Class 19: Pertussis

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Pertussis is a severe lung infection also known as whooping cough. We will begin by investigating the number of Pertussis cases per year in the US.

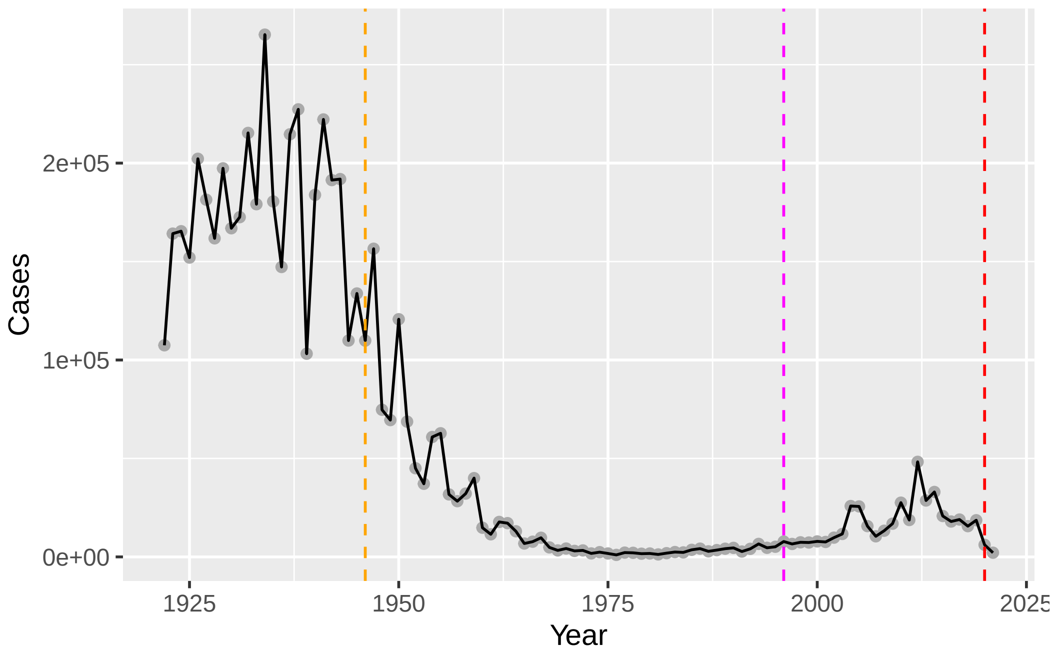
This data is available here

```
echo=FALSE
cdc <- data.frame(
                                 Year = c(1922L,1923L,1924L,1925L,
                                          1926L,1927L,1928L,1929L,1930L,1931L,
                                          1932L,1933L,1934L,1935L,1936L,
                                          1937L,1938L,1939L,1940L,1941L,1942L,
                                          1943L,1944L,1945L,1946L,1947L,
                                          1948L,1949L,1950L,1951L,1952L,
                                          1953L,1954L,1955L,1956L,1957L,1958L,
                                          1959L,1960L,1961L,1962L,1963L,
                                          1964L,1965L,1966L,1967L,1968L,1969L,
                                          1970L,1971L,1972L,1973L,1974L,
                                          1975L,1976L,1977L,1978L,1979L,1980L,
                                          1981L,1982L,1983L,1984L,1985L,
                                          1986L,1987L,1988L,1989L,1990L,
                                          1991L,1992L,1993L,1994L,1995L,1996L,
                                          1997L,1998L,1999L,2000L,2001L,
                                          2002L,2003L,2004L,2005L,2006L,2007L,
                                          2008L,2009L,2010L,2011L,2012L,
                                          2013L,2014L,2015L,2016L,2017L,2018L,
                                          2019L,2020L,2021L),
         Cases = c(107473,164191,165418,152003,
                                          202210,181411,161799,197371,
                                          166914,172559,215343,179135,265269,
                                          180518,147237,214652,227319,103188,
                                          183866,222202,191383,191890,109873,
                                          133792,109860,156517,74715,69479,
                                          120718,68687,45030,37129,60886,
                                          62786,31732,28295,32148,40005,
                                          14809,11468,17749,17135,13005,6799,
                                          7717,9718,4810,3285,4249,3036,
                                          3287,1759,2402,1738,1010,2177,2063,
                                          1623,1730,1248,1895,2463,2276,
                                          3589,4195,2823,3450,4157,4570,
                                          2719,4083,6586,4617,5137,7796,6564,
                                          7405,7298,7867,7580,9771,11647,
                                          25827,25616,15632,10454,13278,
                                          16858,27550,18719,48277,28639,32971,
                                          20762,17972,18975,15609,18617,
                                          6124,2116)
       )
```

```
head(cdc)
```

```
  Year  Cases
1 1922 107473
2 1923 164191
3 1924 165418
4 1925 152003
5 1926 202210
6 1927 181411
```

```
library(ggplot2)
ggplot(cdc, aes(Year, Cases)) +
  geom_point(col="darkgray") +
  geom_line() +
  geom_vline(xintercept=1946, linetype="dashed", col="orange") +
  geom_vline(xintercept=1996, linetype="dashed", col="magenta") +
  geom_vline(xintercept=2020, linetype="dashed", col="red")
```



