Potential Outcome and Randomized Control Trial

Credit : J. Josse, J. Peters, B. Neal, S. Wager

Potential outcome framework (Neyman, 1923, Rubin, 1974)

For a set of i.i.d. subjects $i = 1, \cdots, n$, we observe a tuple (T_i, X_i, Y_i),

- Treatment $T_i \in \{0, 1\}$
- Covariates $X_i \in \mathbb{R}^d$
- Outcome $Y_i \in \mathbb{R}$

Covariates			Treatment	Outcome
X_1	X_2	X_3	T	Y
5	1	F	1	10
-1	2	M	1	5
...	...	...		
6	4	M	0	6

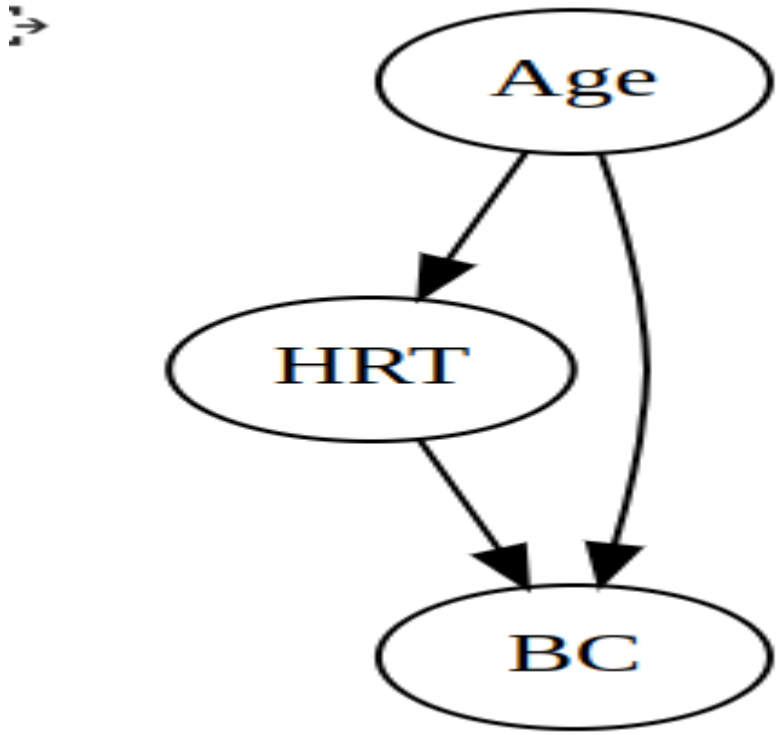
Potential outcome framework (Neyman, 1923, Rubin, 1974)

A practical example (Jérolon et al. (2021))

- (HRT) : Hormone Replacement Therapy
- (A) : Age
- (BC) : Breast Cancer Risk

Causal effect of (HRT) on (BC) taking into account the covariate (A)?

Potential outcome framework (Neyman, 1923, Rubin, 1974)



Potential outcome framework (Neyman, 1923, Rubin, 1974)

- Covariates $X_i \in \mathbb{R}^d$
- T_i binary treatment, Y_i outcome.
- for each individual i, two potential outcomes:
  - $Y_i(0)$ outcome if we do not apply the treatment (ie $T_i = 0$)
  - $Yi(1)$ outcome if we apply the treatment (ie $T_i = 1$)

X_1	X_2	X_3	T	Y	Y(0)	Y(1)
5	1	F	1	10	?	10
-1	2	M	1	5	?	5
⋮	⋮	⋮	⋮	⋮	⋮	⋮
...	...	...	0	6	6	?
...	...	...	1	8	?	8
6	4	M	0	4	4	?

Potential outcome framework (Neyman, 1923, Rubin, 1974)

- only one of the two is observed
- the potential outcomes that you do not (and cannot) observe are known as counterfactuals because they are counter to fact (reality)

X_1	X_2	X_3	T	Y	Y(0)	Y(1)
5	1	F	1	10	?	10
-1	2	M	1	5	?	5
⋮	⋮	⋮	⋮	⋮	⋮	⋮
...	...	...	0	6	6	?
...	...	...	1	8	?	8
6	4	M	0	4	4	?

