class 18: Pertussis Resurgence Mini Project

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First we will examine and explore Pertussis case numbers in the US as tracked by the CDC: https://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html

> Q1. With the help of the R "addin" package datapasta assign the CDC pertussis case number data to a data frame called cdc and use ggplot to make a plot of cases numbers over time.

We can use the datapasta package to scrape this data from the website into R:

```
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)
```

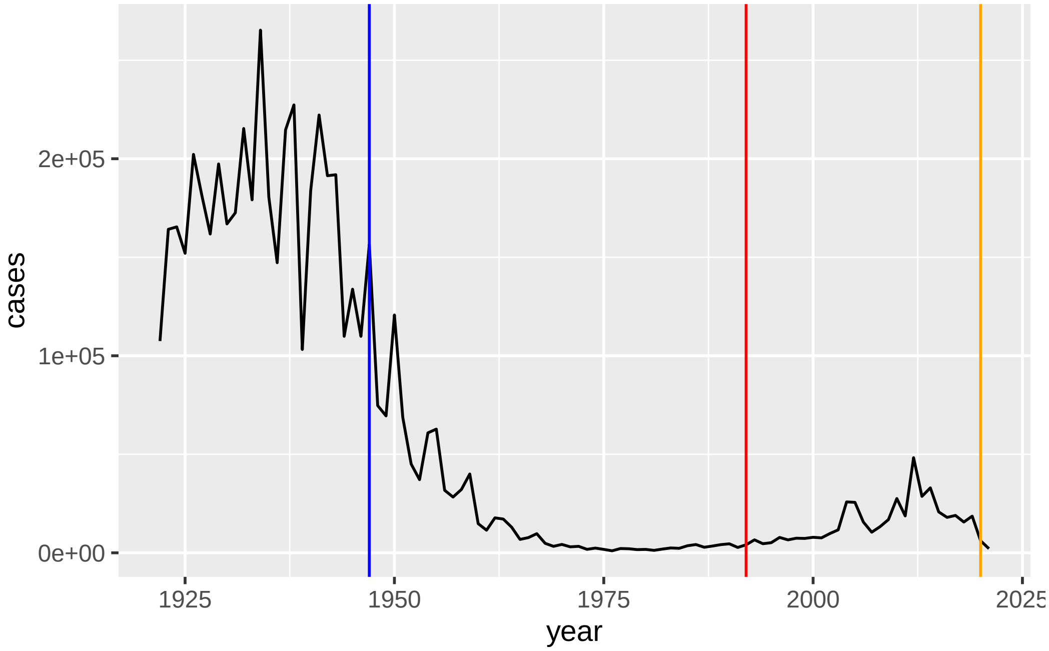
```
  year  cases
1 1922 107473
2 1923 164191
3 1924 165418
4 1925 152003
5 1926 202210
6 1927 181411
```

I want a plot of cases per year with ggplot

> Q2. Using the ggplot geom_vline() function add lines to your previous plot for the 1946 introduction of the wP vaccine and the 1996 switch to aP vaccine (see example in the hint below). What do you notice?

```
library(ggplot2)

ggplot(cdc) + aes(year, cases) + geom_line() + geom_vline(xintercept = 1947, col='blue') +
  geom_vline(xintercept=1992, col='red') +
  geom_vline(xintercept=2020, col='orange')
```



> Q3. Describe what happened after the introduction of the aP vaccine? Do you have a possible explanation for the observed trend?

About a couple decades after the introduction of the aP vaccine, we see a resurgence of pertussis cases (not as much as pre 1950, but still a considerable amount). A possible explanation could be that the newer generation of humans is resistant to the effects of the vaccine, making it less effective.

Access data from the CMI-PB project

This database (like many modern projects) uses an API to return JSON format data.

