DID Analysis: Zika and Birth Rates

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Setting and Data

The data and analysis for this section come from Taddeo et al. (2022). We are interested in understanding the impact of the 2015–2016 Zika virus epidemic on birth rates in Brazil. The epidemic was quite localized within Brazil, with over 65\% of cases arising in the northeastern state of Pernambuco, while the southern state of Rio Grande do Sul had no reported cases. The authors collected administrative data on live births from 185 municipalities in Pernambuco and 497 in Rio Grande do Sul from 2008 to 2016.

The goal of the analysis is to test the hypothesis that the Zika epidemic led to a reduced birth rate in the highly-affected state of Pernambuco and estimate the effect of this shock. Rio Grande do Sul will be used as the control (untreated) unit.

The data are available in the `zika.Rda` file. `zika_full` contains the full data set, by muncipality, while `zika_summ` summarizes this to the two states. The full data set is available, posted by the original authors.

First, load the data into R.

```r
load(file="../data/zika.Rda")
```

Libraries

Throughout the workshop, we will use the `tidyverse` environment for data cleaning and plotting, but the operations for the methods we are learning can be conducted in base R as well. The `knitr` package is used for formatting table output into the document.

To get clustered standard errors for the regression-based DID analyses, we use linear mixed effects models fit using the `lme4` package, although other options are available.

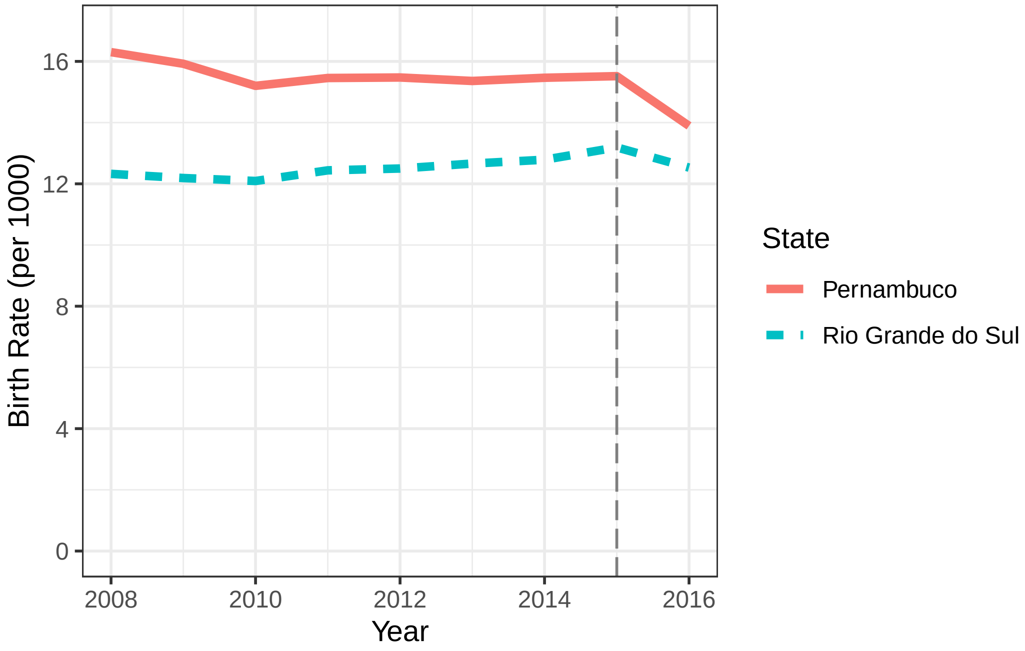
We now load the required libraries.

```r
## If you have not installed these packages before,
##  run the following line:
# install.packages(c("tidyverse","knitr","lme4"))
## Either way, the packages must be loaded:
require(tidyverse)
require(knitr)
require(lme4)
```

