R Lab 7 - Estimation, Part III: g-computation, IPTW, and TMLE estimation for longitudinal data using the ltmle package

Advanced Topics in Causal Inference

Assigned: November 16, 2021

Lab due: November 23, 2021 on bCourses. Please answer all questions and include relevant R code. You are encouraged to discuss the assignment in groups, but should not copy code or interpretations verbatim. Upload your own completed lab to bCourses.

Last lab:

"Traditional" longitudinal parametric g-computation estimator, g-computation estimator based on the ICE representation of the longitudinal g-computation formula, TMLE based on the ICE representation of the longitudinal g-computation formula (by hand).

Goals for this lab:

- 1. Implement ICE g-computation, IPTW, and TMLE using the ltmle package for all of the data structures/causal questions presented in the R Labs we have presented throughout the semester.
- 2. Performance and properties of these estimators.

1 Introduction and Motivation

In R Labs 4 and 6, we delved into estimation of causal parameters presented in R Lab 2. We hand-coded each of the estimators – IPTW, g-computation (parametric and ICE), and TMLE – to understand their inner workings. Lucky for us, in practice we don't have to hand-code these estimators to use them. The ltmle package implements them in one line!

Warning: remember that to infer any causality for a generated estimate, we must carefully and thoughtfully go through the roadmap learned in class.



Figure 1: Last lab! Thanks for a great semester:)

1.1 This lab

For each data structure, we will give you the variables in O (the data), causal question, target causal parameter (and its value), and definition of counterfactual outcomes. We will estimate all of the values of the causal parameters we defined in previous labs using IPTW, g-computation, and TMLE. We'll also interpet what these values mean. At the end of the lab, we'll comment on the properties of each of the estimators, drawing from the estimator performance results.

Refer back to R Lab 1 for variable definitions.

Before getting started, make sure you have loaded the ltmle package:

> library(ltmle)

1.2 To turn in:

For each of the 4 data structures listed below, answer the following questions:

- 1. Implement TMLE, IPTW, and g-computation estimators using the ltmle() function.
- 2. Show the point estimate and inference results for each of the estimators.
- 3. Interpret one of the three estimates. Make sure to comment on inference.
- 4. Comment on the estimators' performance and properties. We will give you performance results at the end of the lab.

Data Structure 1: $O = (W, A, L, \Delta, \Delta Y)$

Causal question: What is the absolute difference in expected test score if all students slept 8 or more hours compared to if all students slept less than 8 hours, under a hypothetical intervention to ensure that everyone takes the statistics test?

Causal parameter:

$$\Psi^F(P_{U,X}) = E_{U,X}[Y_{a=1,\Delta=1}] - E_{U,X}[Y_{a=0,\Delta=1}] = 5.871$$

Where the counterfactual $Y_{a,\Delta=1}$ is a random student's test score if, possibly contrary to fact, the student's sleep status had been A=a and his/her test score was observed ($\Delta=1$). The true value of the causal parameter can be interpreted as follows: the counterfactual expected test score would be 5.87 points higher if all students got 8 hours of sleep than if all students got less than 8 hours of sleep the night before their statistics test, with no loss to follow up.