Potential outcome framework (Neyman, 1923, Rubin, 1974)

Notion of intervention

- One may intervene on an input variable, setting a given value for one of the input variable
- What is the corresponding value of the outcome?

Potential outcome framework (Neyman, 1923, Rubin, 1974)

An example

We simulate an example

$$T = f_1(a_1 \cdot X + \varepsilon_1)$$

$$Y = f_2(a_2 \cdot T + b_2 \cdot X + \varepsilon_2)$$

where $(X, \varepsilon_1, \varepsilon_2)$ are mutually independent random variables with given distribution.

Potential outcome framework (Neyman, 1923, Rubin, 1974)

Notion of intervention

Intervening on T, setting $T := t$ means that we replace the system with

$$T := t$$

$$Y = f_2(a_2 \cdot t + b_2 \cdot X + \varepsilon_2)$$

where (X, ε_2) are two independent random variables with given distribution.

Potential outcome framework (Neyman, 1923, Rubin, 1974)

Notion of counterfactual

- We assume now that we have observed $(X, T, Y) = (1, -1, 1)$ with $f_1 = f_2 := t \mapsto t$, $a_1 = a_2 = b_2 = 1$.
- One can find the values of the noises $(\varepsilon_1^*, \varepsilon_2^*)$ corresponding to the observation $(X, T, Y) = (1, -1, 1)$
- If we now set another value t_{new} for T, we then deduce the value of X and Y corrsponding to $(T, \varepsilon_1, \varepsilon_2) = (t_{new}, \varepsilon_1^*, \varepsilon_2^*)$

Potential outcome framework (Neyman, 1923, Rubin, 1974)

We first consider a simple case without covariates.

Basic definitions

- Individual Causal Effect of individual i,

$$\tau_i := Y_i(1) - Y_i(0)$$

- Fundamental problem of causal inference : $Y_i(0)$ and $Y_i(1)$ cannot be both observed!
- Hence the individual treatment effect cannot be computed in practice

Potential outcome framework (Neyman, 1923, Rubin, 1974)

(A) : we observe n i.i.d. samples (T_i, Y_i)

Basic definitions

- Average treatment effect (ATE), $\tau = \mathbb{E}[Y_i(1) - Y_i(0)]$
- Estimation from observational data?
- A causal quantity (for e.g. $\mathbb{E}[Y(t)]$) is identifiable if we can compute it from a purely statistical quantity (for e.g. $\mathbb{E}[Y|T = t]$)

Shall we need additional assumptions?

Assumptions

Stable-Unit-Treatment-Value Assumption (Rubin, 1980)

- the outcome for individual i is assumed not depend on whether other individuals got treated or not (i.e. no interference between units)
- that there are not multiple versions of a treatment : if the treatment is a surgery then the surgery is assumed to be identically performed by all surgeons

Q: If the treatment is vaccination, is SUTVA met?

Assumptions

Additional assumptions

- Consistency. If the treatment is T, then the observed outcome Y is the potential outcome under treatment T. Formally,

$$T = t \Rightarrow Y = Y(t)$$

- Ignorability / Exchangeability (Randomized Control Trials)

$$(Y(0, Y(1)) \perp\!\!\!\perp T$$

Individuals are randomly assigned their treatment

Consequences

Using the previous assumptions we deduce that

$$\begin{aligned}
\tau &= \mathbb{E}[Y_i(1)] - \mathbb{E}[Y_i(0)] \\
&= \mathbb{E}[Y_i(1)|T=1] - \mathbb{E}[Y_i(0)|T=0] \text{ (consistency)} \\
&= \mathbb{E}[Y_i|T=1] - \mathbb{E}[Y_i|T=0] \text{ (ignorability)}
\end{aligned}$$

