

Letters to the Editor

On the comparability of population-based and hospital-based case-control studies**Comparación de estudios de casos y controles poblacionales y estudios de casos y controles hospitalarios**

Dear Editor:

We read with great interest the methodological note recently published in *Gaceta Sanitaria* by Ruano-Ravina et al,¹ addressing one of the most important, but sadly often misunderstood, methodological issues in case-control studies. However, the authors ignored Olli Miettinen's² concept of a case-control design, currently accepted as a specific sampling technique within "dynamic populations".³

The assumption that the case-control design is a more efficient way of conducting and analyzing cohort studies underlies their methodological strength, and has to be taken into account from planning to the interpretation of results.² When ranking study designs according to their potential to achieve valid conclusions, the differences between population-based and hospital-based case-control studies largely reflect the extent to which each of them is likely to come near the concept of a cohort analysis.

The first step in the conduct of population-based case-control studies is the identification of the study base, preceding the selection of participants and therefore named "primary", which may be seen as equivalent to the definition of the cohort in a cohort design. The study base may be seen as an imaginary cohort that the researchers are able to define but whose elements are not all evaluated for the study purpose. The first great challenge in such case-control studies is the identification of all cases who meet the eligibility criteria arising from the study base. A second challenge is the set up of an appropriate strategy for sampling and evaluation of controls from the study base. Usually a large proportion of cases and a small proportion of available controls are evaluated. Selection bias is avoided when equal sampling fractions are achieved for exposed and non-exposed cases as well as for exposed and non-exposed controls, so that both cases and controls represent the exposure experience of their source populations, within strata that will be used for stratification in the analysis.⁴

Hospital-based differ from population-based studies because the study base is defined secondarily to the identification of cases. Cases are selected regardless of the population from which they arise (e.g. all cases from a given hospital receiving patients from different settings). An effort is then made to identify the study base corresponding to the selected cases. This often translates into important difficulties in the definition of the population from which the controls are to be selected (the source population for cases). Case-control comparisons are likely biased when controls are selected from an ill-defined study base and consequently do not represent the exposure experience of the true source population. However, the procedures for both case and control selection and evaluation tend to be logistically less demanding. Also, differences in the extent and nature of information biases may favor hospital-based studies.

Both primary and secondary base designs can reach equally valid conclusions (at least from the standpoint of internal validity). The biggest challenge in hospital-based studies will never be the assembling of a control group similar to the one that would be desirable for a population-based study, but the selection of controls that adequately estimate the exposure distribution in the corresponding study base. Hospital and population controls can only be expected to be similar in the extent to which the characteristics of population and hospital cases overlap. If a scenario of population and hospital cases being sampled from the same source population happens to occur, the comparison of population and hospital controls still needs to take into account the expected different participation of the controls in these settings.

Ruano-Ravina et al¹ compare controls selected for two different case-control studies conducted in the same region but in different periods. The cases for the population-based study are expected to reflect the exposure experience of the population of Santiago de Compostela Public Health District developing lung cancer, while those from the hospital-based study should be representative of the Spanish population receiving treatment for lung cancer in the hospital(s) involved in the study. In theory these designs correspond to two different source populations, making the comparison between the two groups of controls meaningless, to the extent that the study bases do not overlap. Unfortunately, there is no detailed description of the case selection procedures and yielding in the methodological note or in the original publications. If the study bases do overlap (data on referral patterns in the geographical area of interest would have to be provided to test the truth of this proposition), then both studies have in fact the same base (primary or secondary), and the comparison of different types of controls reflects differences in sampling strategies for controls rather than differences in the type of study.

Either way, the methodological note by Ruano-Ravina et al¹ could benefit from a formal adjustment to follow the conceptual approach to case-control studies of "modern epidemiology".

References

1. Ruano-Ravina A, Pérez-Ríos M, Barros-Dios JM. Population-based versus hospital-based controls: are they comparable?. *Gac Sanit.* 2008;22:609–13.
2. Miettinen OS. The "case-control" study: valid selection of subjects. *J Chronic Dis.* 1985;38:543–8.
3. Zhang FF, Michaels DC, Mathema B, et al. Evolution of epidemiologic methods and concepts in selected textbooks of the 20th century. *Soz Präventivmed.* 2004;49:97–104.
4. Rothman KJ, Greenland S, Lash TL. Case-control studies. In: Rothman KJ, Greenland S, Lash TL, editors. *Modern Epidemiology*, 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 111–27.

Nuno Lunet* y Ana Azevedo

Porto University Medical School, Hygiene and Epidemiology, Porto, Portugal

*Corresponding author.

E-mail address: nlunet@med.up.pt (N. Lunet).