- 1. Load DataStructure1.RData using the load() function. Make sure you have specified the correct file path. You should see 4 new things come up in your global environment:
 - ObsData1 this is a dataframe of 1,000 observations that follows Data Structure 1's observed data.
 - Psi.F1 this is the true $\Psi^F(P_{U,X})$ value for the target causal parameter $E_{U,X}[Y_{a=1,\Delta=1}] E_{U,X}[Y_{a=0,\Delta=1}]$ (generated in lab 2).
 - generate_data1 this is the function that generates n copies of Data Structure 1.
 - generate_data1_intervene we won't be using this function in this lab, so if you'd like you can erase it from your global environment using the rm() function.
 - > rm(generate_data1_intervene)
- 2. Examine ObsData1 using the head() function to re-familiarize yourself with the data.
- 3. Estimate the target causal parameter using the ltmle() function:
 - (a) Before calling the ltmle() function, within ObsData1, change the outcome DeltaY to be 0 if it is NA > ObsData1\$DeltaY[is.na(ObsData1\$DeltaY)] = 0
 - (b) Call the ltmle function. Within it, make sure to specify the following arguments: data, Anodes = c("A", "Delta") (i.e., the variables we're intervening on), Lnodes, and Ynodes = "DeltaY".
 - (c) Additionally, within the function specify the intervention on A we care about. In this case, we're interested in the difference in the mean outcome when A=1 and $\Delta=1$ minus A=0 and $\Delta=1$. Thus, set the argument abar to list(c(1,1), c(0,1)).
 - (d) Also within the function, specify the argument stratify = TRUE. Why do we need to ensure that we are stratifying on the intervention nodes?
 - (e) If the Qform and gform arguments are not specified, ltmle by default estimates each conditional distribution as an additive/main term function of all variables that precede it. Here, that is not the case. We need to specify the gform and Qform arguments as character vectors of the formula used to estimate the outcome regressions/treatment mechanism/missingness mechanism using a linear or logistic regression. Within the function, specify the Qform for L and ΔY , and gform for A and Δ , according to their correct specifications from R Lab 1:

$$\begin{split} A &= \mathbb{I} \big[U_A < expit(0.2^*W) \big] \\ L &= W + A + U_L \\ \Delta &= \mathbb{I} \big[U_\Delta < expit(2^*W + A - L + 3) \big] \\ Y &= L + 5^*A + 3^*W - 0.25^*A^*W + U_Y \end{split}$$

which translates to the following linear models:

$$\begin{split} g_0(A=1|W) &= expit(\beta_0 + \beta_1 W) \\ E_0[L|A,W] &= \beta_0 + \beta_1 W + \beta_2 A \\ P_0(\Delta=1|A,W,L) &= expit(\beta_0 + \beta_1 W + \beta_2 A + \beta_3 L) \\ E_0[Y|W,A,L] &= \beta_0 + \beta_1 L + \beta_2 A + \beta_3 W - \beta_4 A W \end{split}$$

Translated into R code:

- 4. Store the results in an object called results1. Show the causal parameter estimates using TMLE and IPTW by using the summary() function and specifying the argument "tmle" and "iptw", respectively.
- 5. Estimate the causal parameter using g-computation, and store these results as results1.gcomp. Show the g-computation estimates by using the summary() function and specifying the argument "gcomp".
- 6. Choose one of the three estimates implemented above and interpret.

Data Structure 2: $O = (\bar{L}(4), \bar{A}(4), Y)$

Causal question: How would the expected exam score at the end of the study (i.e., after t = 4 days) have differed if all students had gotten 8 or more hours of sleep every night during the entire study (i.e., at t = 1, 2, 3, 4 days) versus if all students had gotten less than 8 hours of sleep every night during the entire study (i.e., at t = 1, 2, 3, 4 days)?

Causal parameter:

$$\Psi^F(P_{U,X}) = E_{U,X}[Y_{\bar{a}(4)=1}] - E_{U,X}[Y_{\bar{a}(4)=0}] = 13.6183$$

Where the counterfactual $Y_{\bar{a}(4)}$ is a random student's test score if, possibly contrary to fact, the student's sleep status for the past 4 nights before the test was $\bar{A} = \bar{a}$. The expected counterfactual test score would be 13.62 points higher if all students had gotten 8 hours of sleep for the 4 nights leading up to the test than if all students got less than 8 hours for all 4 nights.

- 1. Load DataStructure2.RData using the load() function. A few things should come up in your global environment:
 - ObsData2 this is a dataframe of 1,000 students that follows Data Structure 2 from previous labs.
 - Psi.F2 this is the true $\Psi^F(P_{U,X})$ value for the target causal parameter $E_{U,X}[Y_{\bar{a}(4)=1}] E_{U,X}[Y_{\bar{a}(4)=0}]$ (generated in lab 2).
 - TrueMSMbeta1 this is the true $\Psi^F(P_{U,X})$ value for the target causal parameter β_1 from $m(\bar{a}|\beta)$, our MSM.
 - TrueMSMbeta1_wts this is the true $\Psi^F(P_{U,X})$ value for the target causal parameter β_1 from $m(\bar{a}|\beta)$, our weighted MSM.
 - generate_data2 this is the function that generates n copies of Data Structure 2.
 - generate_data2_intervene we won't be using this function in this lab, so if you'd like you can erase it from your global environment using the rm() function.
- 2. Examine ObsData2 using the head() function to re-familiarize yourself with the data.
- 3. Estimate the target causal parameter using the ltmle() function:
 - (a) Make sure to specify the data, Anodes, Lnodes, Ynodes arguments according to the corresponding variables in ObsData2.

