Machine Learning for Causal Inference

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Machine learning cannot automate causal inference… but maybe it can help some difficult parts of estimating causal effects

Review: Estimands, estimators, and estimates

Normal regression estimates associations. But we want ***causal*** estimates: what would happen if ***everyone*** in the study were exposed to x vs if ***no one*** was exposed.

estimand

Ingredients

- 150g unsalted butter, plus extra for greasing
- 150g plain chocolate, broken into pieces
- 150g plain flour
- ½ tsp baking powder
- ½ tsp bicarbonate of soda
- 200g light muscovado sugar
- 2 large eggs

Method

1. Heat the oven to 160C/140C fan/gas 3. Grease and base line a 1 litre heatproof glass pudding basin and a 450g loaf tin with baking parchment.

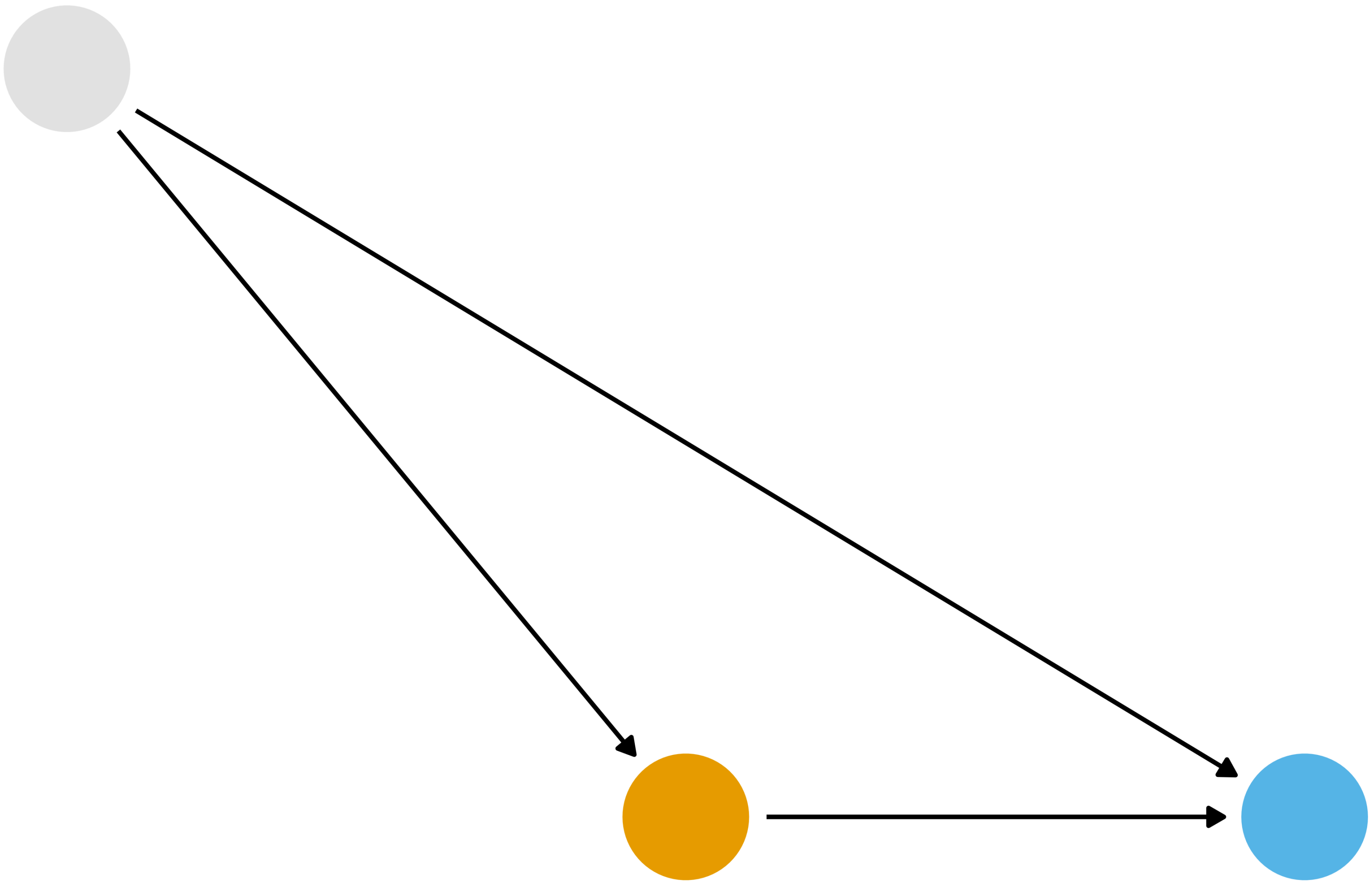
2. Put the butter and chocolate into a saucepan and melt over a low heat, stirring. When the chocolate has all melted remove from the heat.

estimator

estimate

Image source: Simon Grund

What part of the DAG do we want to try to deal with?



