Efficient treatment assignment in a regression discontinuity design? Simulations and validation in a large randomized controlled trial

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Submitted

ABSTRACT

Introduction

The quasi-experimental regression discontinuity (RD) design may provide valid treatment effect estimates but is inefficient compared to a randomized controlled trial (RCT). We aimed to compare different assignment approaches to increase the statistical efficiency of the RD design.

Methods

In Monte Carlo simulations, a random (R^2=0), low (R^2=7%) and highly (R^2=31%) correlating variable with outcome was used for treatment assignment. Patients were sampled from the CRASH trial, with a dichotomous outcome simulated. The treatment effect was analyzed with both local logistic regression and logistic regression with spline adjustment. To assess the relative statistical efficiency, standard errors (SE) of the different treatment assignment strategies were compared with an RCT of the same total sample size. This procedure was repeated in CRASH (n=9,554) as a case study.

Results

In the simulations, treatment effect estimates were unbiased. To obtain the same efficiency as an unadjusted RCT, RD required 2.8 times as many patients when using an assignment variable not correlating with outcome, and approximately 3.3 times as many patients when using an assignment variable highly correlating with outcome, using local regression. Compared to an adjusted RCT, the relative efficiency was not dependent on the correlation between the assignment variable and outcome since the adjustment affects the efficiency of an RCT as well. In the case study similar results were found.

Conclusion

The relative efficiency of the RD design is not dependent on the correlation between the assignment variable and outcome. We recommend researchers to use assigment variables that are feasible in clinical practice.

INTRODUCTION

The regression discontinuity (RD) design is a quasi-experimental design to study effectiveness of treatment. In the RD design, treatment is assigned to a subset of patients based on a baseline variable; e.g. older patients receive treatment. The RD design has been described as the next best design after a randomized controlled trial (RCT)(1): it enables causal inference of the treatment effect without randomizing patients to a treatment- or control group. The crucial feature of the RD design compared to observational designs is the exchangeability of patients around the cut-off of the assignment variable, making causal inference between treatment and outcome possible.(2-4) In some cases, the RD design might be attractive because randomization is avoided and the RD strategy closely resembles clinical practice.

A substantial drawback is that it requires far larger numbers of patients compared to an RCT.(5-7) Goldberger proved that this reduced precision stems from the correlation between the assignment variable and (binary) treatment indicator. This is because the treatment indicator is itself a function of the assignment variable and both must be included to model the outcome in RD.(7, 8) Different assignment variables can be used for treatment allocation in an RD design. Bor et al. suggested that "the assignment variable could be any continuous pretreatment measure including the outcome measure at baseline, or another measure of risk; a baseline covariate that is loosely correlated with the outcome; or even a random number, in which case regression discontinuity is identical to an RCT".(9) Since it is known that an RCT is more efficient than RD, we hypothesize that RD based on a poorly correlating assignment variable with outcome - thus more similar to treatment allocation in an RCT – results in more efficient treatment effect estimates compared to treatment effect estimates from an RD with treatment assignment based on a variable highly correlating with outcome.

In this study, we aim to compare different assignment approaches to increase the statistical efficiency of the RD design. We hereto performed a simulation study and analyzed data from a large RCT.

METHODS

Simulation study set up

According to the key steps and decisions in simulation studies described by Morris et al.(10), we performed Monte Carlo simulations to compare the efficiency of different assignment strategies in RD. For 5,000 patients, baseline prognostic characteristics were drawn from the "Corticosteroid Randomisation After Significant Head injury" (CRASH) trial.(11) A dichotomous outcome measure was simulated for each patient, with odds ratios for treatment of 0.8 and 1.0, corresponding to a small true effect and no effect respectively. We evaluated three approaches to assign treatment in RD. A random (R^2 = 0%), low (R^2 = 7%) - and a higher (R^2 = 31%) correlating variable with outcome was used to assign treatment. For all three strategies, treatment was assigned to the 50% of patients above the median value of the assignment variable. RD was analyzed with local logistic regression analysis to estimate a local treatment effect for the area around the cut-off for treatment assignment. Also, logistic regression models were used to estimate the treatment effect, adjusted for the assignment variable in a restricted cubic spline (RCS) term. Simulations were repeated 10,000 times. The standard errors (SEs) of the effect estimates from the RCT and the different RD approaches were compared as a measure of efficiency. The ratio of variances between an RCT and different RD assignment approaches were calculated with the following formula: $(SE_{RD} / SE_{RCT})^2$. The simulation code is provided in the Appendix.