- (b) Specify the intervention on \bar{A} we care about. In this case, we're interested in the difference in mean outcome when $\bar{A}=1=(a(1)=1,a(2)=1,a(3)=1,a(4)=1)$ minus $\bar{A}=0=(a(1)=0,a(2)=0,a(3)=0,a(4)=0)$. Thus, set the argument abar to list(c(1,1,1,1), c(0,0,0,0)).
- (c) Recall that each of the variables is a linear, additive function of all of the variables that precede it. Thus, we don't have to specify the Qform or gform arguments here, as these are the defaults for ltmle.
- 4. Store the results in an object called results2. Show the causal parameter estimates using TMLE and IPTW.
- 5. Finally, estimate the causal parameter using g-computation. Store these results as results2.gcomp and show the results for the g-computation estimator.
- 6. Choose one of the three estimates used above and interpret.

Bonus!

This section is optional, but could be useful if you are thinking of estimating parameters of an MSM for your project.

<u>Causal question 2:</u> How does cumulative days getting 8 or more hours of sleep affect students' statistics exam scores at the end of the study, assuming a linear relationship between total number of days on which a student got 8 or more hours of sleep and expected exam score?

Causal parameter 2:

$$\Psi^{F}(P_{U,X}) = m(\bar{a}|\beta) = E[Y_{\bar{a}}] = \beta_0 + \beta_1 \sum_{t=1}^{4} a(t)$$

Here we are interested in β_1 – for one additional night of 8 or more hours of sleep, what is the change in students' mean counterfactual test score?. The true dose-response curve's slope is 3.4. This means that, for one more night of 8 or more hours of sleep, students' statistics test scores increase by 3.4 points, on average.

- 1. Set n equal to the number of rows/observations in ObsData2.
- 2. Set up the arguments we will use to estimate the parameter using ltmleMSM().
 - (a) Initialize regimes, a binary array with dimensions: n by number of Anodes by the possible number of counterfactual treatment regimes.
 - (b) Initialize sumA, a vector of NAs of length equal to the number of possible counterfactual treatment regimes, where we will store the cumulative nights of sleep, or $\sum_{t=1}^{4} a(t)$, for each treatment regime.
 - (c) Make abar, a matrix of the possible counterfactual treatment regimes, with column names each of the A nodes:

```
> abar = as.matrix(expand.grid(c(0,1), c(0,1), c(0,1), c(0,1)) > colnames(abar) = c("A1", "A2", "A3", "A4")
```

(d) Within a for loop, store each treatment regime n times in the 3^{rd} dimension of the regimes array. Additionally, store $\sum_{t=1}^{4} a(t)$ for that regime:

```
> for (i in 1:16){
+
    regimes[,,i]=matrix(rep(abar[i,],n),byrow=TRUE,nrow=n)
+    sumA[i] = rowSums(regimes[,,i])[1]
+
+ }
```

- (e) Initialize summary.measures, an array with dimensions: the possible number of counterfactual treatment regimes by number of summary measures (*Hint:*, in this case we only want one summary measure) by the number of Ynodes we have.
- (f) Make the name of the second dimension of summary.measures called "sumA"
 - > dimnames(summary.measures)[[2]]=list("sumA")
- (g) Make the 3^{rd} dimension of the summary.measures array equal to a matrix version of sumA:
 - > summary.measures[,,1]=matrix(sumA)
- (h) Define working.msm a character formula for the working MSM. In our case, that would correspond to:
 - > working.msm = "Y ~ sumA"
- 3. Estimate the target causal parameter using the ltmleMSM() function:
 - (a) Make sure to specify the arguments data, Anodes, Lnodes, Ynodes, working.msm, regimes, summary.measures, msm.weights = NULL, and the gform (use the same specification as in the previous section).
- 4. Store the results in an object called results2.MSM. Show the causal parameter estimates using TMLE and IPTW.
- 5. Estimate the causal parameter using g-computation. Store (in results2.MSM.gcomp) and show the results for the g-computation estimator.
- 6. Choose one of the three estimates use above and interpret the significance value. Here, we cannot make interpretations using the value of the coefficient. Why is this? *Hint*: note that the coefficient estimates are based on a transformed Y that is between 0 and 1.