We will use the R package `jsonlite`.

```
library(jsonlite)
```

```
Warning: package 'jsonlite' was built under R version 4.3.3
```

```
subject <- read_json("https://www.cmi-pb.org/api/subject", 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
```

> Q4. How many wP (the older whole-cell vaccine) individuals and aP (newer acellular vaccine) individuals are in this 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
```

```r
head(subject$year_of_birth)
```

```
[1] "1986-01-01" "1968-01-01" "1983-01-01" "1988-01-01" "1991-01-01"
[6] "1988-01-01"
```

Side-Note: Working with dates

We can use the lubridate package to ease the pain of doing math with dates.

```r
library(lubridate)
```

```
Warning: package 'lubridate' was built under R version 4.3.3


Attaching package: 'lubridate'

The following objects are masked from 'package:base':

    date, intersect, setdiff, union
```

```r
today() - ymd("2000-01-01")
```

```
Time difference of 8832 days
```

```r
today() - ymd("2002-6-25")
```

```
Time difference of 7926 days
```

```
time_length(today() - mdy("6-25-2002"), "years")
```

```
[1] 21.70021
```

So what is the age of everyone on our dataset.

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

> 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?

```
library(dplyr)
```

```

Attaching package: 'dplyr'

The following objects are masked from 'package:stats':

    filter, lag

The following objects are masked from 'package:base':

    intersect, setdiff, setequal, union
```

```
#ap
ap <- subject %>% filter(infancy_vac == "aP")
round(summary(ap$age))
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max. 
     21      26      26      26      27      30 
```

```
# wP
wp <- subject %>% filter(infancy_vac == "wP")
round(summary(wp$age))
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max. 
     28      31      36      37      39      56 
```

```r
t.test(ap$age, wp$age)
```

```
	Welch Two Sample t-test

data:  ap$age and wp$age
t = -12.436, df = 65.411, p-value < 2.2e-16
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 -11.950080  -8.643385
sample estimates:
mean of x mean of y 
 26.27944  36.57618 
```

Determine the age of all individuals at time of boost?

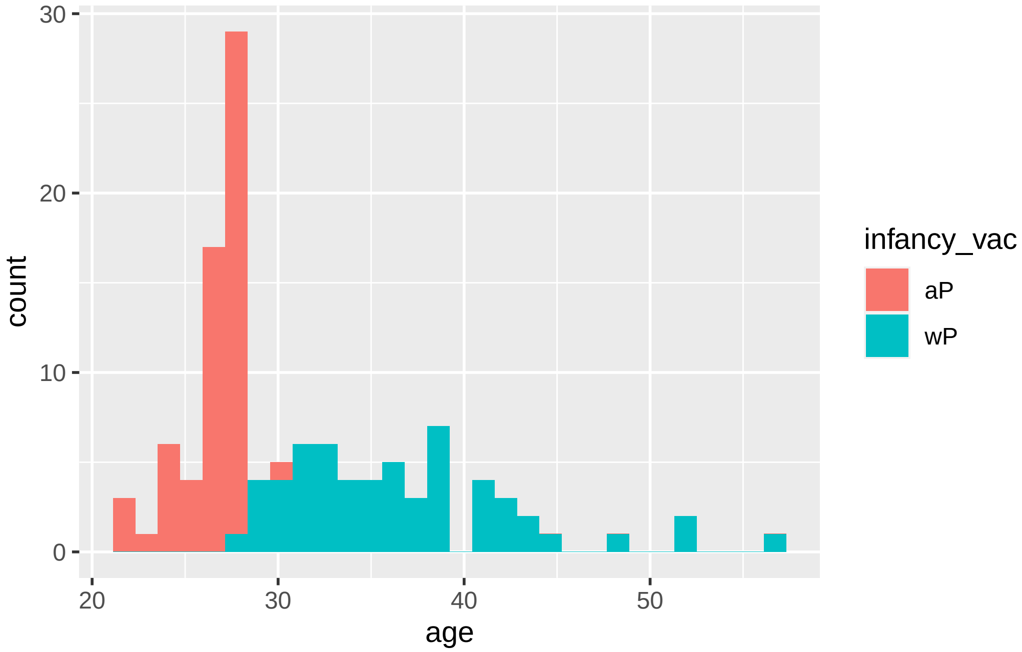
```r
int <- ymd(subject$date_of_boost) - ymd(subject$year_of_birth)
age_at_boost <- time_length(int, "year")
head(age_at_boost)
```