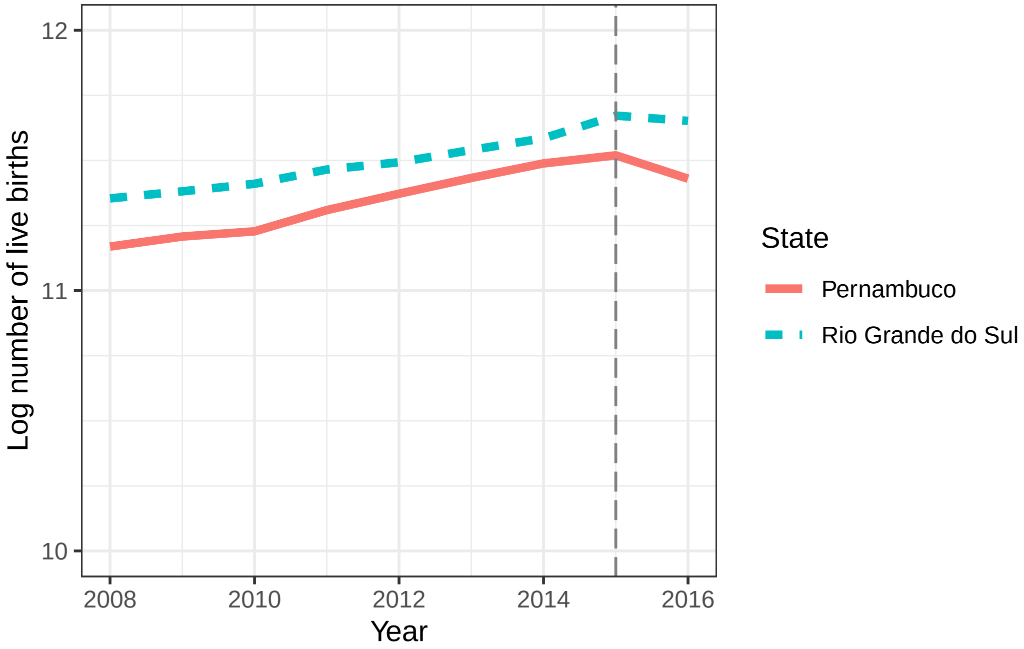
Graphical Exploration

As always, we begin with exploratory data analysis, plotting the time series for visual inspection. Here, we plot the results akin to Figures 2(a) and 2(b) in Taddeo et al. (2022).

```r
## Plot birth rate over time by state:
#| fig-cap: "Plot of live birth rate (per 1,000 population) by year and state, Brazil, 2008-2
#| fig-alt: "A line plot with the line for Pernambuco slowly declining from around 16 in 2008
ggplot(data=zika_summ) +
  geom_line(mapping=aes(x=Year, y=Rate, color=State, linetype=State),
            linewidth=1.5) +
  theme_bw() +
  scale_y_continuous(name="Birth Rate (per 1000)",
                     limits=c(0,17),
                     breaks=seq(0,16,by=4),
                     minor_breaks=seq(0,16,by=2)) +
  geom_vline(xintercept=2015, linetype="longdash", color="grey50")
```