Data Structure 4:
$$O = (L(1), C(1), A(1), Y(2), L(2), C(2), A(2), Y(3))$$

Causal question: How would the counterfactual probability of becoming sick differ under an intervention to get 8 or more hours of sleep for 2 nights before a statistics test versus an intervention to get less than 8 hours of sleep for 2 nights before a statistics test, forcing all students to stay in the class for the time of observation?

Causal parameter:

$$\Psi^{F}(P_{U,X}) = E[Y(3)_{\bar{a}(2)=1,\bar{c}(2)=0}] - E[Y(3)_{\bar{a}(2)=0,\bar{c}(2)=0}]$$
$$= P(Y(3)_{\bar{a}(2)=1,\bar{c}(2)=0} = 1) - P(Y(3)_{\bar{a}(2)=0,\bar{c}(2)=0} = 1) = -0.2604$$

The counterfactual $Y(3)_{\bar{a}(2),\bar{c}(2)=0}$ is the student's illness status on day 3 of the study if, possibly contrary to fact, the student's sleep status was $\bar{A}(2) = \bar{a}(2)$ and he/she remained in the class $\bar{C}(2) = 0$. The difference in counterfactual probability of getting sick if all SPH students got 8 or more hours of sleep every night (setting $\bar{A}(2) = 1$) minus the counterfactual probability of getting sick if all SPH students got fewer than 8 hours of sleep every night (setting $\bar{A}(2) = 0$), ensuring no loss to follow-up by setting $\bar{C}(2) = 0$ (i.e., intervening to ensure that no students drop out of the class) is -26.04%.

- 1. Load DataStructure4.RData. Four things should come up in your global environment:
 - ObsData4 this is a dataframe of 1,000 observations that follows Data Structure 4.
 - Psi.F4 the true $\Psi^F(P_{U,X})$ value for the target causal parameter $P(Y(3)_{\bar{a}(2)=1,\bar{c}(2)=0}=1)$ $P(Y(3)_{\bar{a}(2)=0,\bar{c}(2)=0}=1)$ (generated in lab 2).
 - generate_data4 this is the function that generates n copies of Data Structure 4.
 - generate_data4_intervene we won't be using this function in this lab, so if you'd like you can erase it from your global environment using the rm() function.
- 2. Examine ObsData4 using the head() function to re-familiarize yourself with the data.

- 3. Estimate the target causal parameter using the ltmle() function:
 - (a) Before calling the ltmle function: the ltmle() function requires censoring nodes (i.e., Cnodes) to be a factor variable with levels "censored" and "uncensored". The ltmle package includes a helper function called BinaryToCensoring() that allows us to do this in one line. Recode the censoring nodes in ObsData4 as such. For example, for C1 in ObsData4:
 - > ObsData4\$C1 = BinaryToCensoring(is.censored = ObsData4\$C1)
 Do the same for C2.
 - (b) Call the ltmle() function, specifying the data, Anodes, Lnodes, Cnodes, Ynodes arguments according to the corresponding variable names in ObsData4. Remember there are two Y values here!
 - (c) Also specify survivalOutcome = TRUE.
 - (d) Specify the intervention \bar{A} we care about. Here, we are interested in the difference in mean outcome when $\bar{A}=1$ minus $\bar{A}=0$.
 - (e) Recall that each of the variables is a linear, additive function of all of the variables that precede it. Thus, we don't have to specify the Qform or gform arguments here, as these are the defaults for ltmle.
- 4. Store the results in an object called results4. Show the causal parameter estimates using TMLE and IPTW.
- 5. Estimate the causal parameter using g-computation in an object called results4.gcomp and show its results.
- 6. Choose one of the three estimates used above and interpret.