```
[1] 30.69678 51.07461 33.77413 28.65982 25.65914 28.77481
```

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

```r
ggplot(subject) + aes(age, fill=infancy_vac) + geom_histogram()
```

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



Get more data from CMI-PB

```
specimen <- read_json("http://cmi-pb.org/api/specimen", simplifyVector = T)
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
```

> Q9. Complete the code to join specimen and subject tables to make a new merged data frame containing all specimen records along with their associated subject details:

We need to **join** these two tables (subject and specimen) to make a single new "meta" table with all our metadata. We will use the `dyplyr` join functions to do this:

```
library(dplyr)

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

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

```
head(meta)
```

```
  subject_id infancy_vac biological_sex              ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          1          wP         Female Not Hispanic or Latino White
3          1          wP         Female Not Hispanic or Latino White
4          1          wP         Female Not Hispanic or Latino White
5          1          wP         Female Not Hispanic or Latino White
6          1          wP         Female Not Hispanic or Latino White
  year_of_birth date_of_boost      dataset      age specimen_id
1    1986-01-01    2016-09-12 2020_dataset 38.17933           1
2    1986-01-01    2016-09-12 2020_dataset 38.17933           2
3    1986-01-01    2016-09-12 2020_dataset 38.17933           3
4    1986-01-01    2016-09-12 2020_dataset 38.17933           4
5    1986-01-01    2016-09-12 2020_dataset 38.17933           5
6    1986-01-01    2016-09-12 2020_dataset 38.17933           6
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -3                             0         Blood
2                            1                             1         Blood
3                            3                             3         Blood
4                            7                             7         Blood
5                           11                            14         Blood
6                           32                            30         Blood
  visit
1     1
2     2
3     3
4     4
```

```
5     5
6     6
```

> Q10. Now using the same procedure join meta with titer data so we can further analyze this data in terms of time of visit aP/wP, male/female etc.

Now we can read some of the other data from CMI-PB

```
ab_titer <- read_json("http://cmi-pb.org/api/v4/plasma_ab_titer",
                      simplifyVector = T)
head(ab_titer)
```

```
  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
1 UG/ML                 2.096133
2 IU/ML                29.170000
3 IU/ML                 0.530000
4 IU/ML                 6.205949
5 IU/ML                 4.679535
6 IU/ML                 2.816431
```

One more `inner_join()` to add all our metadata in `meta` on to our `ab_data` table:

```
abdata <- inner_join(ab_titer, meta)
```

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

```
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 infancy_vac biological_sex
1 UG/ML                 2.096133          1          wP         Female
2 IU/ML                29.170000          1          wP         Female
3 IU/ML                 0.530000          1          wP         Female
4 IU/ML                 6.205949          1          wP         Female
5 IU/ML                 4.679535          1          wP         Female
6 IU/ML                 2.816431          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 actual_day_relative_to_boost planned_day_relative_to_boost
1 38.17933                           -3                             0
2 38.17933                           -3                             0
3 38.17933                           -3                             0
4 38.17933                           -3                             0
5 38.17933                           -3                             0
6 38.17933                           -3                             0
  specimen_type visit
1         Blood     1
2         Blood     1
3         Blood     1
4         Blood     1
5         Blood     1
6         Blood     1
```

> Q11. How many specimens (i.e. entries in abdata) do we have for each isotype?

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

```

 IgE  IgG IgG1 IgG2 IgG3 IgG4 
6698 3233 7961 7961 7961 7961 
```

> Q12. What are the different $dataset values in abdata and what do you notice about the number of rows for the most "recent" dataset?

```r
table(abdata$dataset)
```

```
2020_dataset 2021_dataset 2022_dataset 
       31520         8085         2170 
```

2022 has the least amount of specimens collected in this dataset.