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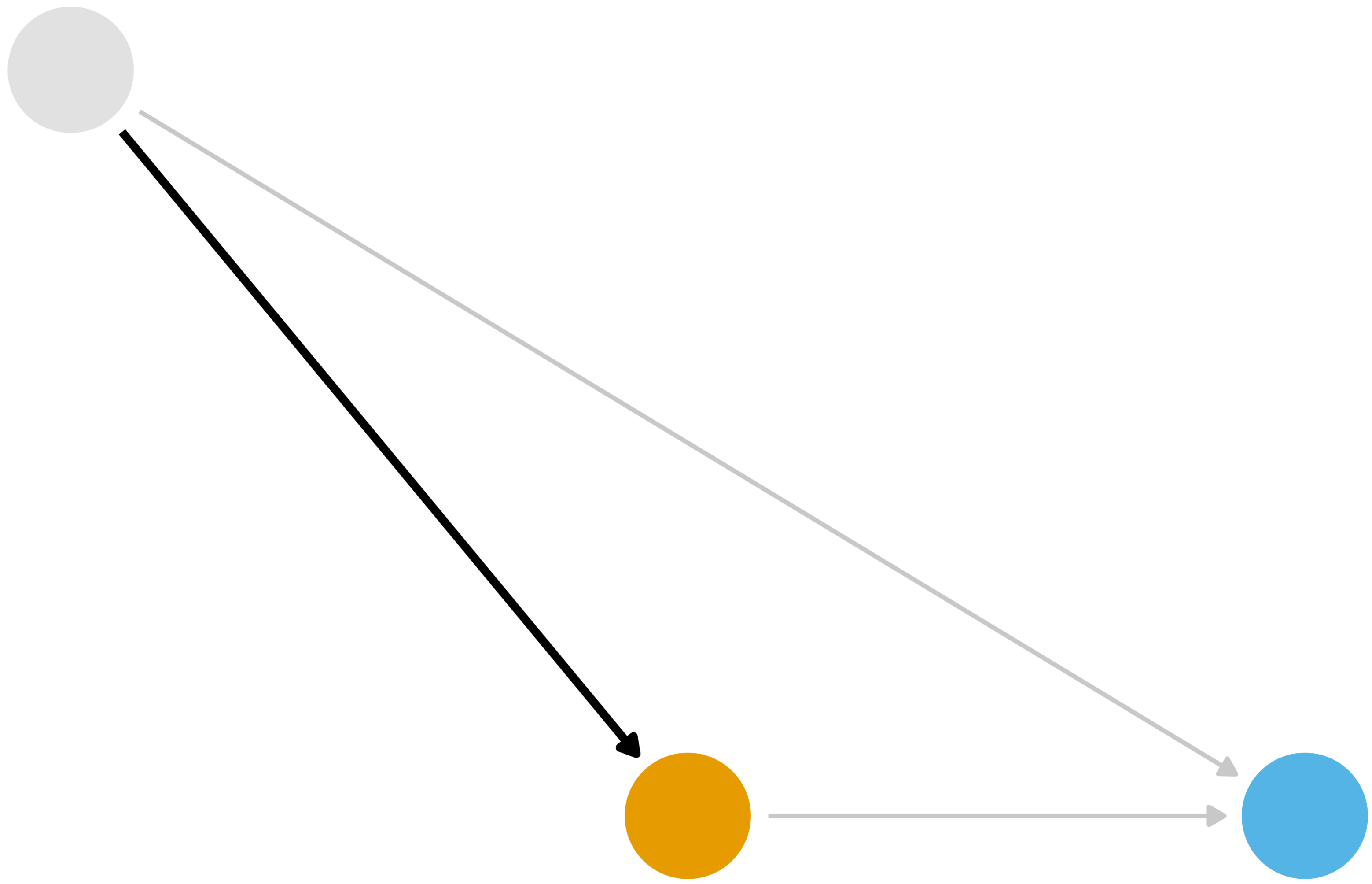

