

Sensitivity Analysis of Untestable Assumptions in Causal Inference

Mathias Lundin



Department of Statistics
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Papers I-IV

List of Papers

The thesis is based on the following papers:

- I. Lundin, M. (2011). Effects of college choice on income in Sweden. Research Report, Department of Statistics, Umeå University, Umeå.
- II. de Luna, X and M. Lundin (2009). Sensitivity analysis of the unconfoundedness assumption in observational studies. *IFAU Working Paper*, 2009:12, Institute for Labour Market Policy Evaluation, Uppsala.
- III. Lundin, M. (2011). Profile likelihood for semiparametric regression. Research Report, Department of Statistics, Umeå University, Umeå.
- IV. Lundin, M. and M. Karlsson (2011). Estimation of causal effects in observational studies with interference between units. Submitted manuscript.

Abstract

This thesis contributes to the research field of causal inference, where the effect of a treatment on an outcome is of interest is concerned. Many such effects cannot be estimated through randomised experiments. For example, the effect of higher education on future income needs to be estimated using observational data. In the estimation, assumptions are made to make individuals that get higher education comparable with those not getting higher education, to make the effect estimable. Another assumption often made in causal inference (both in randomised and nonrandomised studies) is that the treatment received by one individual has no effect on the outcome of others. If this assumption is not met, the meaning of the causal effect of the treatment may be unclear.

In the first paper the effect of college choice on income is investigated using Swedish register data, by comparing graduates from old and new Swedish universities. A semiparametric method of estimation is used, thereby relaxing functional assumptions for the data.

One assumption often made in causal inference in observational studies is that individuals in different treatment groups are comparable, given that a set of pretreatment variables have been adjusted for in the analysis. This so called unconfoundedness assumption is in principle not possible to test and, therefore, in the second paper we propose a Bayesian sensitivity analysis of the unconfoundedness assumption. This analysis is then performed on the results from the first paper.

In the third paper of the thesis, we study profile likelihood as a tool for semiparametric estimation of a causal effect of a treatment. A semiparametric version of the Bayesian sensitivity analysis of the unconfoundedness assumption proposed in Paper II is also performed using profile likelihood.

The last paper of the thesis is concerned with the estimation of direct and indirect causal effects of a treatment where interference between units is present, i.e., where the treatment of one individual affects the outcome of other individuals. We give unbiased estimators of these direct and indirect effects for situations where treatment probabilities vary between individuals. We also illustrate in a simulation study how direct and indirect causal effects can be estimated when treatment probabilities need to be estimated using background information on individuals.

Keywords: Observational studies, semiparametric regression, unconfoundedness, direct and indirect causal effects.

Preface

When I was 18, I was ready to leave school and start to work as an engineer. I was certainly not going to university. Thus, after my military service, I went to the university to get a degree in engineering. One thing was certain, or “almost sure” as statisticians say: I would not become a PhD student! Then I started as a PhD student in the spring of 2003 and as a lecturer at the Department of Statistics in Umeå in 2007. Now my time as a PhD student is ending and I have to start to think about what I want to do besides the lecturing in statistics. One thing is certain: I will not win the Stanley Cup as the captain of the Toronto Maple Leafs. That I do not think, even though...

The most important person for me as a PhD student has been my supervisor Xavier de Luna. Thank you! Without your help this thesis would never have been written. You manage to transform obstacles into possibilities!

I am also very grateful to my co-supervisor Maria Karlsson who has been a great support during the last two years work with the thesis.

I also want to thank all the colleagues at the Department of Statistics. We have a fantastic department where I really feel at home.

Finally, I thank my family for all their love and support.

Umeå, April 2011
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1 Introduction

The field of causal inference is devoted to estimating effects of a cause or treatment on an outcome of interest rather than to find the cause of an effect (Holland, 1986). A treatment can be a medical treatment but can also be more widely defined, e.g., a labour market training program intended to give the participants better chance of finding jobs. To estimate the effect of the medical treatment, randomised trials are often performed where some subjects are given the active treatment and others are used as control subjects. Because of the randomisation, we avoid systematic differences between the treated and the controls, making the estimation of the treatment effect straightforward. As long as the subjects under study are representative of the population of interest, the results can be generalised to this population.

