Generally in the design of case-control studies, the investigator chooses samples from potential cases and controls. The null hypothesis refers to the prevalence of etiologic exposure in these groups. Cases and controls should be as similar as possible, except for factors relating to exposure. The controls should be free from the disease under study. Case-control study is an alternative to the cohort study in terms of resources. The distinction between both studies lies in the sampling procedure in the sense that in a cohort study a sample of people free from the disease under study, representing different categories of the risk factor (potential or known) under study, and follows them up to learn the development of the disease. While in a case-control study, one selects subjects on the basis of presence or absence of the disease at issue and determines their histories regarding the risk factor. In other words, so goes the thinking, in a cohort study the investigative movement is "from cause to effect" and in case-control study "from effect to cause" (1).

In many case-control studies, cases have been chosen from patients treated at a central health facility, such as a hospital. The selection of control group for a case-control study is probably the most important and most difficult decision confronting the investigator. In general controls may be selected either from hospitals or from the community. From hospitals, the controls have come from such diverse sources as autopsy protocols, cancer registries, hospital diagnostic list, hospital services groups, hospital admission rosters, other hospitalized patients or physicians who attended the cases. From the community, or population controls, the controls have come from community neighbours of the cases, retirement communities, friends of the cases, their siblings or the community residents who answered household interview request or random digit-dialled

Berta Kedoteran Mayarakat 1186
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telephone calls. The diversity of these choices suggest either that no specific standards have been established for the decision (2).

The advantages and disadvantages of each source are familiar and have been summarized recently by Cole (3). Hospital controls are readily accessible, usually cooperative and, by virtue of their illness, are likely to have a motivation to recall like the cases do. Controls selected from the same medical care facilities as the cases are more likely to be similar to the case with regards to characteristics leading to admission to the facility. However, they are unsuspected associations between the reason for obtaining medical care and the aetiological factor of study interest. All these advantages cannot be compensated for the invalid conclusions which might be drawn, nor can statistical analysis do.

Controls drawn from the same general population group as the case have the great advantage of providing an estimate of the frequency of the suspected aetiological factor which is not altered by associations with illness or hospitalization. However, several problems may be interfered with obtaining an unbiased estimate from control groups drawn from the general population; population controls are more difficult to locate and less likely to agree to participate in the study, and their ability to recall past events is likely to be different from that of the cases.

Most epidemiologists agree with statement that nature of the cases is the basis for selection of suitable controls, yet they seem unable to agree upon the appropriate source from which to select controls.

Since consideration to choice between two sources of controls is not clear and it is crucial for the validity of the results, Stavinisky and Clarke (4) reported a recent case-control study which used both hospital and population-based controls. They compared these two control groups in the hope of clarifying the issues involving in the choosing between two sources. They pointed out that each type of control has its specific advantages and disadvantages. The hospital, due to referral patterns, has the effects of admission due to socioeconomic variables. In addition, the exposure variable and event of hospitalization may be linked through unknown factor, thereby adversely affecting the validity of a study utilizing hospital controls. On the other hand, while neighbourhood control can
provide useful data the exposure variable, but non participation can be a serious problem. This lead to the concept of using both hospital and neighborhood controls. This experience cannot resolve the controversy about whether a medical care facility or the general population is the best source for a control group.

They had presented the comparison in the hope that it will encourage investigators to use both types of controls, so that the investigators may determine different results would be obtained, what control group differences contribute to these results. Our understanding which regards the bias, if any, would be increased by using both sources of controls. However, the data discussed in Streunkey and Clarke paper cannot be regarded as a real example of use two type of controls in the same study. Their work actually was independent studies. The results would be meaningful if hospital and community controls are obtained simultaneously for the cases. It was suggested that conducting a case-control study, one should take simultaneously hospital and community controls (5).

Berkson postulated that the relative frequency of disease and etiologic exposure factors, as noted in a hospital population, will be biased when compared with the entire community population to which the results are referred (6). The bias will arise because of the different likelihoods of hospitalization for patients with different diseases, in exposure factors, and in combinations of diseases and exposure factors. Fennstein et al (7) have added the discussions of the Berkson bias with the following contributions:

1. To indicate the odd ratio in relation to exposed/unexposed in a case-control study, using an algebraic model that is relative easy for clinical readers to understand.

2. The model has been developed specifically for the three type of the sampling methods that are commonly used in case-control studies. It has been considered to the situations in which the case are hospitalized patients, with the control groups coming from (a) patients hospitalized with other diseases, (b) patients hospitalized with a specific comparative condition and (c) non hospitalized persons in the community.
3. The results demonstrated the relative magnitudes of bias that will be incurred in the mentioned situations, and indicated the needed requirements to avoid bias when the odd ratio is used to estimate the (cohort) risk ratio. The odd ratio will be unbiased if rate of hospitalization for exposed/individual is equal to null, i.e. if exposure to the suspected etiologic agent is not a factor leading to hospitalization. This assumption that the rate hospitalization for exposed person is equal to null, will seldom be realistically tenable. Therefore for most of the entities that come under suspected etiologic agents, the most conservative course is to assume that the rate of hospitalization for exposed person is much more than null. With this assumption the following conclusions have been demonstrated by the fore-going analysis:

1. Berkson's bias will be avoided in case-control studies if the case and control group are chosen from the community. Although applicable for clinical conditions that are not routinely hospitalized, this sampling method was not employed in many of the case-control studies published in the past few decades.

2. If the cases are chosen from a hospitalized population, the mathematical effects of Berkson's bias could not be avoid by choosing the control group from the community: in fact, such a choice will always falsely elevate the odd ratio. Conversely, the mathematical effects will falsely lower the odd ratio if the control group is chosen from hospitalized patients with no disease of study interest.

3. With a hospitalized case group, Berkson's bias can be avoided by using hospitalized control group, having comparison condition for which the rate of hospitalization equals the analogous rate in the case group.

There is no doubt that there is a great deal of skill and judgement required in deciding upon the appropriate control group for a case-control study. Clearly, availability the resources should be considered in the decision. The choices are often highly specific to the investigations being planned and invariably depend on one's understanding of the disease process and hypothesis concerning the pathways by which an exposure is presumed to affect the disease under study.
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