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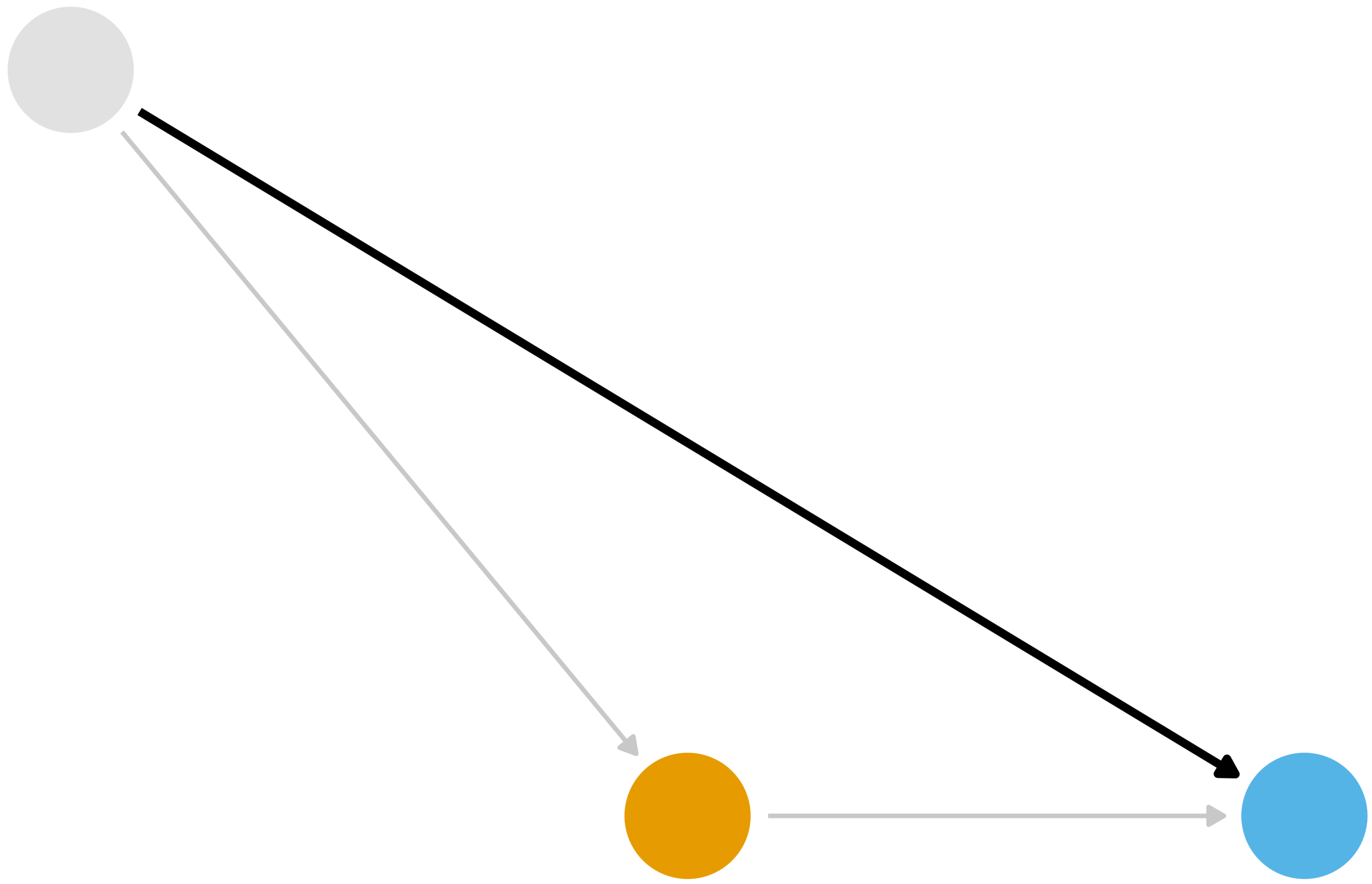
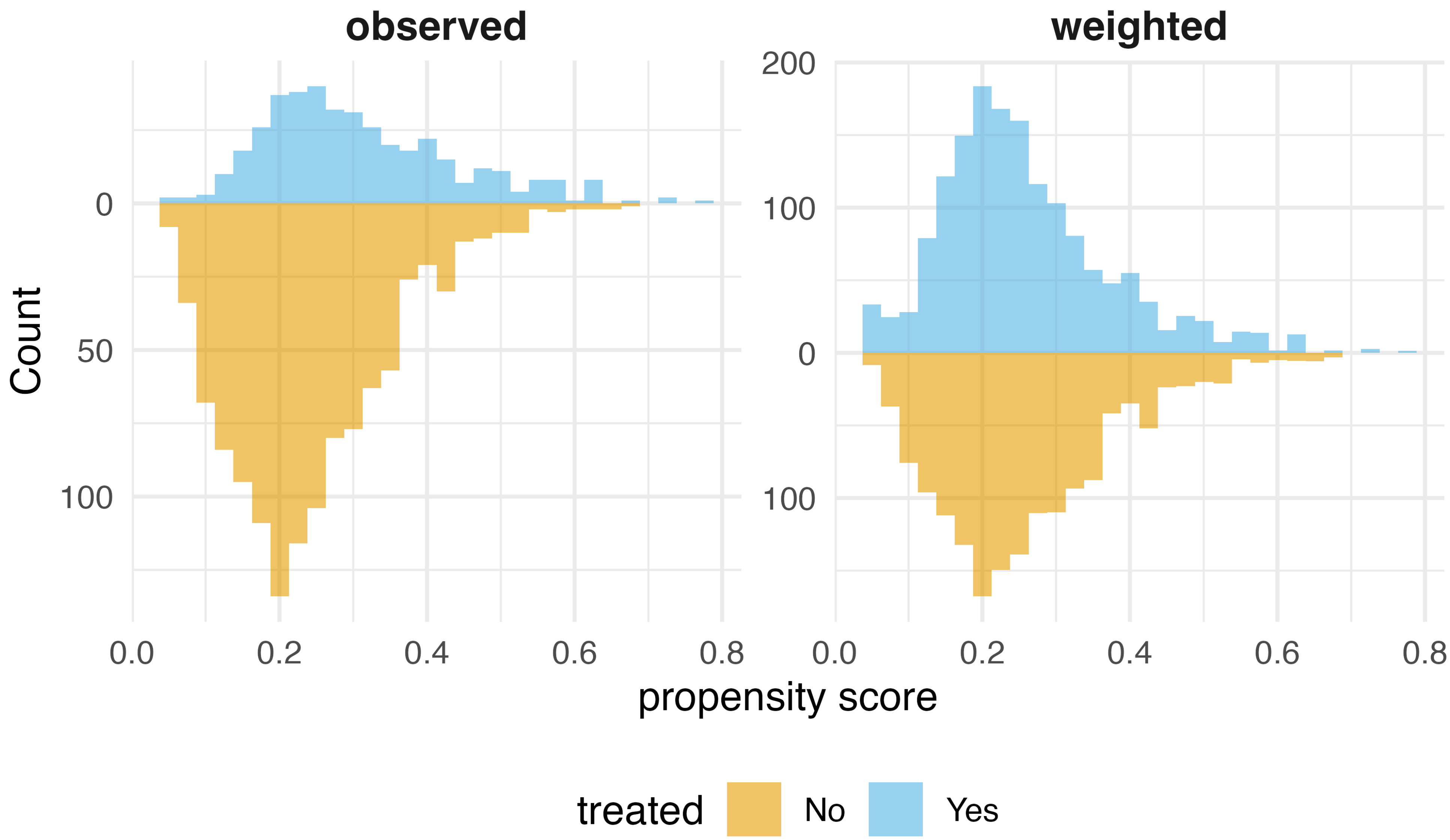