There was a lag in the resurgence after the aP vaccine was introduced. For some reason, the aP vaccine does not last as long in our immune memory at the wP vaccine. Anti-vaxxers also play a role in increasing cases of preventable illnesses.

Exploring CMI-PB

We want to know why this preventable disease is on the upswing. We will investigate the pertussis-specific immune responses over time in wP and aP vaccinated individuals.

We will utilize API-endpoint data in JSON format. We use the jsonlite package to access the data, and `read_json()`

```
library(jsonlite)
subject <- read_json("https://www.cmi-pb.org/api/subject", simplifyVector = TRUE)
specimen <- read_json("https://www.cmi-pb.org/api/specimen", simplifyVector = TRUE)
head(subject)
```

```
  subject_id infancy_vac biological_sex              ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          2          wP         Female Not Hispanic or Latino White
3          3          wP         Female                Unknown White
```

```
4          4          wP           Male Not Hispanic or Latino Asian
5          5          wP           Male Not Hispanic or Latino Asian
6          6          wP         Female Not Hispanic or Latino White
  year_of_birth date_of_boost      dataset
1    1986-01-01    2016-09-12 2020_dataset
2    1968-01-01    2019-01-28 2020_dataset
3    1983-01-01    2016-10-10 2020_dataset
4    1988-01-01    2016-08-29 2020_dataset
5    1991-01-01    2016-08-29 2020_dataset
6    1988-01-01    2016-10-10 2020_dataset
```

```
head(specimen)
```

```
  specimen_id subject_id actual_day_relative_to_boost
1           1          1                           -3
2           2          1                            1
3           3          1                            3
4           4          1                            7
5           5          1                           11
6           6          1                           32
  planned_day_relative_to_boost specimen_type visit
1                             0         Blood     1
2                             1         Blood     2
3                             3         Blood     3
4                             7         Blood     4
5                            14         Blood     5
6                            30         Blood     6
```

Q4. How many aP and wP infancy vaccinated subjects are in the dataset?

```
table(subject$infancy_vac)
```

```

aP wP
60 58
```

Q5. How many Male and Female subjects/patients are in the dataset?

```
table(subject$biological_sex)
```

```
Female   Male 
    79     39 
```

Q6. What is the breakdown of race and biological sex (e.g. number of Asian females, White males etc…)?

```
table(subject$race, subject$biological_sex)
```

```
                                           
                                            Female Male
  American Indian/Alaska Native                  0    1
  Asian                                         21   11
  Black or African American                      2    0
  More Than One Race                             9    2
  Native Hawaiian or Other Pacific Islander      1    1
  Unknown or Not Reported                       11    4
  White                                         35   20
```

Most represented: White females

```
library(tidyverse)
```

```
-- Attaching core tidyverse packages ------------------------ tidyverse 2.0.0 --
v dplyr     1.1.3     v readr     2.1.4
v forcats   1.0.0     v stringr   1.5.0
v lubridate 1.9.3     v tibble    3.2.1
v purrr     1.0.2     v tidyr     1.3.0
-- Conflicts ------------------------------------------ tidyverse_conflicts() --
x dplyr::filter()  masks stats::filter()
x purrr::flatten() masks jsonlite::flatten()
x dplyr::lag()     masks stats::lag()
i Use the conflicted package (<http://conflicted.r-lib.org/>) to force all conflicts to becor
```

```
today()
```

```
[1] "2023-12-06"
```

```
time_length(today() - mdy("08-12-1996"), "years")
```

```
[1] 27.31554
```