Data Structure 0: O = (L(1), A(1), L(2), A(2), Y)

In this section we will estimate the effects of a *dynamic regime*. Recall that a dynamic regime is a rule for assigning treatment based on a subject's characteristics.

Within the context of your pretend GSR project, you can think of the variables in O as:

- L(t) = a standardized measure of the amount of time you napped the night before, for t = 1, 2
- A(t) = a variable indicating whether or not you slept 8 or more hours, for t = 1, 2
- Y = a variable indicating that you are sick on test day

For the causal question corresponding to this data structure, we are assigning treatment (student must get 8 hours of sleep) at each time point based on the subject's observed L (amount of nap time) at that timepoint.

Causal question: What is the expected outcome, Y, if all subjects' treatment at time t was set to 1 if L(t) < 0, otherwise their treatment at time t was set to 0 if $L(t) \ge 0$, for t = 1, 2? What is the probability of getting sick on test day if subjects were assigned to get 8 hours of sleep at time t if their standardized nap time at time t was less than 0, but were assigned to get less than 8 hours of sleep if their standardized nap time was ≥ 0 , for t = 1, 2?

Causal parameter:

$$\Psi^F(P_{U,X}) = E_{U,X}[Y_{d_{\theta}}] = 0.2615$$

Here, the intervention is the decision rule to assign the treatment A(t) a value of 1 if L(t) falls below the threshold $\theta = 0$ for t = 1, 2. The notation for this is:

$$A(t) = \begin{cases} 1, & \text{if } L(t) < 0\\ 0, & \text{if } L(t) \ge 0 \end{cases}$$

For t = 1, 2. Thus, the dynamic regime would be the set of rules $d_{\theta} = (d_{\theta,1}(L(1)), d_{\theta,2}(L(2)))$.

The counterfactual $Y_{d_{\theta}}$ is a random subject's outcome if, possibly contrary to fact, the treatment at time t had been given according to the rule: $d_{\theta}(L(t))$ for t = 1, 2. In other words, a student's health status if, possibly contrary to fact, their sleep regimen had occurred according to a treatment rule based on the amount of time they napped. The counterfactual expected outcome (probability of getting sick) is 0.2615 if all subjects followed the rule $d_{\theta}(L(t))$.

Note that if all students had been assigned 8 hours of sleep the probability of becoming sick would be about 0.6437, and if all students had been assigned less than 8 hours of sleep the probability of getting sick would be about 0.5002 – both of these probabilities of getting sick are higher than assigning treatment based on the dynamic treatment rule. From this we can conclude that getting 8 hours of sleep works for some people, but not others, and assigning 8 hours of sleep in an *individualized* way (i.e., based on subjects' nap habits) yields better outcomes than giving everyone the same sleep schedule (which is something we might've concluded had we only calculated the ATE!).

The Sequential Randomization Assumption (SRA) for dynamic regimes will allow us to identify the causal parameter as a function of the observed data distribution. The SRA for this case is:

$$Y_{d_{\theta}} \perp A(t) | \bar{L}(t), \bar{A}(t-1) \text{ for } t = 1, 2$$

Under the SRA, our g-computation formula (a parameter of the observed data distribution) is then:

$$\Psi^F(P_{U,X}) \stackrel{\text{assumptions}}{=} \sum_{\bar{l}} E_0[Y|A(2) = d(l(2)), L(2) = l(2), A(1) = d(l(1)), L(1) = l(1)]$$