Inverse Probability Weighting (IPW)

1. Fit a model for `x ~ z` where z is all confounders
2. Calculate the propensity score for each observation
3. Calculate the weights
4. Fit a weighted regression model for `y ~ x` using the weights

Inverse Probability Weighting (IPW)



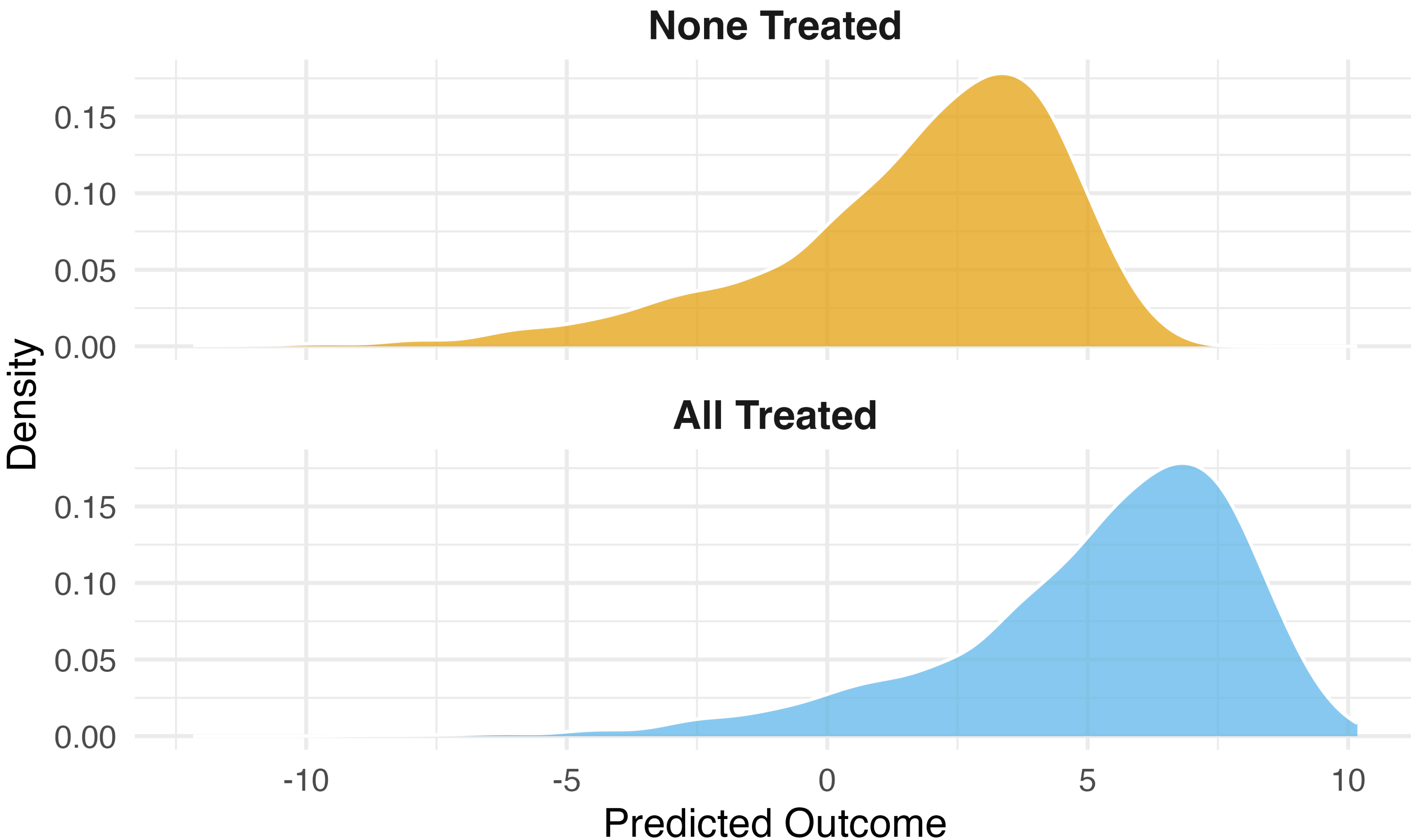
G-computation

1. Fit a model for `y ~ x + z` where z is all confounders
2. Create a duplicate of your data set for each level of `x`
3. Set the value of x to a single value for each cloned data set (e.g `x = 1` for one, `x = 0` for the other)

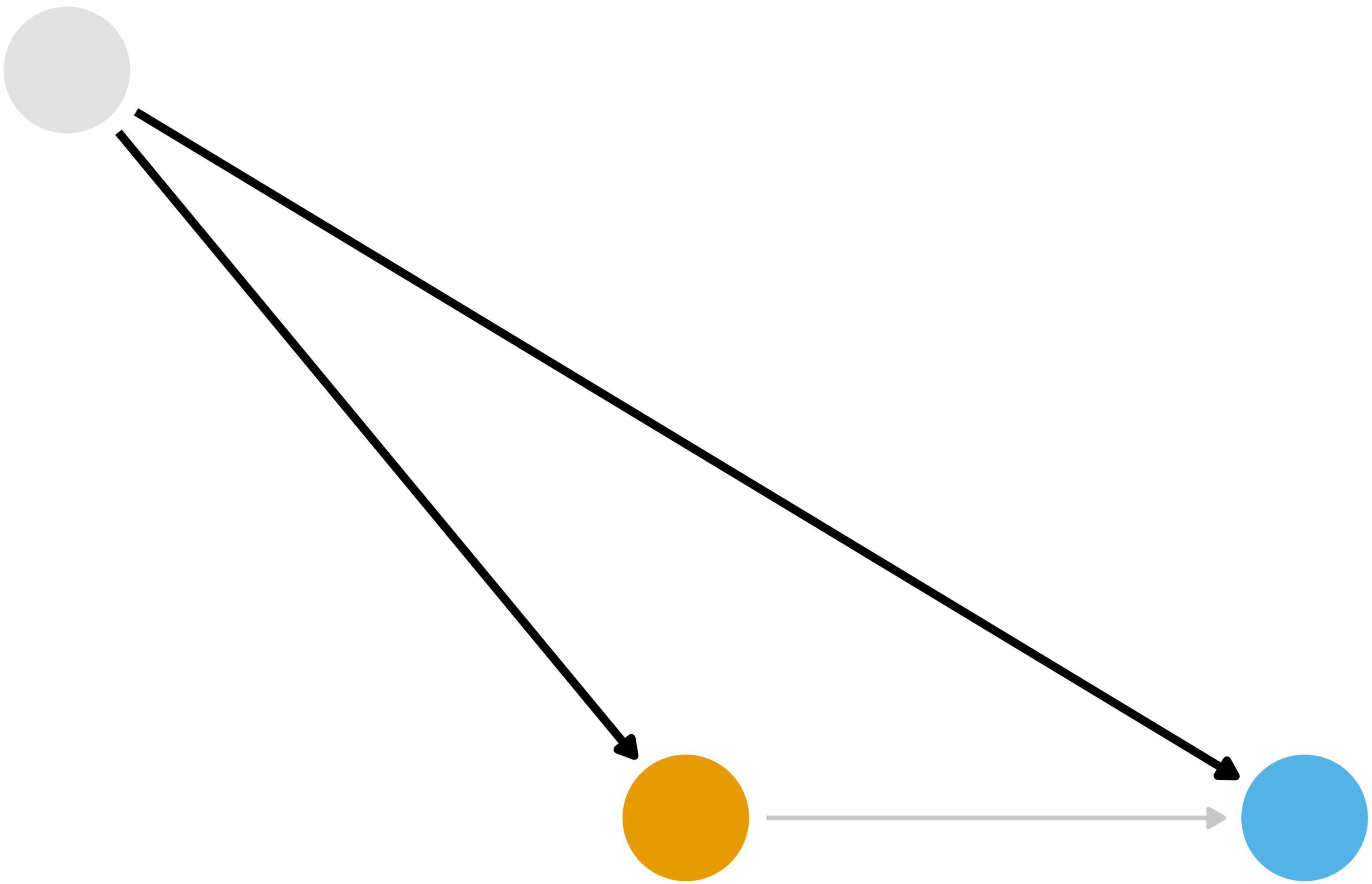
G-computation

1. Make predictions using the model on the cloned data sets
2. Calculate the estimate you want, e.g. `mean(x_1) - mean(x_0)`

G-computation



What part of the DAG do we want to try to deal with?



Two Causal Questions

Does quitting smoking cause weight gain?