The ATE is then identifiable in the case of RCT

Difference in means estimator

Observe n iid samples (T_i, Y_i) each satisfying:

- $Y_i = T_i Y_i(1) + (1 - T_i) Y_i(0)$
- $T_i \perp\!\!\!\perp (Y_i(0), Y_i(1))$

One defines

$$\widehat{\tau}_{DM} = \frac{1}{n_1} \sum_{T=1} Y_i - \frac{1}{n_0} \sum_{T=0} Y_i$$

X_1	X_2	X_3	T	Y	Y(0)	Y(1)
5	1	F	1	10	?	10
...	...	...	0	6	6	?
...	...	...	1	8	?	8
6	4	M	0	4	4	?

ATE=mean(orange)-mean(green)

Difference in means estimator

Properties of $\widehat{\tau}_{DM}$

- $\mathbb{E}[\widehat{\tau}_{DM}] = \tau$ [unbiased estimator]
- $Var(\widehat{\tau}_{DM}) = \frac{Var(Y_i(0))}{n_0} + \frac{Var(Y_i(1))}{n_1}$
- Using CLT, one has

$$\sqrt{n}(\widehat{\tau}_{DM} - \tau) \xrightarrow{(d)} \mathcal{N}(0, V_{DM})$$

with

$$V_{DM} = \frac{Var(Y_i(0))}{\mathbb{P}[T=0]} + \frac{Var(Y_i(1))}{\mathbb{P}[T=1]}$$

- Consequence : one can give CI for $\widehat{\tau}_{DM}$ [see Lab1]

Proof: See chapter 1 Stefan Wager lecture or Theorem 6.3 p. 89 Imbens, Rubin

Difference in means estimator

Properties of $\widehat{\tau}_{DM}$

- conceptually simple estimator and simple to estimate,
- consistent estimator with asymptotically valid inference,
- but is it the optimal way to use the data for fixed finite n?
- What can be problematic even with a RCT in finite sample?

Difference in means estimator

- The outcome Y is daily air quality index. The treatment imposes restrictions on driving to reduce traffic
- Weather (W) has an effect on ozone (hot days have higher levels), independently of treatment
- If we randomly assign treatment to more hot days and control to more cold days, our estimates we exaggerate (or inverse) the treatment effect.
- Large samples: these effects cancel out small samples they matter
- If we could predict and eliminate the effect of weather, we would improve accuracy

Improving DM estimator

Covariate balance

- Under randomization, distribution of the covariates in treated and control groups must be similar.
- If not the case, two possibilities: 1) Randomization was compromised 2) Sampling error (bad luck)

Compare the treatment group and a control group

- If control group looks like treatment group, difference in response likely due to treatment
- if control group does not look like treatment group, difference in response may be confounded by differences in the group

Difference in means estimator

Adding the covariates

- Correct for covariate imbalances
- Increase precision: remove variation in the outcome accounted for by pre-treatment characteristics, thus making it easier to attribute remaining differences to the treatment

A practical example : see notebook

Randomized trials in the linear model

Idea: assume linearity of the responses $Y_i(0)$ and $Y_i(1)$ in the covariates.

Assumptions:

- n iid samples (Xi, T_i, Yi),
- $Y_i(t) = c(t) + X_i\beta(t) + \varepsilon_i(t), t \in \{0, 1\}$ with $\varepsilon_i \perp\!\!\!\perp X_i$
- Set $\mu_t(x) := \mathbb{E}[Y_i(t)|X_i = x]$.
- Assumptions : $\mathbb{E}[\varepsilon_i(t)|X_i] = 0$ and $Var(\varepsilon_i(t)|X_i = x) = \sigma^2$