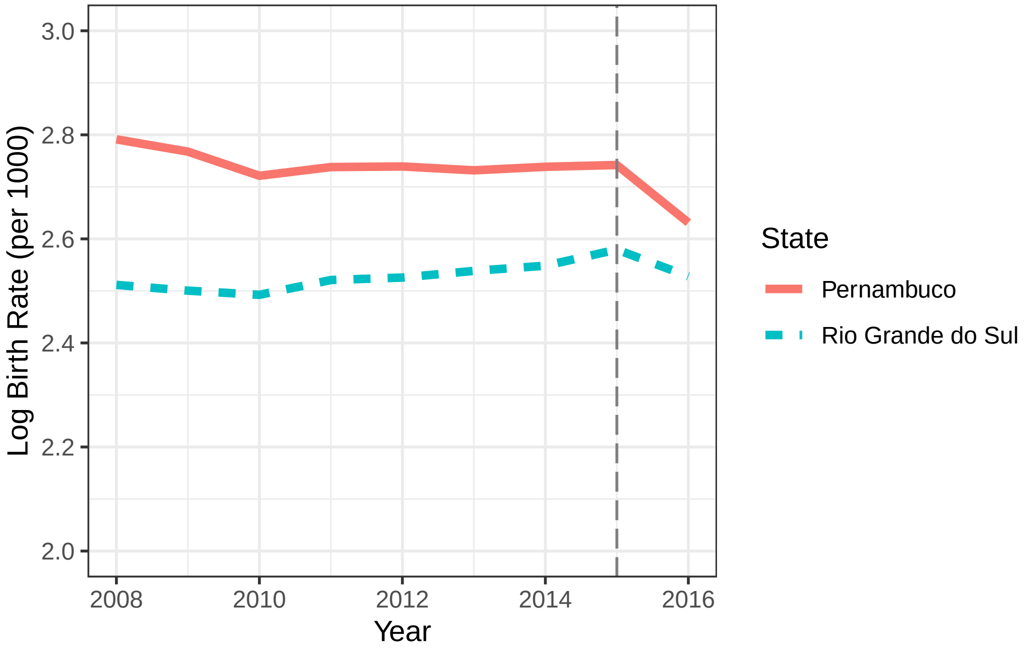


```
## Plot log of number of births over time by state:
#| fig-cap: "Plot of natural log of the number of live births by year and state, Brazil, 2008
#| fig-alt: "A line plot with the line for Pernambuco steadily increasing from around 11.2 in
ggplot(data=zika_summ) +
  geom_line(mapping=aes(x=Year, y=LogBirths, color=State, linetype=State),
            linewidth=1.5) +
  theme_bw() +
  scale_y_continuous(name="Log number of live births",
                     limits=c(10,12),
                     breaks=seq(10,12,by=1),
                     minor_breaks=seq(10,12,by=.25)) +
  geom_vline(xintercept=2015, linetype="longdash", color="grey50")
```



We can also plot the natural log of the birth rate.

```
## Plot log of birth rate over time by state:
#| fig-cap: "Plot of natural log of the rate of live births (per 1,000 population) by year ar
#| fig-alt: "A line plot with the line for Pernambuco declining from 2.8 in 2008 to just abov
ggplot(data=zika_summ) +
  geom_line(mapping=aes(x=Year, y=LogRate, color=State, linetype=State),
            linewidth=1.5) +
  theme_bw() +
  scale_y_continuous(name="Log Birth Rate (per 1000)",
                     limits=c(2,3),
                     breaks=seq(2,3,by=.2),
                     minor_breaks=seq(2,3,by=.1)) +
  geom_vline(xintercept=2015, linetype="longdash", color="grey50")
```



Discussion Question

From these plots, does it appear that parallel trends hold for any of these outcomes? Which seems the most reasonable?

Two-by-Two DID Summary

We can start by examining just two time periods: 2014, prior to the outbreak, and 2016, the first year where the outbreak could have affected live birth rates throughout the year. Note that we exclude 2015, which may have been partially affected. We continue to use the `zika_summ` data set here, looking at the two states as a whole.

```
## Get differences within-units:
did_2x2 <- zika_summ %>%
  dplyr::filter(Year %in% c(2014,2016)) %>%
  pivot_wider(id_cols=State,
              names_from=Year,
              values_from=Rate) %>%
  mutate(`Diff, 2016-2014`=`2016`-`2014`)
## Get differences within years:
yr_diffs <- did_2x2 %>%
  dplyr::filter(State=="Pernambuco") %>%
  dplyr::select(-c(State)) -
  did_2x2 %>%
  dplyr::filter(State=="Rio Grande do Sul") %>%
  dplyr::select(-c(State))
## Combine into presentation table:
did_2x2_f <- did_2x2 %>%
  add_row(bind_cols(State="Diff, Treated-Untreated",
                    yr_diffs))

## Print formatted table of two-by-two analysis:
knitr::kable(did_2x2_f,
             digits=1,
             caption="Table 1. Two-by-two DID analysis of birth rates in Pernambuco and Rio
```

Table 1: Table 1. Two-by-two DID analysis of birth rates in Pernambuco and Rio Grande do Sul, 2016 vs. 2014