However, randomisation is not always practically possible or ethical. If the aim is to estimate the effect of higher education on the probability of finding a job, we cannot, for ethical reasons, randomly select who is going to get higher education and who is not. Thus, we need to make causal inference from observational data. An obstacle for causal inference in observational studies is that the assignment mechanism sorting individuals into treatments is most likely confounded, i.e., there are systematic differences between the treatment groups that are associated with the outcome of interest. Perhaps individuals who chose higher education would have done better on the labour market even without the treatment. For the empirical scientist, it is therefore crucial to find the confounding variables and adjust for these in the estimation of the causal effect of the treatment.

In Paper I of this thesis, we investigate the effect on income of graduating from one of the older Swedish universities instead of from one of the newer universities/colleges. As this is an observational study, we adjust for a number of confounders in the semiparametric estimation of the causal effect of treatment. If there are unobserved confounders that have not been taken into account, the estimation may be biased. Therefore, in Paper II we perform a Bayesian sensitivity analysis of the assumption of unconfoundedness. In Paper III, profile likelihood as a tool for estimation of semiparametric regression models is evaluated in a simulation study. We also describe a semiparametric version of the sensitivity analysis presented in Paper II. In Paper IV, we suggest how indirect causal effects (i.e., effects of the treatment of one individual on the outcome of other individuals) and direct causal effects can be estimated in situations where interference between individuals is present.

In Section 2 of this summary, the topic of causal inference through po-

tential outcomes and the assumptions made are presented. Section 3 gives a summary of the four papers in the thesis and Section 4 gives final remarks and some suggestions for further research.

2 Causal inference using potential outcomes

Suppose that individual i is being randomised to one of two treatments Z , $Z = 0, 1$. Individual i then has two potential outcomes depending on which of the treatments he/she receives. Let $Y_i(1)$ be the outcome measured for an individual i at time t_2 of a treatment $Z_i = 1$ given at time t_1 and $Y_i(0)$ the outcome measured for i at time t_2 of a treatment $Z_i = 0$ given at time t_1 . The causal effect of treatment $Z = 1$ versus $Z = 0$ for i is then $Y_i(1) - Y_i(0)$ (Rubin, 1974). However, this causal effect is in practise impossible to observe as i cannot receive both treatments at the same time.

To overcome the problem that we cannot observe a unit under both treatments we instead focus on an average causal effect in a population. If a group of individuals are randomised to treatments with $0 < \Pr(Z_i = 1) < 1$ for all units, the average causal effect of treatment is defined by

$$\tau = E(Y(1)) - E(Y(0)).$$

Note that due to the randomisation, the treatment assignment is unconfounded, meaning that the potential outcomes are independent of the treatment indicator ($Y(0), Y(1) \perp\!\!\!\perp Z$). Thus,

$$\tau = E(Y(1)|Z = 1) - E(Y(0)|Z = 0),$$

where $E(Y(1)|Z = 1)$ and $E(Y(0)|Z = 0)$ can be estimated from sample data giving an unbiased estimator of τ .

2.1 The unconfoundedness assumption

In observational studies, where treatment assignment is not randomised, the individual treatment probabilities may be dependent of the potential outcomes, thus giving a confounded assignment mechanism. As an example, suppose that people who have high levels of health consciousness are more prone to take vitamin supplement pills than do people who have low levels of health consciousness. To naively estimate the effect on some health-related outcome variable by taking the difference of the averages among the treated and controls would probably overestimate the true effect of the vitamin supplement. This is due to the fact that the treated on average are more health

conscious than the controls and therefore have higher potential outcomes, both under treatment and control. The sample mean in the treatment group will then overestimate the population average potential outcome under treatment and the sample mean in the control group will underestimate the population average potential outcome under control. In this example this would yield an overestimate of the average causal effect of treatment in the population. To estimate the causal effect of vitamin supplement without bias, we need to control for the confounder health consciousness (e.g., by matching) in the estimation. More formally, if the potential outcomes are independent of the treatment assignment mechanism conditional on a set of pretreatment covariates \mathbf{x} (background variables)

$$Y(0), Y(1) \perp\!\!\!\perp Z \mid \mathbf{x},$$

the assignment mechanism is said to be unconfounded.