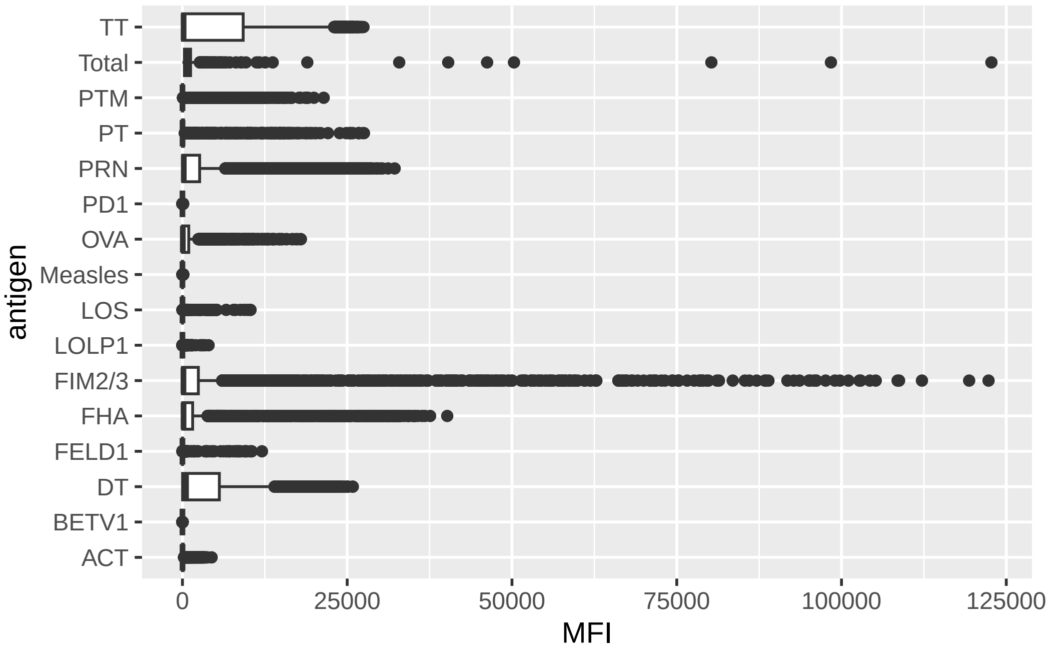
Our first exploratory plot:

```r
table(abdata$antigen)
```

```
    ACT   BETV1      DT   FELD1     FHA  FIM2/3   LOLP1     LOS Measles     OVA 
   1970    1970    3435    1970    3829    3435    1970    1970    1970    3435 
    PD1     PRN      PT     PTM   Total      TT 
   1970    3829    3829    1970     788    3435 
```

```r
ggplot(abdata) + aes(MFI, antigen) + geom_boxplot()
```

```
Warning: Removed 1 rows containing non-finite values (`stat_boxplot()`).
```