Example: The Seven Dwarfs Mine Train

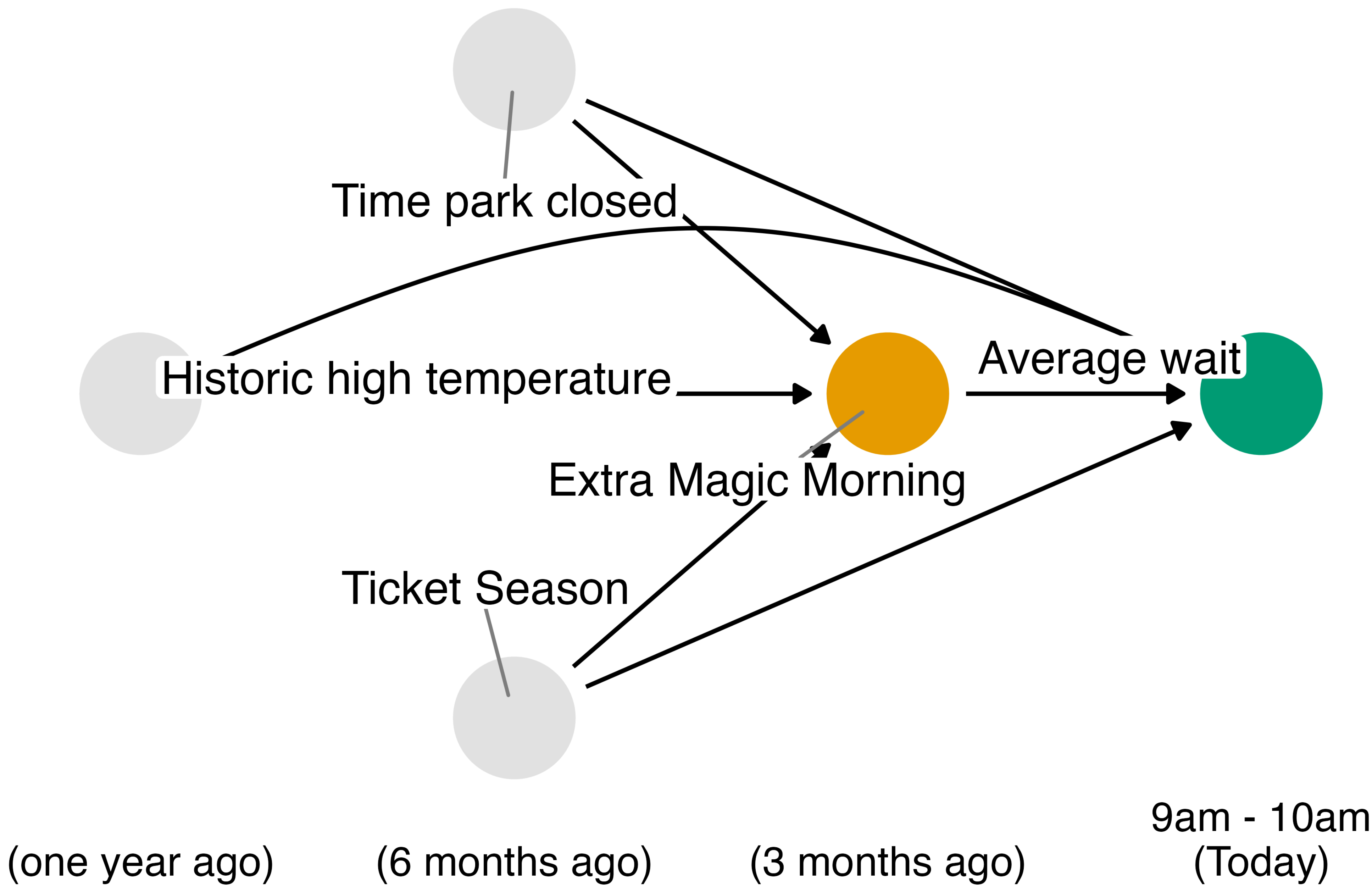
Photo by Anna CC-BY-SA-4.0

Historically, guests who stayed in a Walt Disney World resort hotel were able to access the park during “Extra Magic Hours” during which the park was closed to all other guests.

These extra hours could be in the morning or evening.

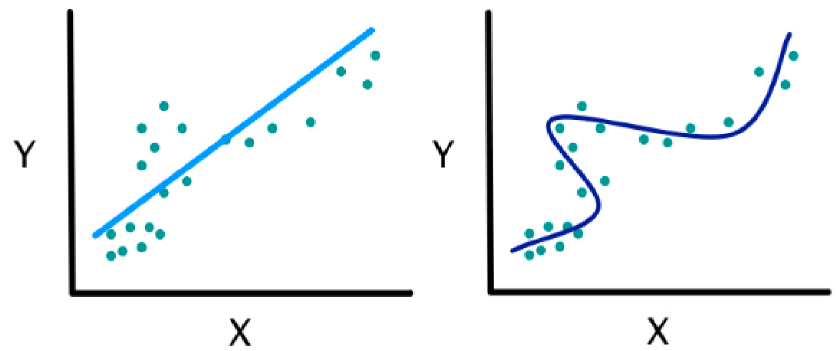
The Seven Dwarfs Mine Train is a ride at Walt Disney World’s Magic Kingdom. Typically, each day Magic Kingdom may or may not be selected to have these “Extra Magic Hours”.

We are interested in examining the relationship between whether there were **“Extra Magic Hours”** *in the morning and* **the average wait time** *for the Seven Dwarfs Mine Train the same day between 9am and 10am.*


Time park closed
Historic high temperature
Average wait
Extra Magic Morning
Ticket Season
9am - 10am
(one year ago)
(6 months ago)
(3 months ago)
(Today)

Machine Learning for Causal Inference

What algorithm should we use to make predictions?



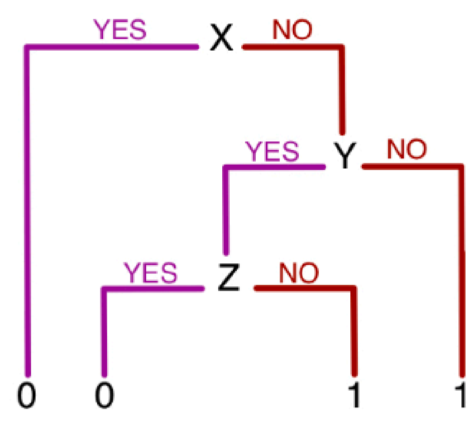
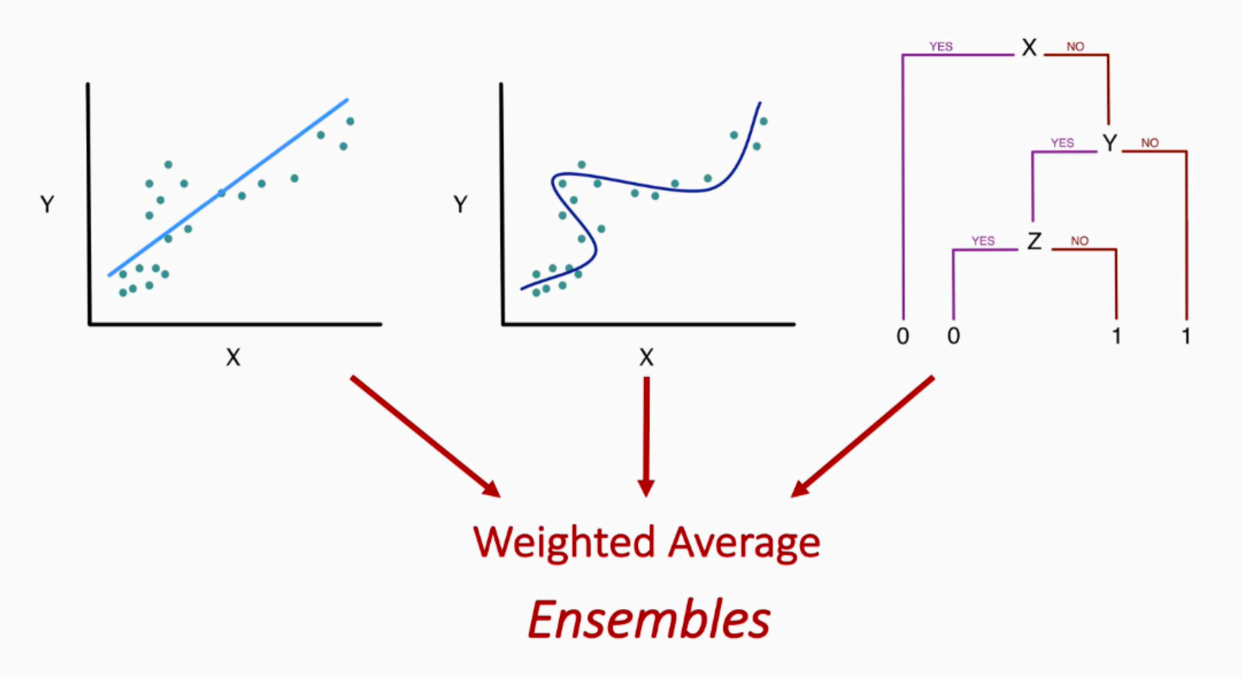