In order to estimate an average causal effect of a treatment we also require (both for observational and randomised studies) that the treatment probability is strictly between 0 and 1 for all units, i.e.,

$$0 < \Pr(Z_i = 1 \mid \mathbf{x}) < 1 \forall i.$$

If this requirement is violated there will be units with certain characteristics \mathbf{x} who never (or always) are treated and therefore cannot be matched against units with the same characteristics but with the opposite treatment status.

The assumption of unconfounded treatment mechanism in observational studies is in principle untestable as we only observe one of the potential outcomes in each treatment group (i.e., $Y(1)$ among the treated and $Y(0)$ among the controls). Instead of testing the assumption we might investigate how sensitive our conclusion of the treatment effect is to violations of the assumption. In Paper II we propose a Bayesian method for performing a sensitivity analysis of the unconfoundedness assumption. In the sensitivity analysis we allow for an unobserved confounder that induces a correlation between the treatment assignment mechanism and the potential outcomes, conditional on the observed covariates \mathbf{x} . The outcome of the proposed sensitivity analysis is two posterior distributions for the causal effect of treatment, one produced when the unconfoundedness assumption holds and the other when there is still a correlation between the potential outcomes and the assignment mechanism after conditioning on \mathbf{x} . If the two posterior distributions differ by much, then inference is sensitive to the unconfoundedness assumption made in the study.

2.2 The stable unit treatment value assumption

In addition to the assumptions described in Section 2.1, there is a stability assumption regarding individual potential outcomes of the units under study. This stability assumption can be divided into two assumptions:

1. There is only one version of each treatment (Neyman and Iwaszkiewicz, 1935).
2. There is no interference between individuals, meaning that a unit's potential outcomes are unaffected by treatments that other individuals receive (Cox, 1958).

Together, these two assumptions are denoted the stable unit treatment value assumption, or SUTVA (Rubin, 1980). If the assumption holds, each unit will have only one potential outcome for both levels of the treatment (assuming a binary treatment), regardless of which of the treatments other individuals under study receive. We can denote SUTVA by

$$Y_i(\mathbf{z}) = Y_i(z_i) \forall i, \mathbf{z},$$

where \mathbf{z} is a vector of treatment statuses of all units being studied. If SUTVA does not hold, the outcome of individual i does not only depend on his/her treatment status but also on the treatment statuses of other units and there is no obvious way to define an average causal effect of the treatment.

For example, consider a vaccination against a contagious disease where the vaccination of an individual may have a positive (risk reducing) indirect effect on others that are not vaccinated because of less exposure. If a high proportion of a community is vaccinated, the risk-reducing effect of vaccination for an individual may be smaller than if he or she is vaccinated in a community where a low proportion of the citizens are vaccinated. Thus, SUTVA is violated and the meaning of the causal effect of vaccination is unclear.

Hudgens and Halloran (2008) defined causal effects of a binary treatment in the presence of interference between units. In their setting, a two-stage randomised experiment, different groups under study are isolated from each other so that individuals in different groups do not interfere with each others potential outcomes while there may be within-group interference. Each group has one of two treatment strategies (e.g., a low proportion of the individuals in the group treated or a high proportion treated). The within-group treatment effects are regarded as direct causal effects while the difference in outcome under control following one group strategy and the outcome under

control in the other group strategy is an indirect causal effect. If the estimated indirect causal effect of treatment is small then SUTVA may be a reasonable assumption, whereas a high estimated indirect effect gives evidence of interference between units. The estimated causal effect of treatment should then be interpreted as a direct causal effect rather than an ordinary causal effect.

In Paper IV of the thesis we extend on the work of Hudgens and Halloran (2008) towards an observational study setting for estimation of direct and indirect causal effects of a treatment.