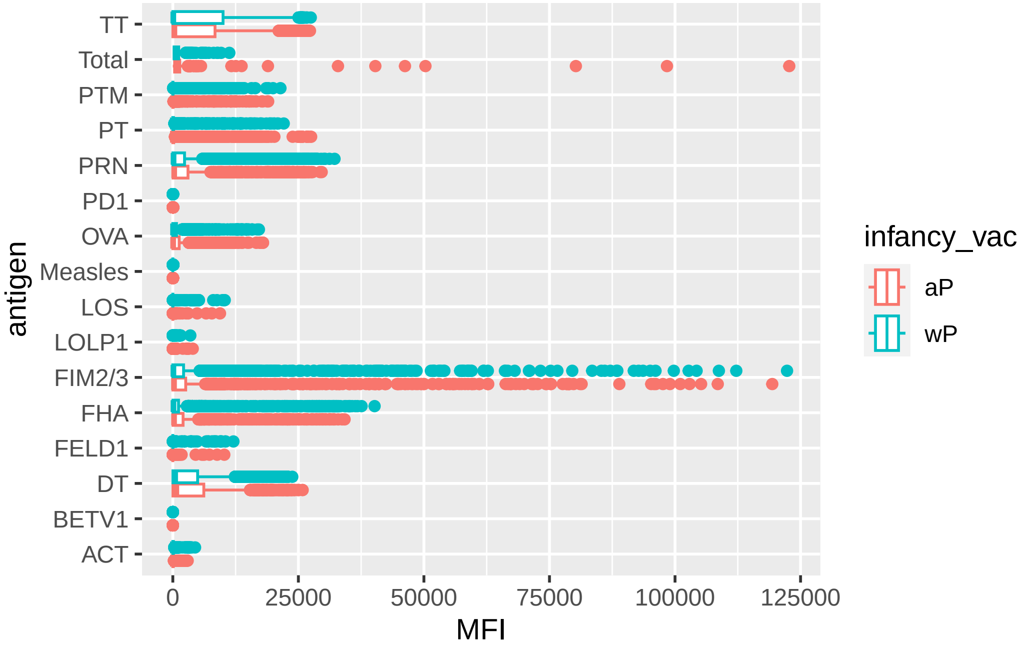


Why are certain antigens and not others very variable in their detected levels here?

Can you facet or even just color by infancy_vac? Is there some difference?

```
ggplot(abdata) + aes(MFI, antigen, color=infancy_vac) + geom_boxplot()
```

```
Warning: Removed 1 rows containing non-finite values (`stat_boxplot()`).
```



There are potentially some differences here but in general it is hard to tell with this whole dataset overview...

```
table(abdata$dataset)
```

```

2020_dataset 2021_dataset 2022_dataset 
       31520         8085         2170 
```

Let's focus in on just the 2021_dataset.

```
abdata.21 <- filter(abdata, dataset == '2021_dataset')
table(abdata.21$dataset)
```

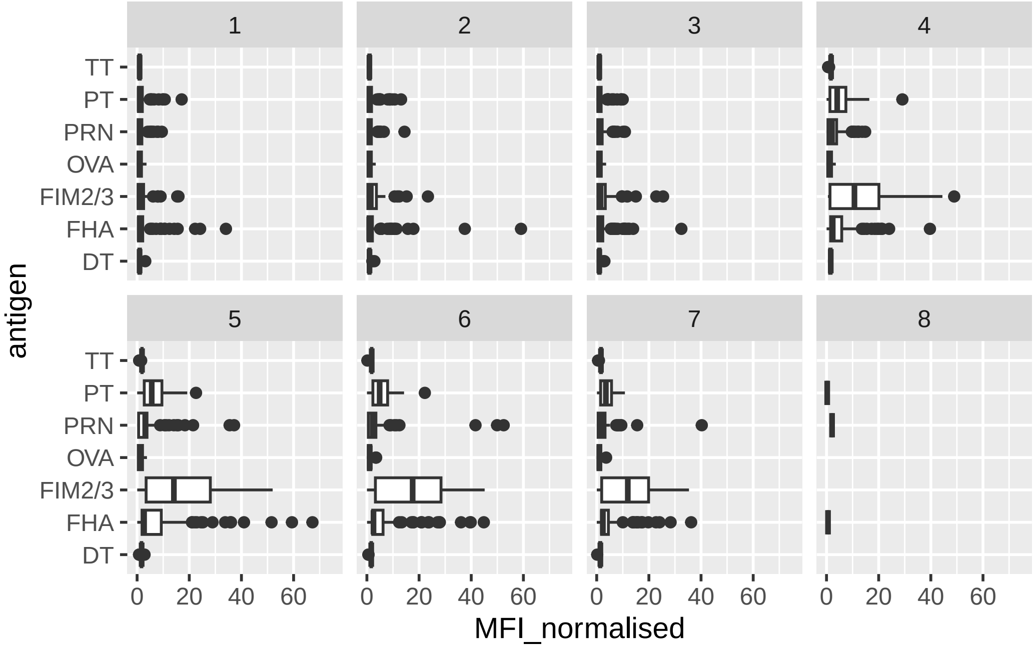
```
2021_dataset
        8085
```

Q13. Complete the following code to make a summary boxplot of Ab titer levels (MFI) for all antigens:

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

ggplot(igg) +
  aes(MFI_normalised, antigen) +
  geom_boxplot() +
    xlim(0,75) +
  facet_wrap(vars(visit), nrow=2)
```

```
Warning: Removed 5 rows containing non-finite values (`stat_boxplot()`).
```

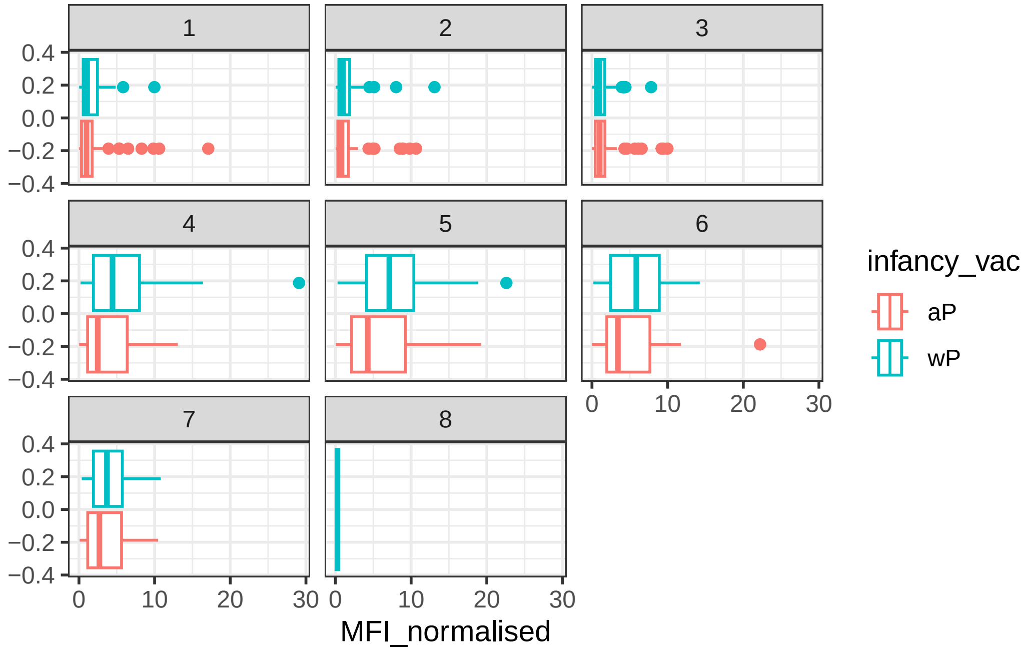


Q14. What antigens show differences in the level of IgG antibody titers recognizing them over time? Why these and not others?

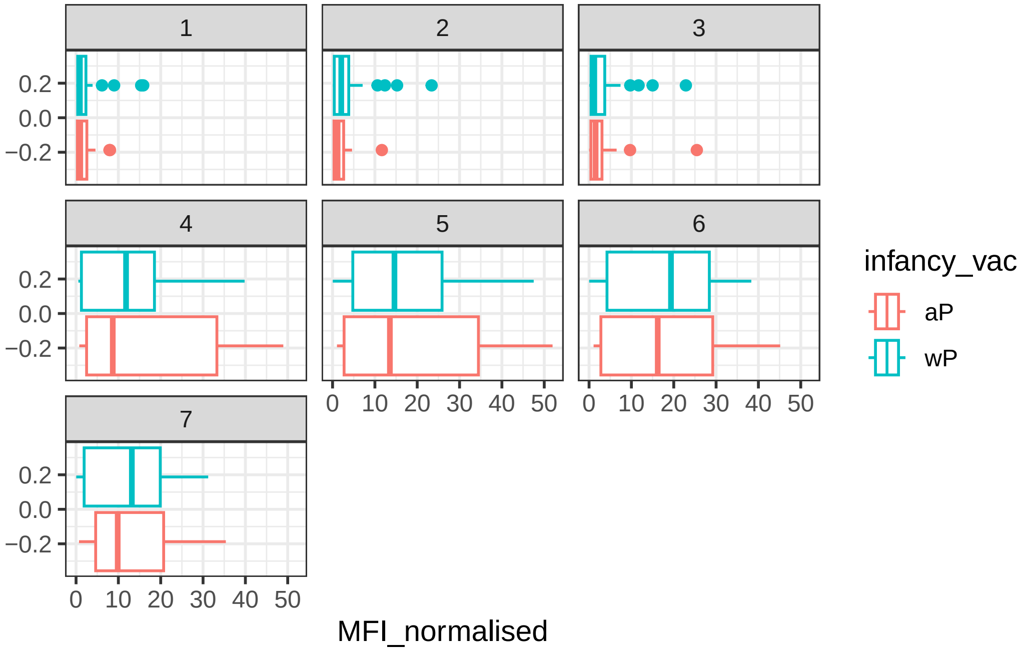
PT and FIM2/3 show a wider range of normalized values. These were included in the vaccine, explaining why this might be the case.