Case study

The CRASH trial(11) was also used to illustrate the potential effect of different assignment approaches on the efficiency of the RD design in empirical data. The CRASH trial assessed the effect of corticosteroids on death and disability after head injury. CRASH enrolled patients between 1999 and 2005, of which 9,554 patients had complete outcome data. Of 10,008 patients included, 5,007 patients were allocated to treatment and 5,001 patients were control patients. To resemble the RD design, we used patients' baseline measures as assignment variable and the primary dichotomous endpoint (14-day all-cause mortality) of CRASH as outcome measure.

Efficient RD assignment approach

Nagelkerke R^2 statistics for all baseline characteristics and the full prediction model with outcome were calculated. The R^2 statistic between treatment allocation - which was completely at random in CRASH - and outcome, in the absence of a treatment effect, would be 0. Next, we assessed three hypothetical treatment assignment variables. First, RD based on a hypothetical completely random assignment variable was performed. In the second assignment strategy, a poorly correlating variable with outcome, age, was used to assign treatment. Finally, in the last setting, the linear predictor of a full prediction model highly correlating with outcome was used to assign treatment. This hypothetical assignment variable was constructed with a logistic regression model containing the most important known predictors for 14-day mortality, namely age, pupillary reactivity and motor score.(12-14) The medians of the assignment variables were used as the cut-off for treatment assignment. To imitate an RD design within the RCT data, we selected treated patients with a value of the assignment variable above the cut-off, and control patients with a value of the assignment variable below the cut-off.

Table 1. Monte Carlo simulations (n=5000, simulations: 10,000 times) comparing RCT with different treatment assignment strategies in regression discontinuity design.

Design	Analysis	Adjustment	Covariate for adjustment	Simulated treatment effect OR = 1.0		Simulated treatment effect OR = 0.8	
				Treatment effect estimate (OR)	Standard error	Treatment effect estimate (OR)	Standard error
Assignment based on (random) variable with no correlation with outcome							
RCT	Logistic regression	-		1.00	0.0660	0.80	0.0681
RCT	Logistic regression	Linear	Random, R^2=0	1.00	0.0660	0.80	0.0682
RD	Logistic regression	-		1.00	0.0660	0.80	0.0681
RD	Logistic regression	RCS	Random, R^2=0	1.00	0.1668	0.80	0.1722
RD	Local logistic regression	-		1.00	0.1095	0.80	0.1129
Assignment based on low correlating (R^2 = 7%) assignment variable with outcome							
RCT	Logistic regression	-		1.00	0.0660	0.81	0.0681
RCT	Logistic regression	Linear	Low correlating assignment variable, R^2=7%	1.00	0.0678	0.80	0.0698
RD	Logistic regression	RCS	Low correlating assignment variable, R^2=7%	1.01	0.2088	0.81	0.2129
RD	Local logistic regression	-		1.00	0.1097	0.80	0.1137
Assignment based on high correlating (R^2 = 31%) assignment model with outcome							
RCT	Logistic regression	-		1.00	0.0597	0.83	0.0607
RCT	Logistic regression	Linear	High correlating assignment variable, R^2=31%	1.00	0.0654	0.80	0.0666
RD	Logistic regression	RCS	High correlating assignment variable, R^2=31%	1.00	0.1898	0.80	0.1924
RD	Local logistic regression	-		1.00	0.1088	0.80	0.1098

So, for example, in the first RD assignment strategy, treated patients with an age > 33 years and control patients with an age ≤ 33 years, were selected to analyze the data as if it was an RD design.