Image source: Sherri Rose

Ensemble Algorithms with SuperLearner



Given a set of candidate algorithms (and hyperparameters), stacked ensembles combine them to minimize (cross-validated) prediction

SuperLearner: Exposure Model

```r
sl_library <- c("SL.glm", "SL.ranger", "SL.gam")

propensity_sl <- SuperLearner(
  Y = as.integer(nhefs_complete_uc$qsmk == "Yes"),
  X = nhefs_complete_uc |>
    select(sex, race, age, education, smokeintensity,
           smokeyrs, exercise, active, wt71) |>
    mutate(across(everything(), as.numeric)),
  family = binomial(),
  SL.library = sl_library,
  cvControl = list(V = 5)
)
```

SuperLearner: Exposure Model

```
1  propensity_sl
```

```
Call:
SuperLearner(Y = as.integer(nhefs_complete_uc$qsmk == "Yes"), X =
mutate(select(nhefs_complete_uc,
    sex, race, age, education, smokeintensity, smokeyrs, exercise,
active,
    wt71), across(everything(), as.numeric)), family = binomial(),
SL.library = sl_library,
    cvControl = list(V = 5))


                   Risk       Coef
SL.glm_All    0.1837871 0.00000000
SL.ranger_All 0.1943978 0.05247478
SL.gam_All    0.1825974 0.94752522
```

SuperLearner: Outcome Model

```r
outcome_sl <- SuperLearner(
  Y = nhefs_complete_uc$wt82_71,
  X = nhefs_complete_uc |>
    select(qsmk, sex, race, age, education, smokeintensity,
           smokeyrs, exercise, active, wt71) |>
    mutate(across(everything(), as.numeric)),
  family = gaussian(),
  SL.library = sl_library,
  cvControl = list(V = 5)
)
```

SuperLearner: Outcome Model

```r
outcome_sl
```

```
Call:
SuperLearner(Y = nhefs_complete_uc$wt82_71, X =
mutate(select(nhefs_complete_uc,
    qsmk, sex, race, age, education, smokeintensity, smokeyrs,
exercise,
    active, wt71), across(everything(), as.numeric)), family =
gaussian(),
    SL.library = sl_library, cvControl = list(V = 5))

                    Risk       Coef
SL.glm_All      55.41405 0.01678317
SL.ranger_All   57.24412 0.13366720
```

Your Turn 1

First, create a character vector `sl_library` that specifies the following algorithms: "SL.glm", "SL.ranger", "SL.xgboost", "SL.gam". Then, Fit a SuperLearner for the exposure model using the `SuperLearner` package. The predictors for this model should be the confounders identified in the DAG: `park_ticket_season`, `park_close`, and `park_temperature_high`. The outcome is `park_extra_magic_morning`.

Fit a SuperLearner for the outcome model using the `SuperLearner` package. The predictors for this model should be the confounders plus the exposure: `park_extra_magic_morning`, `park_ticket_season`, `park_close`, and `park_temperature_high`. The outcome is `wait_minutes_posted_avg`.

Inspect the fitted SuperLearner objects.

08:00

IPW with SuperLearner

```
propensity_scores <- predict(propensity_sl, type = "response")$pred[, 1]

ate_weights <- wt_ate(propensity_scores, nhefs_complete_uc$qsmk)

ipw_model <- lm(
  wt82_71 ~ qsmk,
  data = nhefs_complete_uc,
  weights = ate_weights
)
```

IPW with SuperLearner

```r
tidy(ipw_model)
```

```
# A tibble: 2 × 5
  term        estimate std.error statistic  p.value
  <chr>          <dbl>     <dbl>     <dbl>    <dbl>
1 (Intercept)     1.79     0.280      6.38 2.28e-10
2 qsmkYes         3.31     0.407      8.14 8.30e-16
```

G-computation with SuperLearner

```r
data_all_quit <- nhefs_complete_uc |>
  select(qsmk, sex, race, age, education, smokeintensity,
           smokeyrs, exercise, active, wt71) |>
  mutate(across(everything(), as.numeric)) |>
  mutate(qsmk = 1)

data_all_no_quit <- nhefs_complete_uc |>
  select(qsmk, sex, race, age, education, smokeintensity,
           smokeyrs, exercise, active, wt71) |>
  mutate(across(everything(), as.numeric)) |>
  mutate(qsmk = 0)

pred_quit <- predict(outcome_sl, newdata = data_all_quit)$pred[, 1]
pred_no_quit <- predict(outcome_sl, newdata = data_all_no_quit)$pred[, 1]

mean(pred_quit - pred_no_quit)
```

```
[1] 2.979202
```

Your Turn 2

Implement the IPW algorithm using the SuperLearner propensity scores

Implement the G-computation algorithm using the SuperLearner outcome predictions

08:00

Targeted Maximum Likelihood Estimation (TMLE)

Targeted Learning

- TMLE is a flexible, efficient method for estimating causal effects based in semi-parametric theory

- TMLE solves three problems: doubly robustness, targeted estimation, and valid statistical inference

Targeted Learning: doubly robustness

Targeted Learning: targeted estimation

- In **IPW** and **G-computation**, we estimate the average treatment effect (ATE) using predictions from the exposure and outcome models. But these algorithms optimize for the predictions, not the ATE.