Q15. Filter to pull out only two specific antigens for analysis and create a boxplot for each. You can chose any you like. Below I picked a "control" antigen ("OVA", that is not in our vaccines) and a clear antigen of interest ("PT", Pertussis Toxin, one of the key virulence factors produced by the bacterium B. pertussis).

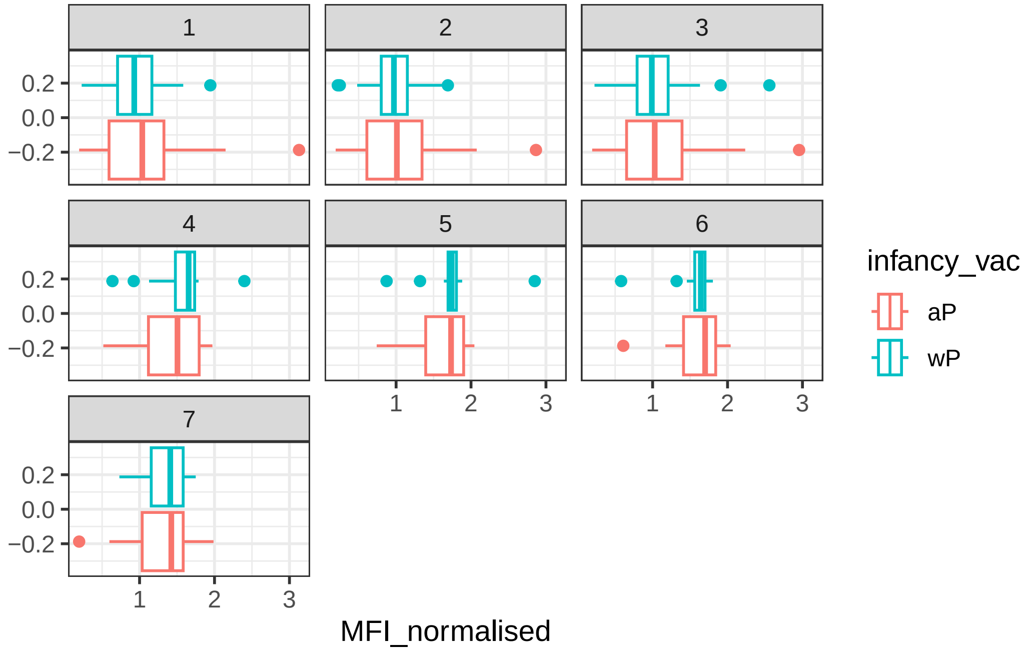
```
filter(igg, antigen=="PT") %>%
  ggplot() +
  aes(MFI_normalised, col=infancy_vac) +
  geom_boxplot(show.legend = T) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



```
filter(igg, antigen=="FIM2/3") %>%
  ggplot() +
  aes(MFI_normalised, col=infancy_vac) +
  geom_boxplot(show.legend = T) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