State	2014	2016	Diff, 2016–2014
Pernambuco	15.5	13.9	-1.6
Rio Grande do Sul	12.8	12.5	-0.3
Diff, Treated–Untreated	2.7	1.4	-1.3

Linear TWFE Model

The two-by-two DID that summarizes to the exposed/unexposed level is the most straightforward, but ignores a lot of the information we have on variability of the outcome. We can incorporate all of the information on the municipalities using the TWFE regression analysis. We start with the linear form. Note that we are now using the `zika_full` data set, which has columns for our outcome (`Rate`), unit identifier (`State`, as a factor variable), time identifier (`year`, coded as 0 for 2014 and 1 for 2016), and whether the exposure was in effect for that observation (`interaction`, coded as 0 for unexposed and 1 for exposed).

```
## Fit linear TWFE model and extract estimate and 95% CI:
zika_lm <- lm(Rate~State+year+interaction,
              data=zika_full)
coef(zika_lm)[c("(Intercept)","year","interaction")]
```

```
(Intercept)        year interaction 
 15.1236895  -0.1013549  -1.2069394 
```

```r
confint(zika_lm, parm="interaction", level=0.95)
```

```
                2.5 %     97.5 %
interaction -1.87173 -0.5421485
```

This gives an effect estimate of -1.21 births per 1,000 population, suggesting a negative effect of the outbreak on birth rates in Pernambuco. The standard errors and confidence intervals should be treated with suspicion, however, as they ignore the correlation between observations in the same municipality in different years.

To correct the standard errors, we can cluster by the municipality using a linear mixed effects model with a random effect for municipality.

```r
## Fit a linear mixed effects model to account for clustering by municipality:
zika_lmer <- lmer(Rate~State+year+interaction+
                    (1|Code),
                  data=zika_full)
fixef(zika_lmer)[c("(Intercept)","year","interaction")]
```

```
(Intercept)        year interaction
 15.1236895  -0.1013549  -1.2069394
```

```r
confint(zika_lmer, parm="interaction", level=0.95)
```

```
Computing profile confidence intervals ...
```

```
                 2.5 %     97.5 %
interaction -1.558305 -0.8555737
```

This gives the same effect estimate of -1.21 births per 1,000 population, with a 95% confidence interval of [-1.558, -0.856], indicating a statistically significant negative effect.

Another approach to clustered inference is the block-bootstrap method.

```r
## First, get a list of unique codes by state
codes <- zika_full %>% dplyr::select(Code,State) %>% distinct()
## Then, write a function that samples codes within each state:
boot_data <- function() slice_sample(codes, by=State, prop=1, replace=TRUE) %>%
  expand_grid(StudyYear=rep(c(2014,2016))) %>%
  left_join(zika_full, by = join_by(Code, State, StudyYear))
```

```
## Set seed for reproducibility:
set.seed(3671)
## Run the sampling and analysis 1000 times to get a distribution:
lm_boot <- replicate(n=1000,
                     expr=lm(Rate~State+year+interaction,
                             data=boot_data())$coefficients["interaction"])
## Examine the median (estimate) and 2.5 and 97.5 percentiles:
quantile(lm_boot, probs=c(0.5,0.025,0.975))
```

```
       50%       2.5%      97.5% 
-1.2033250 -1.5202092 -0.8842974 
```

This method gives an effect estimate of -1.20 births per 1,000 population, with a 95% confidence interval of [-1.520, -0.884], very similar to the previous results.