One has:

$$\begin{aligned}
\tau &= \mathbb{E}[Y_i(1)] - \mathbb{E}[Y_i(0)] \\
&= \mathbb{E}_X\mathbb{E}[Y_i(1)|X_i] - \mathbb{E}_X[Y_i(0)|X_i] \\
&= \mathbb{E}[\mu_1(X_i)] - \mathbb{E}[\mu_0(X_i)] \\
&= \mathbb{E}[c_1 - c_0 + X_i(\beta(1) - \beta(0))]
\end{aligned}$$

Randomized trials in the linear model

- Estimation of $c(t), \beta(t)$?
- The quantity $\mu_t(x) := \mathbb{E}[Y_i(t)|X_i = x]$ should be identifiable
- Assumptions
  - Consistency ,
  - Exchangeability $((Y(0), Y(1)) \perp\!\!\!\perp T)$
  - Covariate balance : $X \perp\!\!\!\perp X$
- Under these assumptions, on has

$$\mathbb{E}[Y_i(t)|X_i = x] = \mathbb{E}[Y_i(t)|X_i = x, T_i = t] = \mathbb{E}[Y_i|X_i = x, T_i = t]$$

Randomized trials in the linear model

This suggests an estimator based on a regression adjustment

$$\frac{1}{n}\sum_i (\widehat{\mu}_1(X_i) - \widehat{\mu}_0(X_i))$$

where $\widehat{\mu}_t(X_i)$ is obtained by regression Y_i on X_i on those observations with $T_i = t$.

Randomized trials in the linear model

OLS estimator

$$\begin{aligned}\widehat{\tau}_{OLS} &= \widehat{c}(1) - \widehat{c}(0) + \overline{X}(\widehat{\beta}(1) - \widehat{\beta}(0)) \\ &= \frac{1}{n}\sum_i ((\widehat{c}(1) + X_i\widehat{\beta}(1)) - (\widehat{c}(0) + X_i\widehat{\beta}(0)))\end{aligned}$$

where $\overline{X} = \frac{1}{n}\sum_i X_i$ and the estimators are obtained by OLS for the two linear models.

We run two separate regressions, make predictions and then obtain treatment effect estimation.

Randomized trials in the linear model

Without loss of generality we additionally assume:

- $\mathbb{P}[T = 0] = \mathbb{P}[T = 0] = 1/2$
- $\mathbb{E}[X] = 0$
- $A = Var(X)$

By definition

$$\begin{aligned}\widehat{\tau}_{OLS} - \tau &= (\widehat{c}(1) - c(1)) - (\widehat{c}(0) - c(0)) + \overline{X}(\beta(1) - \beta(0)) \\ &\quad + \overline{X}((\widehat{\beta}(1) - \beta(1)) - (\widehat{\beta}(0) - \beta(0))\end{aligned}$$

Randomized trials in the linear model

Properties of $\widehat{\tau}_{OLS}$

Noting $V_{OLS} = 4\sigma^2 + \|\beta(1) - \beta(0)\|_A^2$, by central limit theorem we get

$$\sqrt{n}(\widehat{\tau}_{OLS} - \tau) \overset{(d)}{\to} \mathcal{N}(0, V_{OLS})$$

This variance can be compared to V_{DM}, that can be proved to be in this setting

$$V_{DM} = 4\sigma^2 + \|\beta(1) - \beta(0)\|_A^2 + \|\beta(1) + \beta(0)\|_A^2$$

Proof: See chapter 1 Stefan Wager lecture
Examples : see Lab 1

RCT in practice

Gold standard to assess the causal effect of an intervention or treatment on an outcome.

- The allocation of the treatment is under control. The distribution of the covariates for treated and control patients is balanced (as many young/old; diabetic/non diabetic, etc.) so that a simple difference in means estimator can be consistent.
- Control group looks like treatment group: difference in response likely due to treatment.

RCT in practice

Drawbacks

- expensive, take a long time to set,
- small sample size, due to either recruitment difficulties or restrictive inclusion/exclusion criteria.
- narrowly-defined trial sample that is different from the population potentially eligible for the treatment
- Lack of generalizability (external validity) to a target population. Study in one company/hospital/state/country could fail to generalize to others