Q7. Using this approach determine (i) the average age of wP individuals, (ii) the average age of aP individuals; and (iii) are they significantly different?

```
subject$age <- time_length(today() - ymd(subject$year_of_birth), "years")
subject$age_boosted <- time_length(ymd(subject$date_of_boost) - ymd(subject$year_of_birth)
head(subject)
```

```
  subject_id infancy_vac biological_sex               ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          2          wP         Female Not Hispanic or Latino White
3          3          wP         Female                 Unknown White
4          4          wP           Male Not Hispanic or Latino Asian
5          5          wP           Male Not Hispanic or Latino Asian
6          6          wP         Female Not Hispanic or Latino White
  year_of_birth date_of_boost      dataset      age age_boosted
1    1986-01-01    2016-09-12 2020_dataset 37.92745    30.69678
2    1968-01-01    2019-01-28 2020_dataset 55.92882    51.07461
3    1983-01-01    2016-10-10 2020_dataset 40.92813    33.77413
4    1988-01-01    2016-08-29 2020_dataset 35.92882    28.65982
5    1991-01-01    2016-08-29 2020_dataset 32.92813    25.65914
6    1988-01-01    2016-10-10 2020_dataset 35.92882    28.77481
```

aP

```
library(dplyr)

ap <- subject %>% filter(infancy_vac == "aP")
head(ap)
```

```
  subject_id infancy_vac biological_sex              ethnicity
1          9          aP           Male Not Hispanic or Latino
2         13          aP           Male Not Hispanic or Latino
3         18          aP         Female     Hispanic or Latino
4         27          aP         Female Not Hispanic or Latino
5         29          aP           Male     Hispanic or Latino
6         32          aP           Male Not Hispanic or Latino
                                      race year_of_birth date_of_boost
1                                    Asian    1996-01-01    2016-07-25
2                                    White    1997-01-01    2016-07-25
3                   Unknown or Not Reported    1997-01-01    2016-08-29
4                                    Asian    1997-01-01    2016-09-26
5                                    White    1997-01-01    2016-09-26
6 Native Hawaiian or Other Pacific Islander    1997-01-01    2016-10-24
       dataset      age age_boosted
1 2020_dataset 27.92882    20.56400
2 2020_dataset 26.92676    19.56194
3 2020_dataset 26.92676    19.65777
4 2020_dataset 26.92676    19.73443
5 2020_dataset 26.92676    19.73443
6 2020_dataset 26.92676    19.81109
```

```
mean(ap$age)
```

```
[1] 26.02756
```

wP

```
wp <- subject %>% filter(infancy_vac == "wP")
head(wp)
```

```
  subject_id infancy_vac biological_sex              ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          2          wP         Female Not Hispanic or Latino White
3          3          wP         Female                Unknown White
4          4          wP           Male Not Hispanic or Latino Asian
5          5          wP           Male Not Hispanic or Latino Asian
6          6          wP         Female Not Hispanic or Latino White
  year_of_birth date_of_boost      dataset      age age_boosted
```

```
1     1986-01-01    2016-09-12 2020_dataset 37.92745    30.69678
2     1968-01-01    2019-01-28 2020_dataset 55.92882    51.07461
3     1983-01-01    2016-10-10 2020_dataset 40.92813    33.77413
4     1988-01-01    2016-08-29 2020_dataset 35.92882    28.65982
5     1991-01-01    2016-08-29 2020_dataset 32.92813    25.65914
6     1988-01-01    2016-10-10 2020_dataset 35.92882    28.77481
```

```
mean(wp$age)
```

```
[1] 36.32429
```

Q8. Determine the age of all individuals at time of boost?