```
filter(igg, antigen=="DT") %>%
  ggplot() +
  aes(MFI_normalised, col=infancy_vac) +
  geom_boxplot(show.legend = T) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



Q16. What do you notice about these two antigens time courses and the PT data in particular?

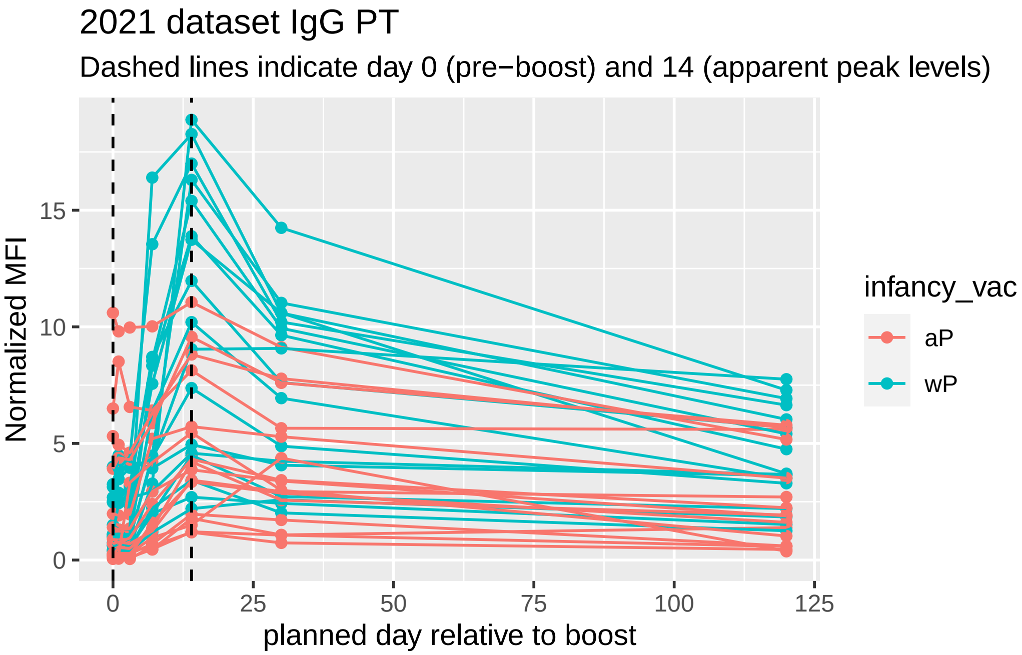
PT and FIM2/3 appear to be generally increasing with the number of visits over time. This is does not appear to be true for DT. This could be indicative of increasing risk for Pertussis.

Focus on PT antigen for IgG levels

```
pt.21 <- filter(abdata.21, isotype == 'IgG', antigen == 'PT')
```

plot of days (time) relative to boost vs MFI

```
ggplot(pt.21) +
  aes(x=planned_day_relative_to_boost, y=MFI_normalised, col=infancy_vac, group=subject_id
    geom_vline(xintercept=0, linetype="dashed") +
    geom_vline(xintercept=14, linetype="dashed") +
  labs(title="2021 dataset IgG PT",
       subtitle = "Dashed lines indicate day 0 (pre-boost) and 14 (apparent peak levels)")
```



Q17. Do you see any clear difference in aP vs. wP responses?

In terms of the PT antigen, we see a clear increase in normalized MFI for the wP infancy vaccination subjects based on this line plot (at 14 days after the boost.