In each scenario, the treatment effect was estimated with both local logistic regression(15) and a logistic regression model with treatment and adjusted for the assignment variable in an RCS term. The treatment effect was expressed as ORs with 95% confidence intervals (95% CI). Analyses were repeated 5,000 times. Random samples of 50% from the complete RCT data were drawn (5,000 times), to calculate the treatment effect from the RCT as a reference estimate. In this way we were able to compare the RD and RCT estimates in the same sample sizes.

To assess the heterogeneity of the treatment effect over the baseline assignment variable, we fitted a model with an interaction term between treatment and the different assignment models to the complete RCT data.

All statistical analyses were performed in R statistical software version 2.15.3 (R Foundation for Statistical Computation, Vienna, Austria) using the *rms* and *gam* packages.

RESULTS

Monte Carlo simulations

Simulations showed that treatment assignment based on a random or poorly correlating variable with outcome, resulted in higher relative efficiency compared to an unadjusted RCT, than RD with treatment assignment based on a higher correlating variable with outcome (Table 2). To obtain the same efficiency as an unadjusted RCT, RD required 2.8 times as many patients when using an assignment variable not correlating with outcome, and approxiamately 3.3 times as many patients when using an assignment variable highly (R^2 31%) correlating with outcome, when RD was analyzed with local regression. The relative efficiency was up to approximately 10 times as low with the strongly correlating assignment variable compared to an unadjusted RCT, when using logistic regression using adjustment. However, compared to an adjusted RCT, the relative efficiency was not dependent on the correlation between the treatment assignment variable and outcome. With local logistic regression, RD required at most 2.8 times as many patients compared to an adjusted RCT in all three assignment strategies (Table 2). In all three treatment assignment approaches, the estimated treatment effects were similar to the simulated treatment effect.

Case study

The median age in CRASH was 33 years (inter quartile range (IQR) 23-47), 2323 (24%) patients died within 14-days after injury. The correlation between the assignment variable

Table 2. Relative efficiency in terms of required sample size in an RD design for different baseline risk assessments compared to an RCT*.

	Assignment based on random variable		Assignment based on low (R^2=7%) correlating variable with outcome		Assignment based on high (R^2 =31%) correlating variable with outcome	
Simulated Odds Ratio	0.8	1.0	0.8	1.0	0.8	1.0
Compared to an unadjusted RCT						
RD no adjustment	1.00	1.00	-	-	-	-
RD RCS adjustment	6.39	6.39	9.78	9.99	10.04	10.12
RD local logistic regression	2.75	2.76	2.79	2.76	3.27	3.32
Compared to an adjusted RCT						
RD no adjustment	1.00	1.00	-	-	-	-
RD RCS adjustment	6.38	6.39	9.31	9.48	8.34	8.42
RD local logistic regression	2.74	2.75	2.65	2.62	2.72	2.77

Formula used to calculate the relative efficiency: $(SE_{RD} / SE_{RCT})^2$

age and 14-day mortality was low (R^2 7%). The correlation between the full model for treatment assignment including age, pupillary reactivity and motor score and mortality was stronger (R^2 31%) (Table 3).

In CRASH treatment had a negative effect on outcome overall. The mean unadjusted OR for treatment on 14-day mortality over in 5,000 subsets of 50% of the RCT was 1.20 [95% CI; 1.05-1.37] and 1.27 [1.08; 1.48] adjusted for the linear predictor defined by age, motor score and pupil reactivity. In the RCT data we found no statistically significant interaction between treatment and both of the assignment variables. However, non-linear RCS functions of the treatment effect over the assignment variable were plotted and showed in Figure 1 and suggests some interaction over the range of the assignment variable. The (local) estimates of the treatment effect in RD varied according to the assignment variable and corresponding cut-off. RD based on a random treatment assignment variable resulted in similar point estimates as the RCT, with and without RCS adjustment and with local logistic regression. The RD estimates were more similar to the global RCT estimates in the approach with assignment based on a poorly correlating variable with outcome compared to RD assignment based on a highly correlated variable with outcome; with assignment based on only age the adjusted ORs for treatment were 1.44 [0.95; 2.19] and 1.13 [0.91; 1.41] estimated with RCS adjusted logistic regression and local logistic regression respectively. In the RD design with assignment based on the higher correlating assignment variable, the estimates were less similar to the RCT effect estimate for treatment; the adjusted OR for treatment estimated with logistic regression was 1.69 [1.01; 2.82]. The estimated OR with local logistic regression was 1.41 [1.12; 1.76]) (Table 4).