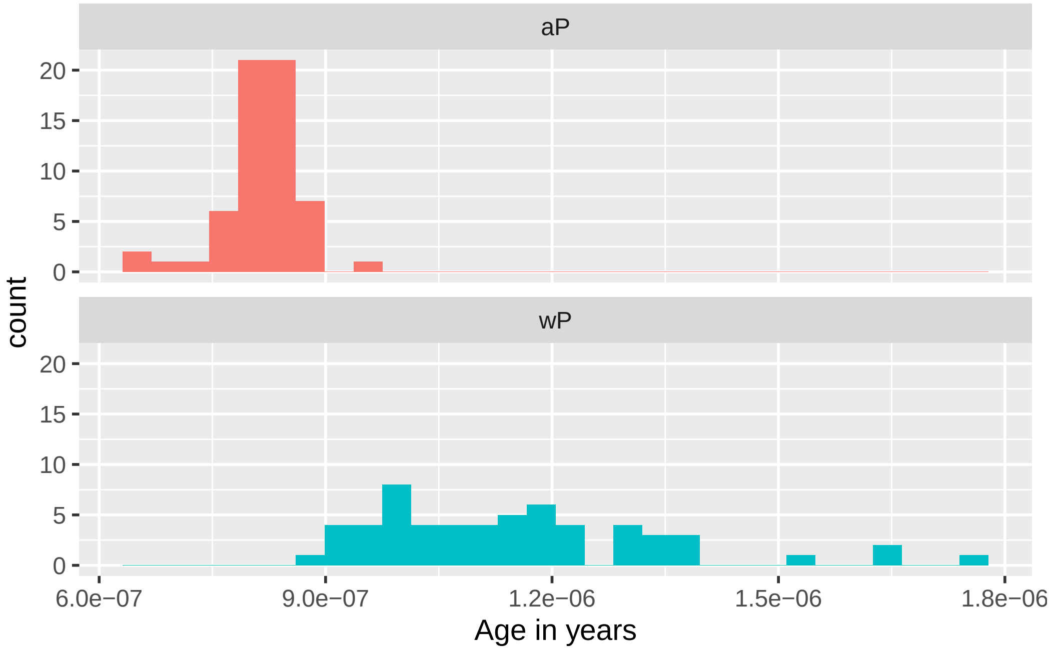
```
mean(subject$age_boosted)
```

```
[1] 25.66682
```

Q9. With the help of a faceted boxplot or histogram (see below), do you think these two groups are significantly different?

```
ggplot(subject) +
  aes(time_length(age, "year"),
      fill=as.factor(infancy_vac)) +
  geom_histogram(show.legend=FALSE) +
  facet_wrap(vars(infancy_vac), nrow=2) +
  xlab("Age in years")
```

```
`stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```



Yes, they appear very different in spread.

```
ap <- subject %>% filter(infancy_vac == "aP")
head(ap)
```

```
  subject_id infancy_vac biological_sex              ethnicity
1          9          aP           Male Not Hispanic or Latino
2         13          aP           Male Not Hispanic or Latino
3         18          aP         Female     Hispanic or Latino
4         27          aP         Female Not Hispanic or Latino
5         29          aP           Male     Hispanic or Latino
6         32          aP           Male Not Hispanic or Latino
                                      race year_of_birth date_of_boost
1                                    Asian    1996-01-01    2016-07-25
2                                    White    1997-01-01    2016-07-25
3                   Unknown or Not Reported    1997-01-01    2016-08-29
4                                    Asian    1997-01-01    2016-09-26
5                                    White    1997-01-01    2016-09-26
6 Native Hawaiian or Other Pacific Islander    1997-01-01    2016-10-24
      dataset      age age_boosted
1 2020_dataset 27.92882    20.56400
2 2020_dataset 26.92676    19.56194
```

```
3 2020_dataset 26.92676    19.65777
4 2020_dataset 26.92676    19.73443
5 2020_dataset 26.92676    19.73443
6 2020_dataset 26.92676    19.81109
```

```
dim(ap)
```

```
[1] 60 10
```

Join functions

```
meta <- inner_join(specimen, subject)
```

```
Joining with `by = join_by(subject_id)`
```

```
head(meta)
```

```
  specimen_id subject_id actual_day_relative_to_boost
1           1          1                           -3
2           2          1                            1
3           3          1                            3
4           4          1                            7
5           5          1                           11
6           6          1                           32
  planned_day_relative_to_boost specimen_type visit infancy_vac biological_sex
1                             0         Blood     1          wP         Female
2                             1         Blood     2          wP         Female
3                             3         Blood     3          wP         Female
4                             7         Blood     4          wP         Female
5                            14         Blood     5          wP         Female
6                            30         Blood     6          wP         Female
               ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
5 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
```

