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Strategies for comparative analyses of registry data

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ABSTRACT

The present paper is a description and summary of methods used in non-randomised cohort data where the comparability of the study groups usually is not granted. Such study groups are formed by a diagnostic or therapeutic intervention, or by other characteristics of the patient or the treatment environment. This is a typical situation in the analysis of registry data. The methods are presented together with an illustrative example of whole-body computed tomography in the early phase of treatment of severe trauma cases. The following approaches are considered: (i) unadjusted direct comparisons; (ii) parallelisation; (iii) subgroup analysis; (iv) matched-pairs analysis; (v) outcome adjustment; and (vi) propensity score analysis. All these approaches have in common that they try to separate, or limit, the influence of confounding variables, which are unevenly distributed among the study groups, but also influence the outcome of interest. They differ in the number of confounders being considered, as well as the number of patients regarded. The more sophisticated the approach, the more effectively such confounding factors could be reduced. However, any method used for the reduction of bias depends on the quality and completeness of recorded confounders. Factors which are difficult or even impossible to be measured could thus not be adjusted for. This is a general limitation of retrospective analyses of cohort data.

Introduction

In recent years data from registries have become increasingly important for health services research. This is especially important in health care areas where the conduct of classical randomised trials is very difficult, or even impossible. The emergency treatment of severely injured patients is such an area because informed consent is difficult to obtain from non-responsive patients.

However, the evidence level of registry studies ranges somewhere between prospective and retrospective observational studies. The main problem with registry studies is not the sample size - there are usually much more patients documented in registries than in clinical trials. It is also a positive aspect that registries include a larger variety of patients with a certain condition while clinical trials usually consider a selected subgroup of cases only. Therefore, registry studies are most appropriate to analyse the effectiveness of routine care. But the main problem of registry studies, however, is data completeness and data correctness, which tend to be lower than in clinical trials. There are usually limited resources for monitoring and source data verification in registries, is not frequently performed. Registries also document considerably less data per case than clinical trials.

But there is a further methodological aspect of registry data analyses, which should be considered more closely here. While descriptive data (like prevalence or incidence rates) profit a lot from a large and representative sample size, problems arise with the comparability of subgroups. If a certain intervention, therapeutic or diagnostic, is analysed in registry data, then the direct comparison of cases with and without that intervention would nearly always give biased results. True comparability would only result from randomizing a sufficiently large number of patients. Registries are comparable with observational studies where treatment decisions are not influenced by an experimental design.

However, there are some analytic strategies, which would allow to reach a certain degree of comparability which sometimes comes close to that of controlled trials. The present paper intends to present and describe six of these strategies, together with their advantages and disadvantages. A summary of these strategies could be found in Table 1. In the first part some general comments on descriptive analyses, especially on the use of confidence intervals, are given.

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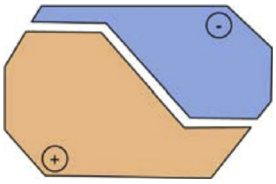
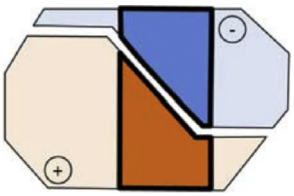
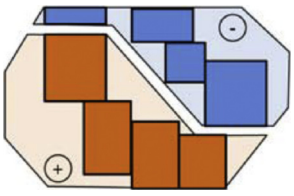
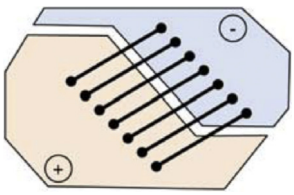
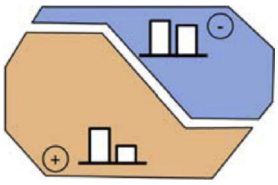
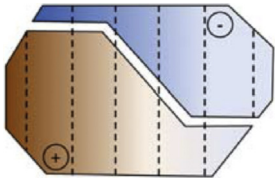
Table 1
Summary of six analytical strategies with the potential to reach a certain degree of comparability which sometimes approximates that of controlled trials.

Method	Pictogram	Description	Advantages	Disadvantages
Direct comparison		No adjustments performed; the groups are compared as they are	Easy to perform	• No comparability of groups Observed differences in outcome could have many reasons
Parallelisation		Comparison is performed in a subgroup of patients defined by some inclusion and exclusion criteria	Comparability somewhat improved Extremes are excluded Easy to perform	• Number of cases reduced Imbalances usually remain
Subgroup analysis		Patients were split into subsets based on a number of criteria; comparisons are performed then in each subgroup	Relatively good comparability within a Subgroup easy to perform	• multiple results only a few criteria could be considered; otherwise the number of subgroups would dramatically increase
Matched Pairs		Based on a number of predefined criteria, pairs of patients are selected and compared who differ only in the intervention (performed, or not)	Very good comparability intuitive understandable equal sample size	• Good comparability only with multiple criteria, but the more criteria, the less pairs Many cases remain unconsidered
Outcome adjustment		Factors that influence the outcome of interest are combined, and the predicted outcome is calculated for each case. Predicted and observed outcome is then compared between those with and without intervention	all cases are included Established tools for outcome adjustment could be used	• Separate adjustment required for each outcome of interest depends on the quality of the Adjustment tool sophisticated multivariate analysis
Propensity score		In a first step, the probability for the intervention is calculated (the propensity score). Then, in a second step, comparisons are made among patients with a similar propensity score	Similarity of cases defined by the probability of receiving the intervention Nearly all cases could be included	• Sophisticated multivariate analysis Sufficient discrimination of the propensity score required

Descriptive statistics

Descriptive data analysis and presentation follow the same rules as in clinical trials. Frequencies are presented as number of subjects and percentage, and continuous variables are presented with a measure of location and a measure of variation, like mean and standard deviation (SD). In case of considerably skewed data, for example length of stay (LOS) in hospital, it is recommended to provide the median with interquartile range, or add at least the median to the mean/SD. The use of mean/SD is by no means limited to normally distributed data, which is a common misunderstanding. It could be calculated from any type of data. But in some cases the median gives important additional information. If mean and median have about the same quantity, then it could be assumed that the data are distributed approximately symmetrically. The range of the observed data (minimum and maximum) could also be helpful, however, these values tend to be biased by outliers and extreme values.

Confidence intervals

For some key results it is further recommended to provide 95% confidence intervals (CI). Such an interval describes very clearly the degree of uncertainty contained in the data. The range of a confidence interval decreases when the sample size increases, reflecting the increasing statistical certainty with which the results