Table 3. Patient characteristics and explained variance with 14-day mortality in the CRASH trial (n = 9,554)

Characteristic	N (%)	$R^{2\#}$
Random treatment allocation	4800 (50)	0^
Age, median (IQR)	33 (23 - 47)	7
Motor score*		22
1	785 (8)	
2	515 (5)	
3	659 (7)	
4	1181 (12)	
5/6	6414 (67)	
Pupillary reactivity		19
Both responsive	8100 (85)	
One responsive	597 (6)	
Both unresponsive	857 (9)	
Predicted probability from full prediction model**, median (IQR)	0.15 (0.08 – 0.31)	31
14-day mortality	2323 (24)	NA

 # Explained variance with 14-day mortality for CRASH
^ independent of the treatment effect (in the absence of treatment effect)
** 1 Makes no movements, 2 Extension to painful stimuli, 3 Abnormal flexion to painful stimuli, 4 Flexion/withdrawal to painful stimuli, 5/6 Localizes painful stimuli / Obeys commands*
***Age, motor score and pupillary reactivity*

DISCUSSION

We investigated the impact on efficiency of different associations of the treatment assignment variable with the outcome under study in the RD design. When assignment in RD was close to at random, or based on a variable that poorly correlates with outcome, estimates were more efficient than RD based on a variable highly correlating with outcome. These comparisons were made with the unadjusted treatment effect estimate from a similarly-sized RCT. However, compared to an adjusted treatment effect estimate from an RCT, the (in)efficiency of the RD design is independent of the correlation between assignment variable and outcome measure. In the case study, RD estimates from assignment based on a random variable or variable poorly correlating with outcome were more similar to the global RCT estimates than the RD estimates from assignment based on a variable highly correlating with outcome. These findings show that the relative efficiency of the RD design is not dependent on the correlation between the treatment assignment variable and outcome.

Table 4. RCT and RD analyses in the CRASH (n=9 554), repeated 5000 times.

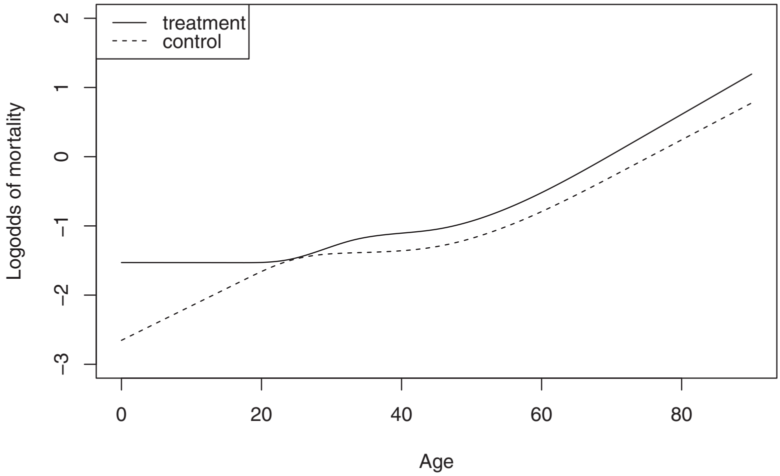
Analysis	Adjustment	Covariate for adjustment	N total	OR (95% CI) for 14-day mortality	Standard error
Randomized controlled trial (50% subset)					
Logistic regression	-		4777	1.20 (1.05-1.37)	0.07
Logistic regression	Linear	Age	4777	1.22 (1.06-1.40)	0.07
Logistic regression	RCS	Age	4777	1.22 (1.07-1.40)	0.07
Logistic regression	Linear	Linear predictor full model	4777	1.27 (1.09-1.48)	0.08
Logistic regression	RCS	Linear predictor full model	4777	1.27 (1.09-1.48)	0.08
Regression discontinuity: assignment based on random variable with no correlation with outcome					
Logistic regression	-		4777	1.20 (1.05-1.37)	0.07
Logistic regression	RCS	Random	4777	1.21 (0.86-1.69)	0.17
Local logistic regression	-		4777	1.20 (0.97-1.50)	0.11
Regression discontinuity: assignment based on low (R^2 = 0.07) correlating assignment model with outcome*					
Logistic regression	RCS	Age	4777	1.44 (0.95-2.19)	0.21
Local logistic regression	-		4777	1.13 (0.91-1.41)	0.11
Regression discontinuity: assignment based on high (R^2 = 0.31) correlating assignment model with outcome**					
Logistic regression	RCS	Linear predictor full model	4777	1.69 (1.01-2.82)	0.26
Local logistic regression	-		4777	1.41 (1.12-1.76)	0.11