2.3 Estimation of causal effects

A semiparametric regression model, used in Paper I, is one alternative for estimating an average causal effect. For simplicity, assume that there is only one confounder, x , that we need to adjust for in the estimation of the causal effect and that the effect of the treatment is the same for all possible values of the confounder. We can specify a semiparametric model for the relationship between the confounder, the treatment and the observed outcome:

$$Y_i = \alpha + f(x_i) + \tau z_i + \varepsilon_i, \quad \varepsilon_i \sim N(0, \sigma^2),$$

where α is a constant, f is a smooth function and τ is the average causal effect of treatment $z = 1$ versus treatment $z = 0$. This additive model can be estimated in different ways. The R package `gam` uses a backfitting algorithm (Hastie and Tibshirani, 1990) to estimate the model. Another approach is to use profile likelihood (Murphy and van der Vaart, 2000) to profile out the function f which is regarded as a nuisance parameter in the estimation of τ . In Paper III of the thesis, we compare these two methods for estimation of τ in a simulation study and find that they produce similar results. Profile likelihood is then considered for a semiparametric version of the Bayesian sensitivity analysis of the unconfoundedness assumption presented in Paper II.

3 Summary of papers

3.1 Paper I: Effects of college choice on income in Sweden

In this paper, effects on labour market earnings of choosing to graduate from one of the old Swedish universities (established 1965 or earlier) instead of one of the newer universities/colleges are evaluated.

We perform semiparametric estimation of the earnings premium from choosing to graduate from an old university instead of a new university using the potential-outcomes framework.

The sample in the study is the cohort of students graduating from senior high school between 1990 and 1996 and then graduating with a three year university degree in business or economics before 2001. Register data is used to gather information on incomes, educations, demographic and socioeconomic variables.

The labour market earnings (annual incomes) are measured during the period 2-6 years after graduation from university and defined as y , the log of annual income given that income is higher than 100,000 SEK. The income restriction of 100,000 SEK has been shown to give a good correspondence to hourly earnings which is used as a measure of labour productivity (Antelius and Björklund, 2000). However, it would not be meaningful only to estimate the effect of college choice on y and therefore we also estimate the effect of college choice on the probability of having an annual income higher than 100,000 SEK.

Results of the estimations show an earnings premium ranging between 5% and 9% during the period two to six years after graduation from choosing to graduate from an old university instead of a new university. On the other hand, graduates from new universities have a higher probability of getting an income higher than 100,000 SEK, although statistically significant only two of the years in the period.

3.2 Paper II: Sensitivity analysis of the unconfoundedness assumption in observational studies

When evaluating a treatment effect with a regression model approach, every covariate affecting both the potential outcomes ($Y(0), Y(1)$) and the assignment mechanism, Z , should be controlled for. If there is a covariate, not controlled for, that affects both $Y(0), Y(1)$ and Z then the unconfoundedness assumption (UA, defined in Section 2.1) does not hold and the estimator of the treatment effect is biased.

The sensitivity analysis proposed in this paper investigates how a small departure from UA, expressed as a correlation between the potential outcomes and the assignment mechanism, given a set of observed covariates, would affect the inference for an estimated treatment effect. A correlation coefficient is a standardised measure of dependence and also intuitively comprehensible to most empirical scientists, making the results of the sensitivity analysis easy to communicate.

A simple example for a treatment evaluation model is obtained with a linear regression model for the potential outcomes, given the covariates \mathbf{x} , with a normally distributed error term:

$$Y(0)|\mathbf{x}; \beta, \sigma^2 \sim N(\beta'\mathbf{x}, \sigma^2)$$

and

$$E(Y(1)) = E(Y(0)) + \tau,$$

where τ is the treatment effect. A logistic regression model is used to describe the treatment assignment mechanism:

$$\Pr(Z = 1|\mathbf{x}; \gamma) = \exp(\gamma'\mathbf{x}) / (1 + \exp(\gamma'\mathbf{x})).$$

Suppose that there is an unobserved covariate, u , that affects the outcome and the treatment indicator as described in the following expanded model:

$$Y(0)|\mathbf{x}, u; \beta, \eta_1, \nu^2 \sim N(\beta'\mathbf{x} + \eta_1 u, \nu^2),$$

and

$$\Pr(Z = 1|\mathbf{x}, u; \gamma, \eta_2) = \exp(\gamma'\mathbf{x} + \eta_2 u) / (1 + \exp(\gamma'\mathbf{x} + \eta_2 u)),$$

where u is assumed to be Bernoulli distributed with $\Pr(u = 1) = 1/2$. UA would not hold if $\eta_1 \eta_2 \neq 0$ because then the bias parameters η_1 and η_2 induce a dependence between $Y(0)$ and Z , given \mathbf{x} .