Discussion Questions

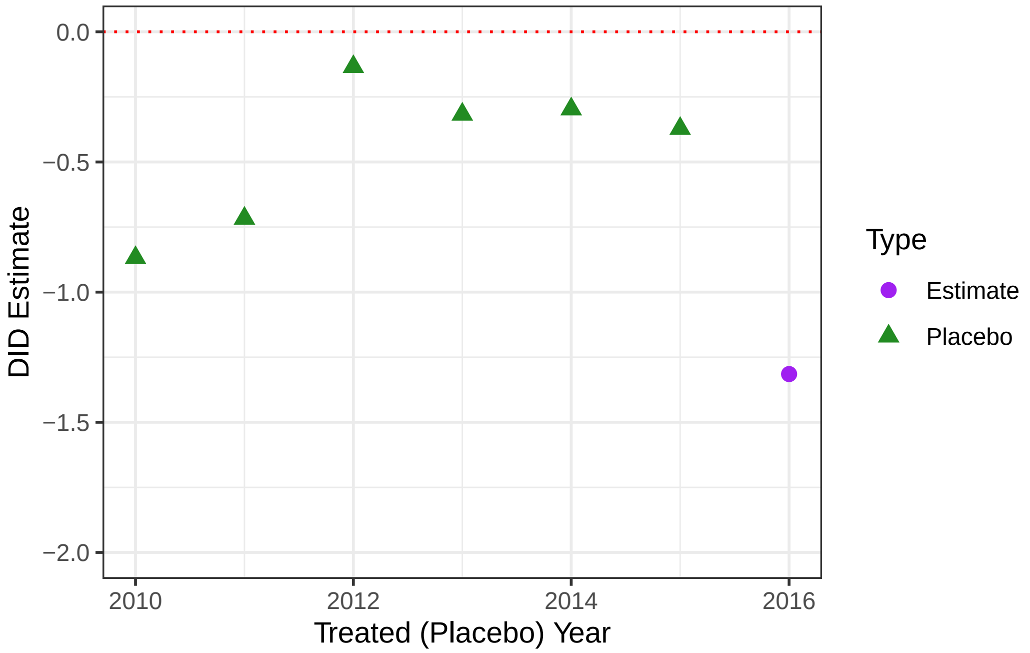
1. How should this result be interpreted?
2. What do the three key assumptions mean for this setting?
3. Which of these assumptions are reasonable? Which are unlikely to be valid?

Placebo Test in Time

We can use the `zika_summ` data set to run the two-by-two DID analysis on all pairs of years that are two years apart, starting with 2010 vs. 2008. Since there were no Zika outbreaks in those prior years, if the parallel trends assumption holds true, the estimates should be distributed around 0.

```
## Create a data set with a row for each pair of years
zika_plac <- tibble(`Treated Year`=unique(zika_summ$Year),
                    `Untreated Year`=`Treated Year`-2) %>%
  dplyr::filter(`Untreated Year` %in% unique(zika_summ$Year)) %>%
  left_join(zika_summ %>% dplyr::select(Year,State,Rate) %>%
              pivot_wider(id_cols=Year, names_from=State, values_from=Rate),
            by=join_by(`Treated Year`==Year)) %>%
  rename(P1=Pernambuco, R1=`Rio Grande do Sul`) %>%
  left_join(zika_summ %>% dplyr::select(Year,State,Rate) %>%
              pivot_wider(id_cols=Year, names_from=State, values_from=Rate),
            by=join_by(`Untreated Year`==Year)) %>%
  rename(P0=Pernambuco, R0=`Rio Grande do Sul`)
## Get the estimate for each pair of years
zika_plac <- zika_plac %>%
  mutate(Estimate=(P1-P0)-(R1-R0),
         Type=factor(if_else(`Treated Year`==2016,
                      "Estimate","Placebo")))
```

```
## Plot two-by-two DID estimates for placebo years:
#| fig-cap: "Plot of two-by-two DID estimates for placebo treatment years (2010-2015) and ac
#| fig-alt: "A scatter plot with points ranging from around -0.868 to -0.135 in the 2010 thr
ggplot(data=zika_plac) +
  geom_point(mapping=aes(x=`Treated Year`, y=Estimate,
                         color=Type, shape=Type),
             size=2.5) +
  theme_bw() +
  labs(x="Treated (Placebo) Year", y="DID Estimate") +
  scale_y_continuous(limits=c(-2,0), breaks=seq(-2,0,by=.5)) +
  scale_color_manual(breaks=c("Estimate","Placebo"),
                     values=c("purple","forestgreen")) +
  geom_hline(yintercept=0, color="red", linetype="dotted")
```