** The median age was used as a cut-off for treatment assignment. Age ≤ 33 receiving no treatment and age > 33 receiving treatment.*
***Assignment based on the linear predictor of age, pupillary reactivity and motor score as predictors for outcome. The median linear predictor was used as a cut-off for treatment assignment.*

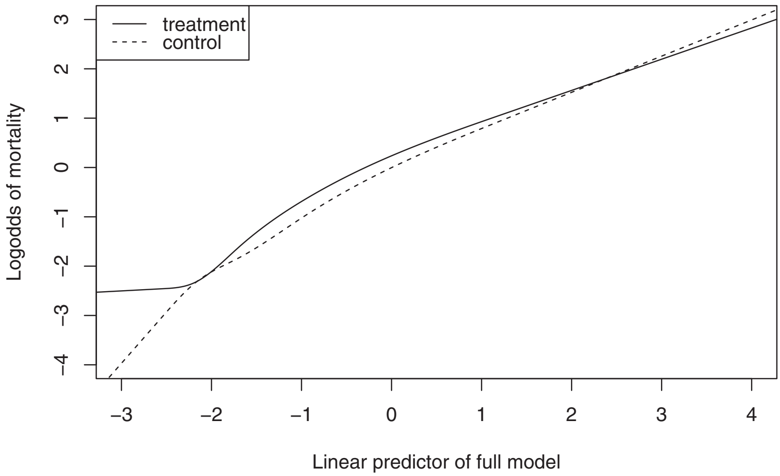
Efficiency of different RD assignment strategies

First, the simulation study shows higher relative efficiency of RD based on a random or poorly correlating variable than RD based on a higher correlating assignment variable, when compared to an unadjusted RCT. We found that RD based on a random variable needs 2.75 times as many patients to have the same statistical power as in an unadjusted RCT, which is similar to what has been described in other studies on the efficiency of RD compared to RCTs.(7, 8, 16, 17)

We note that treatment effect estimates in RD are conditional on the assignment variable. Thus, comparing RD estimates with conditional estimates from an RCT with adjustment for the assignment variable would be the more appropriate comparison. A feature of covariate adjustment with nonlinear models, such as logistic regression, is an increase of the standard error of the conditional treatment effect estimate from an RCT.(18-20) The increase in relative efficiency of RD based on a higher correlating assignment variable is eliminated when the standard errors of estimates are compared to the increased standard errors of the treatment effect estimate from the adjusted RCT, since the increase of standard error of the treatment effect estimated in an adjusted RCT is higher in case of a high correlating assignment variable. In other words, when the RCT estimates are conditioned on the same covariates as used in the RD design, the relative efficiency is independent of the correlation between the assignment variable and the outcome.



*A) Nonlinear rcs function (the function fitted is 14 day mortality ~ treatment * rcs [age]) of the interaction of the treatment effect over the range of age in the CRASH trial. Interaction test of age * treatment was not significant (p = 0.17).*



*B) Nonlinear rcs function (the function fitted is 14 day mortality ~ treatment * rcs [linear predictor of the full model]) of the interaction of the treatment effect over the range of the linear predictor in the CRASH trial. Interaction test of the linear predictor * treatment was not significant (p = 0.99).*

Figure 1. Density plot of the assignment variables and nonlinear restricted cubic spline functions of the interaction of the treatment effects over the range of the assignment variables in the CRASH trial (n=9,554).