In the sensitivity analysis, we consider small departures from UA in terms of the correlation between $Y(0)$ and Z given \mathbf{x} ,

$$\rho(\mathbf{x}) = \text{Corr}(Y(0), z|\mathbf{x}),$$

generated by the bias parameters $\eta = (\eta_1, \eta_2)$. We use a Bayesian approach proposed by Greenland (2005) to conduct a sensitivity analysis of UA where we assign a prior distribution for η so that it generates uniform prior distributions for $\rho(\mathbf{x})$ on $(-0.01, 0.01)$ and $(-0.05, 0.05)$. Values of η are sampled from the prior distribution and the treatment effect, τ , is then estimated with maximum likelihood estimation. The resulting posterior distribution of τ , including both random variation and bias introduced by the correlation, can then be compared with the posterior distribution under UA to see if the treatment effect is sensitive to small departures from UA.

This proposed sensitivity analysis is performed on a toy application based on the LaLonde data (LaLonde, 1986) and on the observational study presented in Paper I. The first example shows little sensitivity to these departures,

whereas the college choice evaluation is more sensitive, although not sensitive enough to alter the inference of a positive treatment from choosing to graduate from one of an old Swedish universities instead of one of the newer universities/colleges.

3.3 Paper III: Profile likelihood for semiparametric regression

In estimation of a causal effect using semiparametric regression, the model can be estimated in different ways. In this paper we investigate by a simulation study how profile likelihood compare with backfitting (which is implemented in the R package `gam`) for the estimation of the parametric part of a semiparametric regression model. We find very similar results between the methods, given the same value of the smoothing parameter. In addition, both methods give results similar to parametric estimation from the correct model although parametric estimation is more efficient.

We then use profile likelihood to suggest a semiparametric version of the Bayesian sensitivity analysis of the unconfoundedness assumption presented in Paper II of the thesis. The semiparametric sensitivity analysis is performed on a simulated dataset.

3.4 Paper IV: Estimation of causal effects in observational studies with interference between units

The stable unit treatment value assumption, SUTVA (Rubin, 1980), states that each unit only has one potential outcome for each level of a treatment. This implies that there are not different versions of a treatment and that there is no interference between units in the study.

For causal inference in the presence of interference between units, Hudgens and Halloran (2008) defined direct and indirect causal effects that rely on two-stage randomisation of treatment. In the first stage groups are randomised into one of two treatment strategies (e.g., either a high proportion or a low proportion of the group is treated) and in the second stage individuals within each group are randomly assigned to treatment (with each individual within a group having the same treatment probability). Interference may be present between members of a group but not between members of different groups.

We extend on the work of Hudgens and Halloran (2008) by deriving unbiased estimators of their proposed causal effects, allowing for unequal individual treatment probabilities in the second stage of randomisation. We

also show how our proposed estimators can be used to estimate these effects when the second stage is not randomised but individual treatment probabilities need to be estimated using background variables.

4 Final remarks and further research

In this thesis we have estimated effect of college choice on income in Sweden. The estimation is based on the unconfoundedness assumption, and therefore a sensitivity analysis of this assumption has been performed. This Bayesian sensitivity requires that the outcome and assignment mechanisms are parametrically specified. An interesting topic for further research would be to perform the semiparametric sensitivity analysis proposed in Paper III of the thesis on the results of the college choice study.

Estimators of direct and indirect causal effects were proposed in Paper IV. Further research is needed in order to find variance estimators of the effects and under which assumption these estimators would be unbiased.

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