$$\times P_0(L(2) = l(t)|A(1) = d(l(1)), L(1) = l(1))$$

$$\times P_0(L(1) = l(1))$$

- 1. Load DataStructureO_dtr.RData using the load() function. Make sure you have specified the correct file path. You should see 4 new things come up in your global environment:
 - ObsDataO_dtr this is a dataframe of 1,000 observations that follows Data Structure 0.
 - Psi.F0_dtr this is the true $\Psi^F(P_{U,X})$ value for the target causal parameter $E_{U,X}[Y_{d_{\theta}}]$.
 - generate_data0_dtr this is a function that generates n copies of Data Structure 0.
 - generate_dataO_dtr_intervene we won't be using this function in this lab, so if you'd like you can erase it from your global environment using the rm() function.
- 2. Examine ObsDataO_dtr to familiarize yourself with the data using the head() function.
- 3. Estimate the target causal parameter using the ltmle() function:
 - (a) Before calling the ltmle() function, make a dataframe of treatment regimes according to the rule we care about, and set it equal to abar. For example, we want the first column of abar to be 1 if L1 in ObsData0 is less than 0, and 0 otherwise. Same for the second column:
 - > abar = cbind(ObsDataO_dtr\$L1 < 0, ObsDataO_dtr\$L2 < 0)
 - (b) Within the ltmle() function, make sure to specify the arguments data, Anodes, Lnodes, and Ynodes according to the corresponding variable names in ObsDataO_dtr. For example, Anodes = c("A1", "A2") and Ynodes = "Y".

- (c) Additionally, specify the abar argument using the object you made previously.
- (d) The outcome regression here is not a main term/additive function of all of the variables that precede it. Thus, we need to specify the Qform argument as a character vector of the formula used to estimate the outcome regression and conditional expectation of L(2). The correct model specifications are:

$$E_0[L(2)|L(1), A(1)] = \beta_0 + \beta_1 L(1) + \beta_2 A(1)$$

$$E_0[Y|\bar{L}(2), \bar{A}(2)] = expit[\beta_0 + \beta_2 L(1)A(1) + \beta_3 L(2)A(2)]$$

- 4. Store the results in an object called results0. Show the causal parameter estimates using TMLE and IPTW by using the summary() function and specifying the argument "tmle" and "iptw", respectively. For example, for TMLE:
 - > summary(results0, "tmle")
- 5. Finally, estimate the causal parameter using g-computation by specifying the same arguments as results0 in the ltmle() function, except include the argument gcomp = TRUE. Store these results as results0.gcomp and show the g-computation estimates by using the summary() function and specifying the argument "gcomp".
- 6. Choose one of the three estimates implement above and interpret.

Performance of estimators

Following are tables describing each estimator's performance (bias, variance, MSE, and proportion confidence interval coverage of the truth) for each data structure/causal parameter. Comment on the strengths and weaknesses of each estimator based on our discussions in class, and draw from the performance results shown below as examples of their properties.

	tmle1	iptw1	gcomp1
Bias	0.006	0.007	0.006
Variance	0.005	0.005	0.005
MSE	0.005	0.005	0.005
Coverage	0.95	1	-

Table 1: Performance - Data Structure 1 for $E_{U,X}[Y_{a=1,\Delta=1}] - E_{U,X}[Y_{a=0,\Delta=1}]$

	tmle2	iptw2	gcomp2
Bias	-0.031	-0.03	-0.097
Variance	0.382	1.152	0.219
MSE	0.383	1.153	0.228
Coverage	0.951	0.986	-

Table 2: Performance - Data Structure 2 for $E_{U,X}[Y_{\bar{a}(4)=1}] - E_{U,X}[Y_{\bar{a}(4)=0}]$

	tmle4	iptw4	gcomp4
Bias	0.002	0.002	0.002
Variance	0.001	0.002	0.001
MSE	0.001	0.002	0.001
Coverage	0.955	0.98	-

Table 3: Performance - Data Structure 4 for $P(Y(3)_{\bar{a}(2)=1,\bar{c}(2)=0}=1) - P(Y(3)_{\bar{a}(2)=0,\bar{c}(2)=0}=1)$

	tmle0	iptw0	gcomp0
Bias	0.0	0.0	-0.001
Variance	0.001	0.001	0.0
MSE	0.001	0.001	0.0
Coverage	0.949	0.955	-

Table 4: Performance - Data Structure 0 for $E_{U,X}[Y_{\theta}]$

Bonus questions:

- 1. Calculate each estimator's bias, variance and MSE to replicate these performance results.
- 2. Why do we omit confidence interval coverage for the g-computation estimator?

2 Optional Feedback

Please attach responses to these questions to your lab. Thank you in advance!

- 1. Did you catch any errors in this lab? If so, where?
- 2. What did you learn in this lab?
- 3. Do you think that this lab met the goals listed at the beginning?
- 4. What else would you have liked to review? What would have helped your understanding?
- 5. Any other feedback?