In the simulations and in the case study two different methods for the analysis of the treatment effect estimate were used: local logistic regression and logistic regression with adjustment for the assignment variable using restricted cubic splines (RCS). The two methods both provided valid treatment effect estimates. However, estimation of the treatment effect using local logistic regression would be the preferred method to use in an RD design since both in the simulations and the case study this method resulted in lower standard errors; local logistic regression provides more efficient estimations.

Validity of different RD assignment strategies

The treatment effects estimated in RCTs can be interpreted as global treatment effects. Interpreting RD estimates as global treatment effect estimates requires the assumption of an identical treatment effect over the full range of the assignment variable. This implies that treatment does not interact with the baseline assignment variable.(2) However, the treatment effect could vary over de range of the assignment variable, as is shown in Figure 1. We were able to plot this effect since we had the RCT data available. In contrast, in a prospective RD design, the assumption of no interaction between treatment and the assignment variable cannot be tested, since the treatment groups each have data on only one side of the cut-off. The RD estimates should thus primarily be interpreted as local treatment effects at the assignment cut-off.(9) This is also illustrated in our case study in CRASH. As expected, RD based on a random treatment assignment variable resulted in the same treatment effect estimates as in the RCTs. The estimates from RD based on a poorly correlating variable with outcome were more similar to the global RCT estimates, compared to the RD estimates with assignment based on a variable highly correlating with outcome. Indeed, the treatment effect varied over the range of the higher correlating variable (Figure 1b). This might reflect a more general explanation that treatment effect heterogeneity over the range of the baseline assignment variable is less likely when an assignment variable has a no correlation with outcome. When treatment assignment is based on a random or poorly correlating variable with outcome in RD, it may be more acceptable to assume a global treatment effect over the range of the assignment variable and the estimates from RD can be interpreted as an average treatment effect.

Implications

We can debate the applicability of a prospective RD design and choosing a variable for treatment assignment. There might be more clinical support to assign treatment to high-risk patients, because these patients have the highest absolute benefit of treatment, when the relative benefit is similar over the whole range of the assignment variable.(21) In an RD design this approach would not increase efficiency. Thus, in RD we do not necessarily have to aim for an assignment variable that strongly correlates with outcome, such as a prognostic model that combines multiple predictors. It could be more practical to apply RD on a single baseline measurement, such as blood pressure, cholesterol level or age. The simplicity of this approach is an advantage. Besides, compared to an unadjusted RCT this approach is more efficient. In clinical practice, it is not uncommon that treatment is assigned based on a single baseline measurement; this treatment assignment strategy highly resembles treatment assignment in an RD design. For example, intensified medical treatment given to very low-birth-weight-babies (weighing less than 1,500 g).(4, 22) Also a CD4 count threshold is used in HIV patients to determine treatment assignment for immediate vs. deferred antiretroviral therapy.(4, 9) In traumatic brain injury, it is recommended to treat patients with intracranial pressure monitoring above 22 mmHg.(23) These are examples of treatment assignment in daily clinical practice that resemble a 'natural' application of the RD design. In theory, observational data of these examples could be used to assess the (local) effectiveness of treatment. Thus, RD based on one single measure as an assignment variable may be a good trade-off between efficiency and feasibility in clinical practice.

Conclusion and recommendations

In conclusion, compared to an unadjusted analysis, the efficiency of an RD design could be increased by using an assignment variable with a low correlation with the outcome of interest. However, the relative efficiency compared to an adjusted analysis of the treatment effect in an RCT, was not dependent on the correlation between the treatment assignment variable and outcome since the adjustment affects the efficiency of an RCT as well. We recommend researchers to use assignment variables that are feasible in clinical practice but do not necessarily have a high correlation with outcome, to facilitate patient inclusion and optimize efficiency in a prospective RD design.