- In **TMLE**, we adjust the predictions to specifically target the ATE. We change the bias-variance tradeoff to focus on the ATE rather than just minimizing prediction error. This is a debiasing step that also improves the efficiency of the estimate!

Targeted Learning: valid statistical inference

- In **IPW** and **G-computation**, we cannot easily get valid confidence intervals with ML. Bootstrapping is often used, but it can be computationally intensive and not always valid.

- In **TMLE**, we can use the influence curve to get valid confidence intervals. The influence curve is a way to estimate the variance of the TMLE estimate, even when using complex ML algorithms.

The TMLE Algorithm

1. Start with SuperLearner predictions for the outcome
2. Calculate the propensity scores using SuperLearner
3. Create the clever covariate using the propensity scores

The TMLE Algorithm

TMLE Step 1: Initial Predictions (on the bounded [0,1] scale)

```r
# For TMLE with continuous outcomes, fit SuperLearner on bounded Y
min_y <- min(nhefs_complete_uc$wt82_71)
max_y <- max(nhefs_complete_uc$wt82_71)
y_bounded <- (nhefs_complete_uc$wt82_71 - min_y) / (max_y - min_y)

# Fit new SuperLearner on bounded outcome
outcome_sl_bounded <- SuperLearner(
  Y = y_bounded,
  X = nhefs_complete_uc |>
    select(qsmk, sex, race, age, education, smokeintensity,
           smokeyrs, exercise, active, wt71) |>
    mutate(across(everything(), as.numeric)),
  family = quasibinomial(),
  SL.library = sl_library,
  cvControl = list(V = 5)
)
```

TMLE Step 1: Initial Predictions (on the bounded [0,1] scale)

```
initial_pred_quit <- predict(outcome_sl_bounded, newdata = data_all_quit)$pred[, 1]
initial_pred_no_quit <- predict(outcome_sl_bounded, newdata = data_all_no_quit)$prec

# Predictions for observed treatment
initial_pred_observed <- ifelse(
  nhefs_complete_uc$qsmk == "Yes",
  initial_pred_quit,
  initial_pred_no_quit
)
```

TMLE Step 2: Clever Covariate

```
clever_covariate <- ifelse(
  nhefs_complete_uc$qsmk == "Yes",
  1 / propensity_scores,
  -1 / (1 - propensity_scores)
)
```

- Not the same as IPW weights!
- Part of the efficient influence function
- Helps target the ATE specifically

TMLE Step 3: Targeting

```
# Fluctuation model - learns how much to adjust
# Use binomial family and work on logit scale
fluctuation_model <- glm(
  y_bounded ~
     -1 +
     offset(qlogis(initial_pred_observed)) +
     clever_covariate,
  family = quasibinomial()
)

epsilon <- coef(fluctuation_model)
epsilon
```

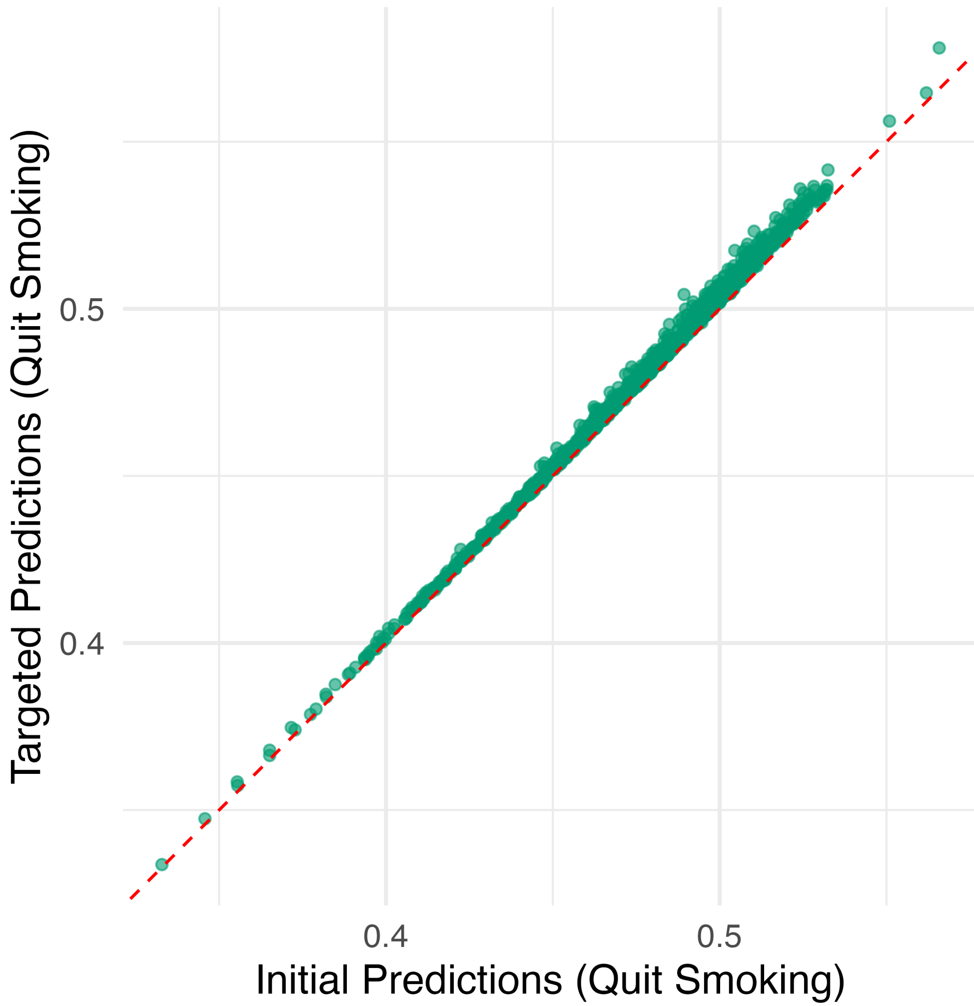
```
clever_covariate
     0.002936146
```

- Small epsilon = initial estimate was good
- Large epsilon = needed more adjustment

