

Comparison of different matching methods in observational studies and sensitivity analysis: The relation between depression and STAI-2 scores

Handan C. Ankarali^a, Vildan Sumbuloglu^a, Ayse Canan Yazici^{b,*}, Irem Yalug^c, Macit Selekler^d

^a Zonguldak Karaelmas University, Faculty of Medicine, Biostatistics Department, Zonguldak, Turkey

^b Başkent University, Faculty of Medicine, Biostatistics Department, Baglica Campus, 06530 Ankara, Turkey

^c Kocaeli University, Faculty of Medicine, Psychiatry Department, Kocaeli, Turkey

^d Kocaeli University, Faculty of Medicine, Neurology Department, Kocaeli, Turkey

Abstract

In researches where two or more groups are desired to be compared, observational and randomized experiments are very frequently used. As the subjects are randomly assigned to the groups in randomized experiments, balance is provided in observed/unobserved covariates of subjects in different groups. As the subjects cannot be randomly distributed into groups in observational studies, balance of observed/unobserved covariates between groups is not provided. This situation causes a biased estimate of the treatment effect. In this research, it is focused on different matching methods in observational studies and elimination of observed covariate effects confounding in the group effect, and these methods are examined comparatively. For this purpose, the effect of depression in 300 migraine patients, obtained from an observational study, on State continuous anxiety scale scores is taken and compared with the five different matching methods. Sensitivity of results is examined and it is researched whether the effect of treatment contains any bias. When results are examined, it is seen that matching methods produce similar results due to the overlap of propensity distribution in groups, high and balanced number of subjects in groups and covariates being not so many in number. The effects of unobserved covariates do not change the effect of treatment significantly. In conclusion, it is seen that, in the estimation of group effect in observational studies, it is possible to eliminate the effects of observed covariates using matching methods and matching quality of matching methods based on the propensity score is high.

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1. Introduction

In researches where two or more groups are desired to be compared, observational and randomized experiments are very frequently used. While the randomized experiments can be designed as cross-sectional or prospective, observational experiments can be designed in many types of research like retrospective, cross-sectional, prospective,

field surveys, administrative records or census data. Randomized experiments and observational studies share a common purpose, namely inference about the effects caused or produced by a treatment, but in observational studies the assignment of experimental units to treatment or control is not based on randomization (McKinlay, 1977). As a consequence of the nonrandomized assignment of units, the treated and control groups may differ systematically prior to the start of the treatment, so that differences in outcome in treated and control groups can reflect either effects caused by the treatment, or inherent pre-treatment differences, or both (Cochran & Rubin,

* Corresponding author. Tel.: +90 312 2341010/1568.

E-mail address: aysecanan@yahoo.com (A.C. Yazici).

1973; Perkins, Tu, Underhill, Zhou, & Murray, 2000). In certain cases, observational studies can be advantageous; and in others, the randomized studies. Namely, observational studies take less time, more easily adjusted and cost less when compared with randomized studies. Furthermore, there is no obligation to follow the ethical and logistic rules. On the contrary, there are no biases in results obtained from randomized studies. However, the accuracy of results obtained from a well-adjusted observational study will be almost the same as the results in randomized studies (Perkins et al., 2000).

As stated above, differences originating from observed and unobserved covariates between groups to be compared in observational studies bring about biased estimates. The concept of bias here expresses the systematic differences observed between treatment and control groups in terms of one or more covariates. There are two analytical ways to eliminate this bias. These are; (1) those that focus on the relationship between covariates and outcomes and (2) those that focus on the relationship between covariates and assignment of patients to treatment or control (Rosenbaum & Rubin, 1983). The first strategy models the response directly, for example, through use of multiple linear regression or multiple logistic regression. The second strategy, which uses propensity scores (PS), is an attempt to reconstruct, after the fact, a situation similar to random assignment, albeit only with respect to observed covariates.

Matching has become a popular approach to estimate causal treatment effects. Various matching algorithms are developed and in recent years, the most frequently used are the matching methods based on propensity score. After randomized distribution of groups in terms of observed covariates using the matching methods, there can still be bias in the estimate of group effect. These are called hidden bias and they include unobserved covariate effects. This effect is examined using the sensitivity analysis. A sensitivity analysis in an observational study is an attempt to display and clarify the extent to which inferences about a treatment effect vary over a range of plausible assumptions about unmeasured pre-treatment (Rosenbaum & Rubin, 1983).

Purpose of this study is to compare the covariate matching with four matching methods based on propensity score and test the sensitivity of results. With this aim, focus has been made on the relation between the existence of depression, a psychiatric disorder, in migraine patients and the State continuous anxiety scale scores (STAI-2), and the matching methods have been compared taking these data into consideration.

2. Material and methods

2.1. Propensity scores (PS)

Propensity score (PS) is the probability of being assigned to a particular treatment conditional on a set of

observed covariates, \mathbf{X}_i ($i = 1, 2, \dots, n$). The PS for individual i is defined as:

$$P(\mathbf{x}_i) = e(\mathbf{x}_i) = \Pr(Z_i = 1 | \mathbf{X}_i = \mathbf{x}_i)$$

Z_i : 1 = Treatment group; \mathbf{X}_i is the vector of observed covariates.

As the values \mathbf{x}_i and Z_i are independent, following equation can be formed:

$$\begin{aligned} \Pr(Z_1 = z_1, \dots, Z_n = z_n | \mathbf{X}_1 = \mathbf{x}_1, \dots, \mathbf{X}_n = \mathbf{x}_n) \\ = \prod_{i=1}^n e(\mathbf{x}_i)^{z_i} \{1 - e(\mathbf{x}_i)\}^{1-z_i} \end{aligned}$$

Subjects are then matched or grouped into subclassifications based on their PS. Because, measured covariates of two subjects with same PS values are also the same and one of these subjects is assigned to the treatment, where the other is assigned to the control; thus, matching is provided (Aassve, Davia, Lacovou, & Mazzuco, 2005). Here, terms ‘treatment’ and ‘control’ are the common names for two groups desired to be compared. In this study, the depressive group is considered as the treatment and non-depressive as the control.

The most widely used model in obtaining PS values is the logistic regression model which requires no assumptions relating to the variable distributions. Moreover, the discriminant analysis, linear regression models and recently, the tree-based models are used for this purpose.

Prior to the calculation of PS values, variables to be included in the PS model should be decided. All pre-treatment covariates, which is collected before treatment assignment, related to both the treatment and outcome are included in the PS model. It is also very important not to include the outcome in the PS model. In addition covariates that are known to be related to the treatment assignment but not to the outcome should not be included because they may potentially reduce the effectiveness of the subclassification in balancing the distributions of confounding covariates (Bryson, Dorsett, & Purdon, 2002). Covariates related to the response but not to the treatment assignment may also be included in the model to ensure that their distributions remain balanced across the treatment groups while balancing the other relevant covariates (Perkins et al., 2000). Another important issue is whether to include covariates collected after treatment assignment in the PS model. Using post-treatment covariates to predict treatment assignments result in biased estimates of the treatment effect. For this reason, it is not recommended to include such types of covariates in PS model (Rosenbaum, 1984).

Furthermore, univariate tests are most widely used to select proper ones among the variables defined above for the PS model. However, there is no complete consensus on this issue. In this study, variables to be taken into the PS model are decided using both univariate and multiple tests. In the first stage, the relationships between baseline covariates and depression groups and STAI-2 scores are

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