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APPENDIX 1

```
## Activation of required libraries
library(rms)
library(foreign)
library(gam)

set.seed(100)

n_patients          <- 5000
treatment_effect  <- 0
n_sim      <- 10000
Est_Effect            <- matrix(nrow = n_sim, ncol=24)
colnames(Est_Effect)          <- c("Tx-effect RCT1", "se RCT1",
          "Tx-effect RCT2", "se RCT2",
          "Tx-effect RCT3", "se RCT3",
          "Tx-effect RCT4", "se RCT4",
          "Tx-effect RCT5", "se RCT5",
          "Tx-effect RDrandom1", "se RDrandom1",
          "Tx-effect RDrandom2", "se RDrandom2",
          "Tx-effect RDrandom3", "se RDrandom3",
          "Tx-effect RDlow1", "se RDlow1",
          "Tx-effect RDlow2", "se RDlow2",
          "Tx-effect RDhigh1", "se RDhigh1",
          "Tx-effect RDhigh2", "se RDhigh2")

for(i in 1:n_sim){
index      <- sample(1:nrow(data), replace = TRUE, size = n_patients)
data$motor          <- as.factor(data$motor)
data$pupils_i        <- as.factor(data$pupils_i)
data$random        <- rnorm(10008, 50, 12.5)
CRASH_sim <- data[index, c("age", "motor","pupils_i", "random")]
CRASH_sim$pupils_i1        <- CRASH_sim$pupils_i==1
CRASH_sim$pupils_i2        <- CRASH_sim$pupils_i==2
CRASH_sim$motor1           <- CRASH_sim$motor==2
CRASH_sim$motor2           <- CRASH_sim$motor==3
CRASH_sim$motor3           <- CRASH_sim$motor==4
CRASH_sim$motor4           <- CRASH_sim$motor==5
CRASH_sim$lp1    <- with(CRASH_sim, 0)
```

```
CRASH_sim$lp2   <- with(CRASH_sim, 0.0289 * age)
CRASH_sim$lp3   <- with(CRASH_sim, 0.0336 * age + 0.7878 * motor1 + 0.2312 * motor2
+ -0.2916 * motor3 + -1.3765 * motor4 + 0.9090 * pupils_i1 + 1.7841 * pupils_i2)

## Randomized controlled trial
# Treatment "Randomize all patients"
CRASH_sim$T_RCT          <- as.numeric(runif(n_patients) <= 0.5)
# Outcome "Randomize all patients"
CRASH_sim$O_RCTlp1       <- with(CRASH_sim, plogis(-1.1355 + lp1 + treatment_effect
* T_RCT)> runif(nrow(CRASH_sim)))
CRASH_sim$O_RCTlp2       <- with(CRASH_sim, plogis(-2.2671 + lp2 + treatment_effect
* T_RCT)> runif(nrow(CRASH_sim)))
CRASH_sim$O_RCTlp3       <- with(CRASH_sim, plogis(-1.9675 + lp3 + treatment_effect
* T_RCT)> runif(nrow(CRASH_sim)))
## Regression discontinuity, assignment with random variable
#Treatment "Regression discontinuity design"
CRASH_sim$T_RDD_R        <-        as.numeric(median(CRASH_sim$random)<CRASH_
sim$random)

#Outcome "Regression discontinuity design"
CRASH_sim$O_RDD_R        <- with(CRASH_sim, plogis(-1.1355 + lp1 + treatment_effect
* T_RDD_R)> runif(nrow(CRASH_sim)))

## Regression discontinuity, assignment with low correlating variable
#Treatment "Regression discontinuity design"
CRASH_sim$T_RDD_L        <- as.numeric(median(CRASH_sim$lp2)<CRASH_sim$lp2)

#Outcome "Regression discontinuity design"