```
6 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
       age age_boosted
1 37.92745    30.69678
2 37.92745    30.69678
3 37.92745    30.69678
4 37.92745    30.69678
5 37.92745    30.69678
6 37.92745    30.69678
```

```r
titer <- read_json("https://www.cmi-pb.org/api/v4/plasma_ab_titer", simplifyVector = TRUE)
abdata <- inner_join(titer, meta)
```

```
Joining with `by = join_by(specimen_id)`
```

```r
head(abdata)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgE               FALSE   Total 1110.21154       2.493425
2           1     IgE               FALSE   Total 2708.91616       2.493425
3           1     IgG                TRUE      PT   68.56614       3.736992
4           1     IgG                TRUE     PRN  332.12718       2.602350
5           1     IgG                TRUE     FHA 1887.12263      34.050956
6           1     IgE                TRUE     ACT    0.10000       1.000000
   unit lower_limit_of_detection subject_id actual_day_relative_to_boost
1 UG/ML                 2.096133          1                           -3
2 IU/ML                29.170000          1                           -3
3 IU/ML                 0.530000          1                           -3
4 IU/ML                 6.205949          1                           -3
5 IU/ML                 4.679535          1                           -3
6 IU/ML                 2.816431          1                           -3
  planned_day_relative_to_boost specimen_type visit infancy_vac biological_sex
1                             0         Blood     1          wP         Female
2                             0         Blood     1          wP         Female
3                             0         Blood     1          wP         Female
4                             0         Blood     1          wP         Female
5                             0         Blood     1          wP         Female
6                             0         Blood     1          wP         Female
               ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
```

```
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
5 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
6 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
       age age_boosted
1 37.92745    30.69678
2 37.92745    30.69678
3 37.92745    30.69678
4 37.92745    30.69678
5 37.92745    30.69678
6 37.92745    30.69678
```

How many isotypes are we measuring for all these individuals?

```
table(abdata$isotype)
```

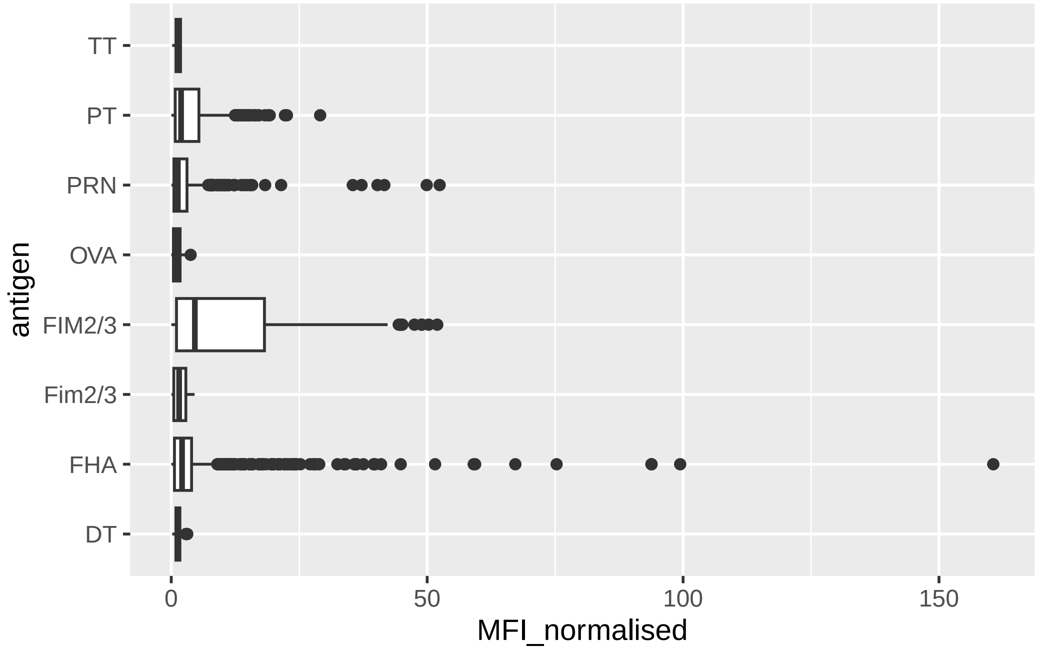
```
 IgE  IgG IgG1 IgG2 IgG3 IgG4
6698 3240 7968 7968 7968 7968
```