Re-Scaling: Natural Log

One approach that might improve the parallel trends assumption in this case is to use a log transformation. We implement this using the linear mixed effects model to get a cluster-robust confidence interval.

```
## Fit TWFE model with clustering by municipality and log-scale:
zika_log_lmer <- lmer(LogRate~State+year+interaction+(1|Code), data=zika_full)
summary(zika_log_lmer)
```

```
Linear mixed model fit by REML ['lmerMod']
Formula: LogRate ~ State + year + interaction + (1 | Code)
   Data: zika_full

REML criterion at convergence: -77.6

Scaled residuals:
    Min      1Q  Median      3Q     Max 
-4.7117 -0.3414  0.0739  0.4163  3.0462 

Random effects:
 Groups   Name        Variance Std.Dev.
 Code     (Intercept) 0.04955  0.2226  
 Residual             0.02402  0.1550  
Number of obs: 1364, groups:  Code, 682

Fixed effects:
                        Estimate Std. Error t value
(Intercept)             2.699193   0.019942 135.355
StateRio Grande do Sul -0.386474   0.023360 -16.544
year                   -0.017260   0.009832  -1.756
interaction            -0.070706   0.018877  -3.746

Correlation of Fixed Effects:
            (Intr) StRGdS year  
SttRGrnddSl -0.854              
year         0.000 -0.210       
interaction -0.345  0.404 -0.521
```

```
confint(zika_log_lmer, level=0.95)
```

```
Computing profile confidence intervals ...
```

```
                              2.5 %       97.5 %
.sig01                   0.20779243  0.237716262
.sigma                   0.14689761  0.163351936
(Intercept)              2.66012593  2.738260691
StateRio Grande do Sul -0.43223814 -0.340709224
year                    -0.03652934  0.002008589
interaction             -0.10770239 -0.033708693
```

```
## Exponentiate estimates and CI to get RR estimates:
exp(summary(zika_log_lmer)$coefficients["interaction","Estimate"])
```

```
[1] 0.9317362
```

```
exp(confint(zika_log_lmer, level=0.95))
```

```
Computing profile confidence intervals ...
```

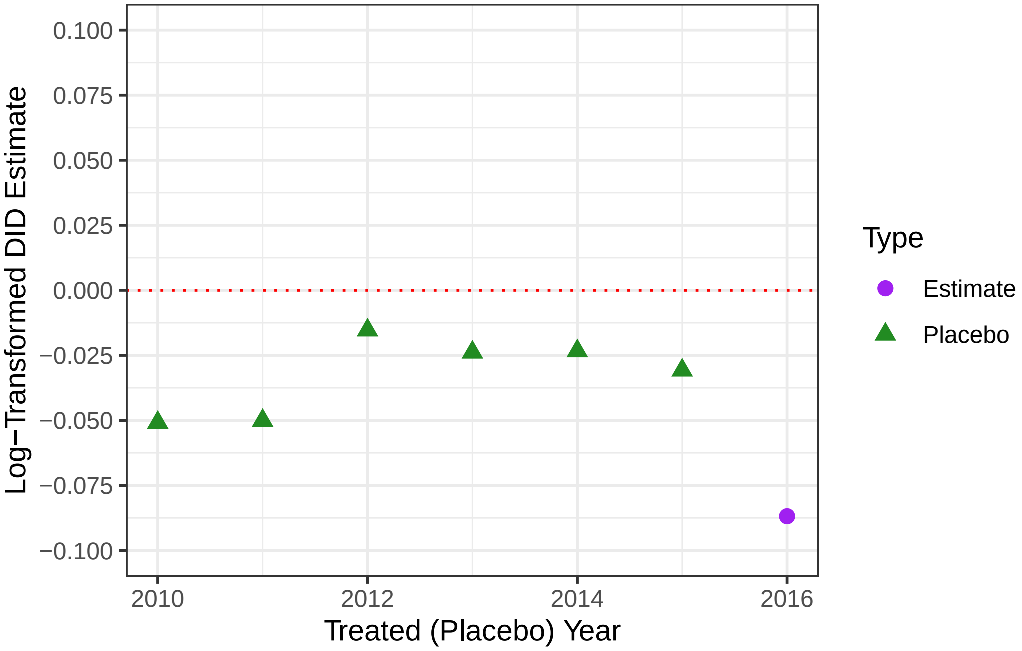
```
                             2.5 %     97.5 %
.sig01                   1.2309576  1.2683493
.sigma                   1.1582354  1.1774510
(Intercept)             14.2980895 15.4600719
StateRio Grande do Sul   0.6490548  0.7112657
year                     0.9641298  1.0020106
interaction              0.8978948  0.9668531
```