CRASH_sim$O_RDD_L        <- with(CRASH_sim, plogis(-2.2671 + lp2 + treatment_effect
* T_RDD_L)> runif(nrow(CRASH_sim)))

## Regression discontinuity, assignment with high correlating variable
#Treatment "Regression discontinuity design"
CRASH_sim$T_RDD_H        <- as.numeric(median(CRASH_sim$lp3)<CRASH_sim$lp3)

#Outcome "Regression discontinuity design"
CRASH_sim$O_RDD_H        <- with(CRASH_sim, plogis(-1.9675 + lp3 + treatment_effect
* T_RDD_H)> runif(nrow(CRASH_sim)))
```

```
#fit RCT
fit_RCT1 <- lrm(O_RCTlp1 ~ T_RCT, data = CRASH_sim, x=T, y=T)
fit_RCT2 <- lrm(O_RCTlp2 ~ T_RCT, data = CRASH_sim, x=T, y=T)
fit_RCT3 <- lrm(O_RCTlp2 ~ T_RCT + lp2, data = CRASH_sim, x=T, y=T)
fit_RCT4 <- lrm(O_RCTlp3 ~ T_RCT, data = CRASH_sim, x=T, y=T)
fit_RCT5 <- lrm(O_RCTlp3 ~ T_RCT + lp3, data = CRASH_sim, x=T, y=T)
#fit RD with assignment based on random variable
fit_RDD_random1        <- lrm(O_RDD_R ~ T_RDD_R, data = CRASH_sim, x=T, y=T)
fit_RDD_random2        <- lrm(O_RDD_R ~ rcs(random) + T_RDD_R, data = CRASH_
sim, x=T, y=T)
fit_RDD_random3        <- gam(O_RDD_R ~ lo(random) + T_RDD_R, family = bino-
mial, data = CRASH_sim)
#fit RD with assignment based on low correlating variable
fit_RDD_low1    <- lrm(O_RDD_L ~ rcs(lp2) + T_RDD_L, data = CRASH_sim, x=T, y=T)
fit_RDD_low2    <- gam(O_RDD_L ~ lo(lp2) + T_RDD_L, family = binomial, data =
CRASH_sim)
#fit RD with assignment based on high correlating variable
fit_RDD_high1   <- lrm(O_RDD_H ~ rcs(lp3) + T_RDD_H, data = CRASH_sim, x=T, y=T)
fit_RDD_high2   <- gam(O_RDD_H ~ lo(lp3) + T_RDD_H, family = binomial, data =
CRASH_sim)

Est_Effect[i, ]    <- c(fit_RCT1$coefficients["T_RCT"],
        sqrt(fit_RCT1$var["T_RCT", "T_RCT"]),

        fit_RCT2$coefficients["T_RCT"],
        sqrt(fit_RCT2$var["T_RCT", "T_RCT"]),

        fit_RCT3$coefficients["T_RCT"],
        sqrt(fit_RCT3$var["T_RCT", "T_RCT"]),

        fit_RCT4$coefficients["T_RCT"],
        sqrt(fit_RCT4$var["T_RCT", "T_RCT"]),

        fit_RCT5$coefficients["T_RCT"],
        sqrt(fit_RCT5$var["T_RCT", "T_RCT"]),



        fit_RDD_random1$coefficients["T_RDD_R"],
```

```
        sqrt(fit_RDD_random1$var["T_RDD_R", "T_RDD_R"]),

        fit_RDD_random2$coefficients["T_RDD_R"],
        sqrt(fit_RDD_random2$var["T_RDD_R", "T_RDD_R"]),

        fit_RDD_random3$coefficients["T_RDD_R"],
        (sqrt(diag(vcov(fit_RDD_random3)))["T_RDD_R"]),



        fit_RDD_low1$coefficients["T_RDD_L"],
        sqrt(fit_RDD_low1$var["T_RDD_L", "T_RDD_L"]),

        fit_RDD_low2$coefficients["T_RDD_L"],
        (sqrt(diag(vcov(fit_RDD_low2)))["T_RDD_L"]),



        fit_RDD_high1$coefficients["T_RDD_H"],
        sqrt(fit_RDD_high1$var["T_RDD_H", "T_RDD_H"]),

        fit_RDD_high2$coefficients["T_RDD_H"],
        (sqrt(diag(vcov(fit_RDD_high2)))["T_RDD_H"]))

}

#Mean Effect estimate of treatment and standard error
colMeans(Est_Effect,na.rm=T)
```