```
igg <- abdata %>%
  filter(isotype == "IgG")
head(igg)
```

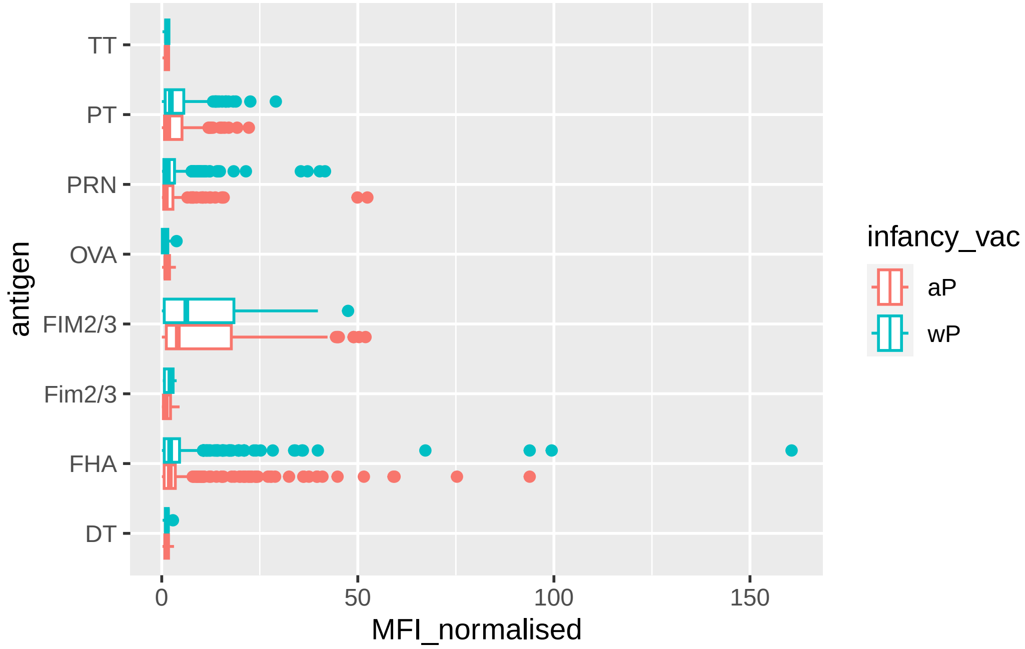
```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgG                TRUE      PT   68.56614       3.736992
2           1     IgG                TRUE     PRN  332.12718       2.602350
3           1     IgG                TRUE     FHA 1887.12263      34.050956
4          19     IgG                TRUE      PT   20.11607       1.096366
5          19     IgG                TRUE     PRN  976.67419       7.652635
6          19     IgG                TRUE     FHA   60.76626       1.096457
   unit lower_limit_of_detection subject_id actual_day_relative_to_boost
1 IU/ML                 0.530000          1                           -3
2 IU/ML                 6.205949          1                           -3
3 IU/ML                 4.679535          1                           -3
4 IU/ML                 0.530000          3                           -3
5 IU/ML                 6.205949          3                           -3
6 IU/ML                 4.679535          3                           -3
  planned_day_relative_to_boost specimen_type visit infancy_vac biological_sex
```

```
1                              0         Blood     1           wP          Female
2                              0         Blood     1           wP          Female
3                              0         Blood     1           wP          Female
4                              0         Blood     1           wP          Female
5                              0         Blood     1           wP          Female
6                              0         Blood     1           wP          Female
                ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4                 Unknown White    1983-01-01    2016-10-10 2020_dataset
5                 Unknown White    1983-01-01    2016-10-10 2020_dataset
6                 Unknown White    1983-01-01    2016-10-10 2020_dataset
       age age_boosted
1 37.92745    30.69678
2 37.92745    30.69678
3 37.92745    30.69678
4 40.92813    33.77413
5 40.92813    33.77413
6 40.92813    33.77413
```

```
ggplot(igg) + aes(MFI_normalised, antigen) +
         geom_boxplot()
```



```
ggplot(igg) + aes(MFI_normalised, antigen, col=infancy_vac) +
        geom_boxplot()
```



