospective nature, it is difficult to determine the unbiased effect of those changeable internal and external risk factors on the occurrence of sports injuries. Many internal risk factors for injury cannot be measured shortly after the injury was sustained. For example, when assessing the effect of dynamic quadriceps strength on the occurrence of MCL sprains, isokinetic machines have to be used to obtain the most valid estimate. Since it is unethical to measure the player's strength directly after the injury was sustained, the value of this changeable internal risk factor can only be determined during the injured players' rehabilitation process. It then becomes impossible to determine the association of interest since the strength level of the cases is unknown at the time of injury.

Van Mechelen and colleagues[32] recently studied the inability to determine the effect of a changeable internal risk factor on the occurrence of injuries. The relationship between ROM of the hip joint and running-related injuries was investigated. ROM was measured 1 year after running-related injuries were sustained by the cases. Controls were runners who did not sustain injuries and were measured at the same time as cases. It is difficult to determine the direction of the relationship between the study factor and outcome since ROM is expected to decline as the result of having sustained an injury. Thus, the difference in ROM between cases and controls may be increased at the time of data collection relative to the time of injury. This means the study may have overestimated the effect of ROM on injury occurrence.

Figure 2 shows the hypothetical decline of strength as a result of sustaining an injury. Depending on the duration of the injury, for example, the quadriceps strength will decline. The difference between the level of quadriceps strength of cases and controls at the time of data collection will be less than at the time of the injury if it could have been measured. As a result, the OR found by the study will underestimate the true OR if increased

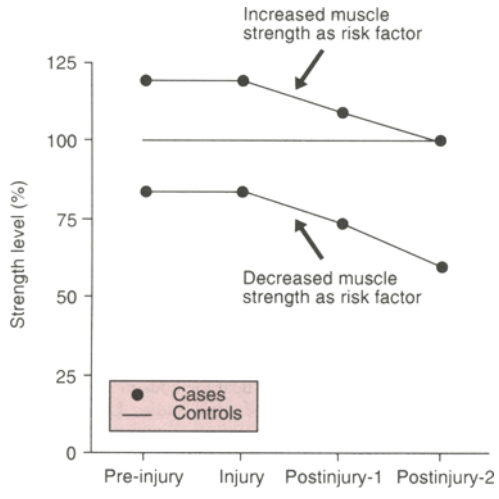

Fig. ...e of association (positive or negative) as a result of the occurence of a medical collateral ligament injury.

level of strength predisposed the players to sustain MCL injuries. If decreased level of strength was associated with increased risk of MCL injuries, the true OR will be overestimated by the study since the difference between cases and controls is increased at the time of data collection relative to the time of injury occurrence.

The magnitude of the bias of the OR depends on the time of data collection since players were injured which also depends on the severity of the injury among others. One way to overcome the potential bias in this example is to measure the quadriceps strength of the uninjured leg shortly after the injury occurrence among cases. This assumes no prior strength difference between the injured and uninjured leg of a player. Although this may be a solution in this example, other internal risk factors such as agility or flexibility cannot be measured shortly after the occurrence of the injury.

One of the ways to assess the relationship between changeable internal and external risk factors and injury occurrence is to measure them before the injury is sustained. This means that changeable risk factors of all players eligible to be enrolled in the study should be measured by using a prospective study design. This would sometimes require serial measurement to detect change in the risk factor. The collection of risk factors before the occurrence of the injuries provides stronger data for predicting injury. However, it increases the cost substantially as a result of the larger sample size.

Another way to overcome the measurement of changeable risk factors, is to use available information on risk factors collected for reasons other than research. For example, if most athletic trainers determine some measure of strength for American football players at the beginning of the season it can be used in the analysis of the study. The use of those measurements has one important limitation: the information was not collected for research purposes. This means that validity and reliability of the measurements may not be adequate for use in a study.

5.2 Acute and Overuse Injuries

The distinction between acute and overuse injuries has also implications for the applicability of case-control studies. This type of study is better suited for the study of injuries with relatively rapid onset because it is easier to discriminate between factors that caused the injury from factors that may have occurred after the injury was sustained.[11] For many overuse injuries it is unknown exactly when the onset of the injury occurred. The salient presence of an injury may have affected several changeable internal and external risk factors. Suppose the effect of hamstring flexibility on the occurrence of running-related hamstring strains was assessed by using a case-control design. In some athletes the onset of a hamstring strain is very gradual. Because of pain at the beginning of a running session, they do not perform stretching exercises as frequently as they once did, thereby reducing hamstring flexibility. As a result, the relationship between hamstring flexibility and the occurrence of hamstring strain is biased.

6. Conclusions

The case-control study is a frequently used study design in disease epidemiology. Many advantages

of using the case-control approach exist: (i) it is highly informative; (ii) the timeliness of information on risk factors; (iii) relatively low cost; and (iv) applicability for studying rare sports injuries. Case-control studies have not been used frequently to assess risk factors associated with sports injury occurrence.

Limitations of this type of design also need to be identified. When conducting a case-control study, special consideration has to be given to the occurrence of potential biases. Selection bias, information bias and confounding may all result in a mistaken estimate of association between a risk factor and injury occurrence. In addition, the case-control design is better suited for the study of acute injuries with risk factors that remain stable after their occurrence.

Future studies on the aetiology of sports injuries should use study designs that have provided valid estimates of effect of risk factors on disease occurrence. The case-control design is an example. Several advanced designs have been developed to study the aetiology of various diseases more efficiently.[37-39] More advanced statistical methods have to be utilised when applying these advanced study designs. For example, since risk factors (e.g. quadriceps strength) do not remain constant over time, statistical techniques have to be able to adapt to those changing conditions. Another essential feature of future study designs is that they must reflect the multifactorial nature of the aetiology of sports injuries. No single factor produces the occurrence of injuries. By not controlling for the effect of other variables (i.e. confounders), a mistaken estimate of effect may result.

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