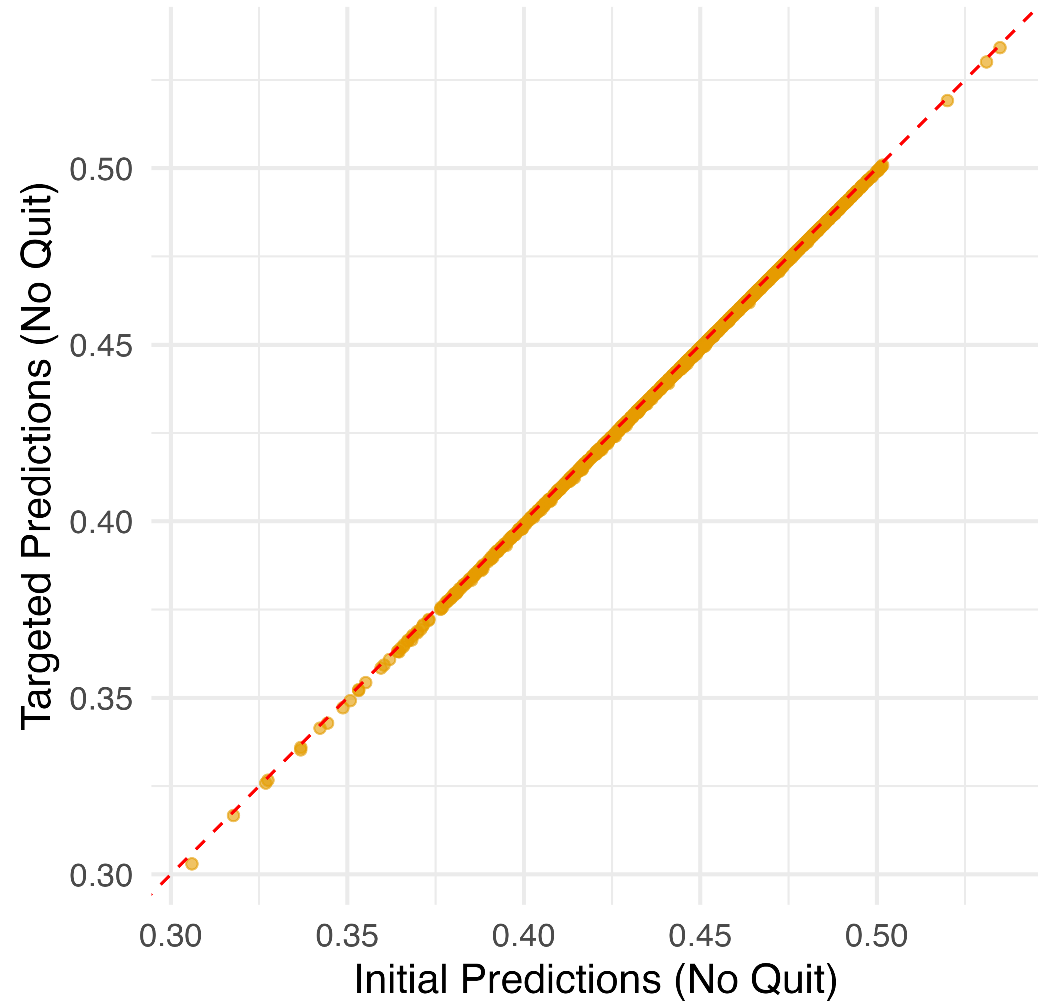
TMLE Step 4: Update Predictions

```
# Update predictions on logit scale, then transform back
logit_pred_quit <- qlogis(initial_pred_quit) + epsilon * (1 / propensity_scores)
logit_pred_no_quit <- qlogis(initial_pred_no_quit) + epsilon * (-1 / (1 - propensity

# Transform back to probability scale
targeted_pred_quit <- plogis(logit_pred_quit)
targeted_pred_no_quit <- plogis(logit_pred_no_quit)
```



Targeted Predictions (Quit Smoking)
0.5
0.4
0.4
0.5
Initial Predictions (Quit Smoking)



Targeted Predictions (No Quit)
0.50
0.45
0.40
0.35
0.30
0.30
0.35
0.40
0.45
0.50
Initial Predictions (No Quit)

Your Turn 3

Calculate initial predictions for treated/control scenarios

Create the clever covariate using propensity scores

Fit the fluctuation model with offset and no intercept

Update predictions with the targeted adjustment

10:00

TMLE ATE

```r
initial_ate <- mean(
  initial_pred_quit - initial_pred_no_quit
  # Transform back to original scale for ATE
) * (max_y - min_y)

targeted_ate <- mean(
  targeted_pred_quit - targeted_pred_no_quit
) * (max_y - min_y)

tibble(initial = initial_ate, targeted = targeted_ate)
```

```
# A tibble: 1 × 2
  initial targeted
    <dbl>    <dbl>
1    2.75     3.15
```

TMLE Inference

```r
targeted_pred_observed <- ifelse(
  nhefs_complete_uc$qsmk == "Yes",
  targeted_pred_quit,
  targeted_pred_no_quit
)

# IC uses bounded outcomes and predictions
ic <- clever_covariate * (y_bounded - targeted_pred_observed) +
      targeted_pred_quit - targeted_pred_no_quit - targeted_ate / (max_y - min_y)

# Standard error on original scale
se_tmle <- sqrt(var(ic) / nrow(nhefs_complete_uc)) * (max_y - min_y)

# 95% CI
tibble(
  ate = targeted_ate,
  se = se_tmle,
  lower_ci = targeted_ate - 1.96 * se_tmle,
  upper_ci = targeted_ate + 1.96 * se_tmle
)
```

TMLE Inference

```
# A tibble: 1 × 4
    ate    se lower_ci upper_ci
  <dbl> <dbl>    <dbl>    <dbl>
1  3.15 0.447     2.27     4.02
```

Using the tmle Package

```r
library(tmle)

tmle_result <- tmle(
  Y = nhefs_complete_uc$wt82_71,
  A = as.integer(nhefs_complete_uc$qsmk == "Yes"),
  W = nhefs_complete_uc |>
    select(sex, race, age, education, smokeintensity,
           smokeyrs, exercise, active, wt71) |>
    mutate(across(everything(), as.numeric)),
  Q.SL.library = sl_library,
  g.SL.library = sl_library
)

tibble(
  ate = tmle_result$estimates$ATE$psi,
  lower_ci = tmle_result$estimates$ATE$CI[[1]],
  upper_ci = tmle_result$estimates$ATE$CI[[2]]
)
```

```
# A tibble: 1 × 3
    ate lower_ci upper_ci
  <dbl>    <dbl>    <dbl>
1  3.44     2.56     4.31
```

Your Turn 4

Calculate the TMLE ATE and compare to the initial (g-computation) estimate

Work through the code to compute the variance and CIs (nothing to change here)

05:00

Key Takeaways

Resources

Targeted Learning **by Mark van der Laan and Sherri Rose (THE book… see the sequel for longitudinal problems)**

Introduction to Modern Causal Inference **by Alejandro Schuler and Mark van der Laan (Great introduction to the math and theory)**