```r
head(igg)
```

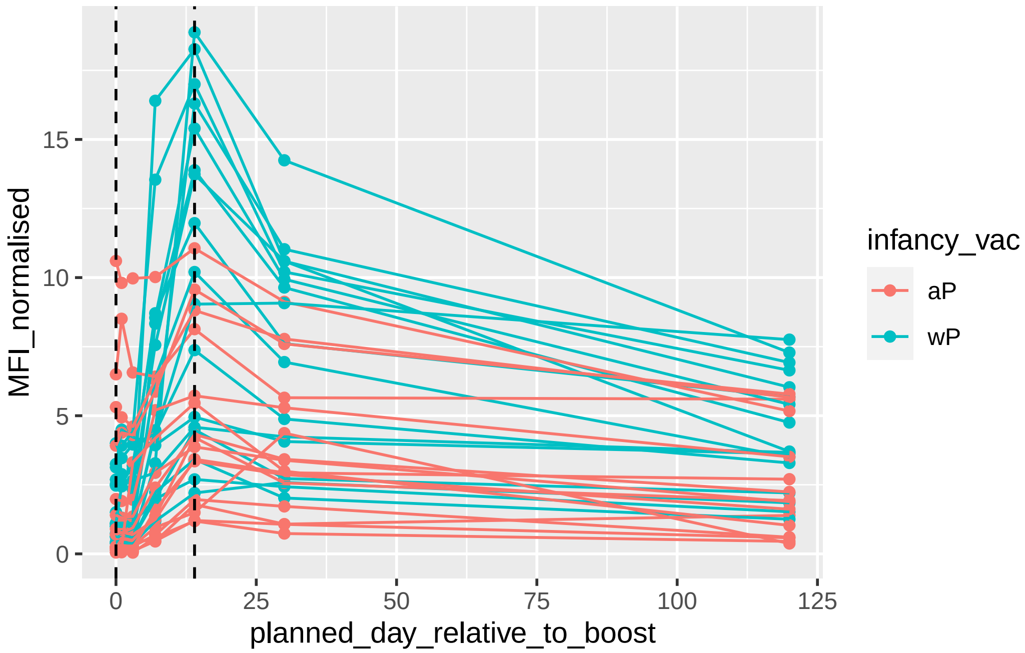
```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgG                TRUE      PT   68.56614       3.736992
2           1     IgG                TRUE     PRN  332.12718       2.602350
3           1     IgG                TRUE     FHA 1887.12263      34.050956
4          19     IgG                TRUE      PT   20.11607       1.096366
5          19     IgG                TRUE     PRN  976.67419       7.652635
6          19     IgG                TRUE     FHA   60.76626       1.096457
   unit lower_limit_of_detection subject_id actual_day_relative_to_boost
1 IU/ML                 0.530000          1                           -3
2 IU/ML                 6.205949          1                           -3
3 IU/ML                 4.679535          1                           -3
4 IU/ML                 0.530000          3                           -3
5 IU/ML                 6.205949          3                           -3
6 IU/ML                 4.679535          3                           -3
  planned_day_relative_to_boost specimen_type visit infancy_vac biological_sex
1                             0         Blood     1          wP         Female
2                             0         Blood     1          wP         Female
3                             0         Blood     1          wP         Female
4                             0         Blood     1          wP         Female
5                             0         Blood     1          wP         Female
6                             0         Blood     1          wP         Female
               ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4                Unknown White    1983-01-01    2016-10-10 2020_dataset
5                Unknown White    1983-01-01    2016-10-10 2020_dataset
6                Unknown White    1983-01-01    2016-10-10 2020_dataset
       age age_boosted
1 37.92745    30.69678
2 37.92745    30.69678
3 37.92745    30.69678
4 40.92813    33.77413
5 40.92813    33.77413
6 40.92813    33.77413
```

```r
#igg %>%
  #filter(antigen == "PT", dataset == "2020_dataset")
```

To focus in on IgG to the Pertussis Toxin (PT) antigen in the 2021 dataset:

```
igg.pt <- igg %>%
  filter(antigen == "PT", dataset == "2021_dataset")
```

```
ggplot(igg.pt) +
  aes(planned_day_relative_to_boost, MFI_normalised,
      col=infancy_vac,
      group=subject_id) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept = 0, linetype = "dashed", col="black") +
  geom_vline(xintercept = 14, linetype = "dashed", col="black")
```


MFI_normalised
planned_day_relative_to_boost
infancy_vac
aP
wP