This approach gives an effect estimate of -0.0707 births per 1,000 population, with a 95% confidence interval of [-0.108, -0.0337], indicating a statistically significant negative effect. On the multiplicative scale, by exponentiating, we get an estimate of 0.932 with a 95% CI of [0.898, 0.967].

We can check the placebo in-time plot for the log-transformed outcome.

```
## Add log-transformed DID estimate to placebo data set:
zika_plac <- zika_plac %>% mutate(LogEstimate=log(P1/P0)-log(R1/R0))
```

```
## Plot two-by-two log-transformed DID estimates for placebo years:
#| fig-cap: "Plot of two-by-two log-transformed DID estimates for placebo treatment years (20
#| fig-alt: "A scatter plot with points ranging from around 0 to -0.05 in the 2010 through 20
ggplot(data=zika_plac) +
  geom_point(mapping=aes(x=`Treated Year`, y=LogEstimate,
                         color=Type, shape=Type),
             size=2.5) +
  theme_bw() +
  labs(x="Treated (Placebo) Year", y="Log-Transformed DID Estimate") +
  scale_y_continuous(limits=c(-0.1,0.1), breaks=seq(-0.1,0.1,by=.025)) +
  scale_color_manual(breaks=c("Estimate","Placebo"),
                     values=c("purple","forestgreen")) +
  geom_hline(yintercept=0, color="red", linetype="dotted")
```



Discussion Questions

1. Do the placebo tests support the observed effect being a true causal effect?
2. Do they indicate potential bias in one direction or another?

Additional Options

Further modeling is possible. In this case, the authors also proposed Poisson and Negative Binomial models for the live birth counts in the DID framework. Further details on model fitting and interpretation can be found in the article.

The following code can be run to fit the Poisson GLM with bootstrap CI or GLMM, clustered by municipality:

```
# To execute this code into the document, change the previous line to true
## Fit Poisson GLM:
zika_glm <- glm(Births~State+year+interaction+offset(log(Pop)), data=zika_full,
                family=poisson(link="log"))
summary(zika_glm)
## Compute bootstrap 95% CI for Poisson GLM:
set.seed(4008335)
glm_boot <- replicate(n=1000,
                      expr=glm(Births~State+year+interaction+offset(log(Pop)),
                               data=boot_data(),
                               family=poisson(link="log"))$
                        coefficients["interaction"])
glm_boot_res <- quantile(glm_boot, probs=c(0.5,0.025,0.975))
## Exponentiate results:
exp(c(Estimate=unname(coef(zika_glm)["interaction"]),
      CI.Lower=glm_boot_res["2.5%"],
      CI.Upper=glm_boot_res["97.5%"]))
## Fit Poisson GLMM, clustered by municipality:
zika_glmer <- glmer(Births~State+year+interaction+offset(log(Pop))+(1|Code),
                    data=zika_full,
                    family=poisson(link="log"))
zika_glmer_CI <- confint(zika_glmer, parm="interaction", level=0.95)
## Exponentiate results:
exp(c(Estimate=unname(summary(zika_glmer)$coefficients["interaction","Estimate"]),
      CI.Lower=zika_glmer_CI["interaction","2.5 %"],
      CI.Upper=zika_glmer_CI["interaction","97.5 %"]))
```

Discussion Question

How do transformations of the outcome change the interpretation of the estimate and of the assumptions required?