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Matching versus Regression in Observational Studies

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A large number of biomedical studies whose aim is assessing treatment effects or comparing groups of patients rely on observational data. Various registries house a wealth of observational data which can be used to make conclusions about the treatment effectiveness. Such collection of data lends itself to retrospective (historical) cohort studies which are carried out at the present time and look to the past to examine disease, treatment, and outcomes. These studies utilize the entire cohort of patients who satisfy criteria for inclusion in the study and whose information is available in the registry. Their patient characteristics, disease and treatment description, along with the outcome data (e.g., survival status, disease recurrence) which were assessed in the past, are reconstructed for analysis. An alternative design for analyzing observational data is matched cohort studies. In this case, subjects are paired based on their treatment assignment. Pairs are formed to include individuals who differ with respect to treatment but may be matched on certain baseline characteristics. The matching can be done either on covariate values themselves (for example, treated and untreated patients are matched on gender, age, and disease stage) or based on propensity score1. In the latter approach, the first step involves building a logistic regression model to predict the probability of receiving treatment, given a set of covariates. Each subject in the data set is then assigned a so called "propensity score" which is their estimated probability of being a treated case. Then treated cases and untreated controls with approximately the same propensity score are chosen to form a pair. Once matching is done, occurrence of the outcome of interest is ascertained. It is a common perception by clinicians that a matched study is the best option to perform needed comparisons

between groups of patients. It is believed that matching minimizes variability caused by extraneous variables and makes the groups balanced with respect to key factors which may influence the outcome. In particular, it is appealing that tables of patient characteristics make the groups appear similar, and creates an impression that a matched cohort study may be treated as a randomized trial where possible confounding is removed. However, besides matching, analytic tools such as regression modeling can also be used to remove confounding and adjust for imbalances between the groups. Regression modeling deals with confounding as effectively as matching techniques and in many cases regression may be preferred to matching. While matching aims to reduce bias it may suffer from loss of efficiency which results from restricting the analysis to a subset of patients. This issue can be especially notable if the matching ratio is low. The value of matching in case-control studies has been discussed by many, and numerous publications indicate that such an approach is not always beneficial2. Discarding observations in the matching process will typically result in smaller sample sizes and may lead to increased variance which will obscure existing differences between groups. There is a body of research devoted to improving matching and estimation quality in matched studies under specific conditions (overview and extensive reference list is provided by Stuart3). However, matched studies followed by simple unadjusted analysis are very common and frequently chosen instead of more flexible regression models. A recent study focused on time-to-event studies and compared the performance of matched studies and regression techniques applied to simulated cohorts of patients4. In survival analysis studies, matching is usually followed by a stratified or marginal Cox model which accounts for dependence between subjects within a pair or cluster. However, the investigation4 showed that a Cox regression model applied to the entire cohort was often a more powerful tool in detecting a treatment effect. Matched studies result in a smaller sample size which can lead to reduced power. If possible, an investigator should strive to find a larger number of untreated controls for each treated subject because a greater matching ratio mitigates much of the power loss associated with the sample size reduction occurring in matched studies. Furthermore, results from a given matched data set may be different from those obtained if the matching procedure was to be repeated and a different set of controls was to be selected, illustrating the variability inherent in the study design. Selecting a matched study design may be justified when there is a need to reduce the number of individuals. For example, a study may require additional data collection on patients in the final dataset which is time or labor intensive (such as manual chart review or interpretation

of lab results or images); matching can be completed on readily available patient characteristics and then researchers can obtain the additional (more costly) data for the reduced study population. . In most other cases, a regression model applied to the entire study cohort can effectively address confounding and maximizes power by using all the data available. However, utmost care is needed with the regression model to adequately capture the relationship between covariates and outcome and provide a proper adjustment for these covariates. This includes ensuring that model assumptions hold, checking for significant interactions between variables and including important ones in the model, assessing the functional form of the relationship between quantitative covariates (e.g. age) and outcome, and ensuring sufficient overlap of patient characteristics to allow for a proper risk adjustment. Complying with assumptions and conditions to ensure the adequacy of the analysis and conclusions that follow are not only pertinent to regression modeling. There are many pitfalls in the matching process and analysis that may affect their feasibility and performance as well2, 3, 5. A well-chosen regression model has the advantage over matched studies of using all patient information available leading to increased efficiency.

References

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