Lab 18

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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>

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

> Q1 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.

```
cdc <- data.frame(
                                 year = c(1922L,1923L,1924L,192
                                          1926L,1927L,1928L,192
                                          1932L,1933L,1934L,193
                                          1937L,1938L,1939L,194
                                          1943L,1944L,1945L,194
                                          1948L,1949L,1950L,195
                                          1953L,1954L,1955L,195
                                          1959L,1960L,1961L,196
                                          1964L,1965L,1966L,196
                                          1970L,1971L,1972L,197
                                          1975L,1976L,1977L,197
                                          1981L,1982L,1983L,198
                                          1986L,1987L,1988L,198
                                          1991L,1992L,1993L,199
                                          1997L,1998L,1999L,200
                                          2002L,2003L,2004L,200
                                          2008L,2009L,2010L,201
                                          2013L,2014L,2015L,201
                                          2019L,2020L,2021L),
         No.Reported.Pertussis.Cases = c(107473,164191,165418,1
                                          202210,181411,161799,
                                          166914,172559,215343,
                                          180518,147237,214652,
                                          183866,222202,191383,
                                          133792,109860,156517,
                                          120718,68687,45030,37
                                          62786,31732,28295,321
                                          14809,11468,17749,171
                                          7717,9718,4810,3285,4
                                          3287,1759,2402,1738,1
                                          1623,1730,1248,1895,2
                                          3589,4195,2823,3450,4
                                          2719,4083,6586,4617,5
                                          7405,7298,7867,7580,9
                                          25827,25616,15632,104
                                          16858,27550,18719,482
                                          20762,17972,18975,156
                                          6124,2116)
       )

View(cdc)
```

```
head(cdc)
```

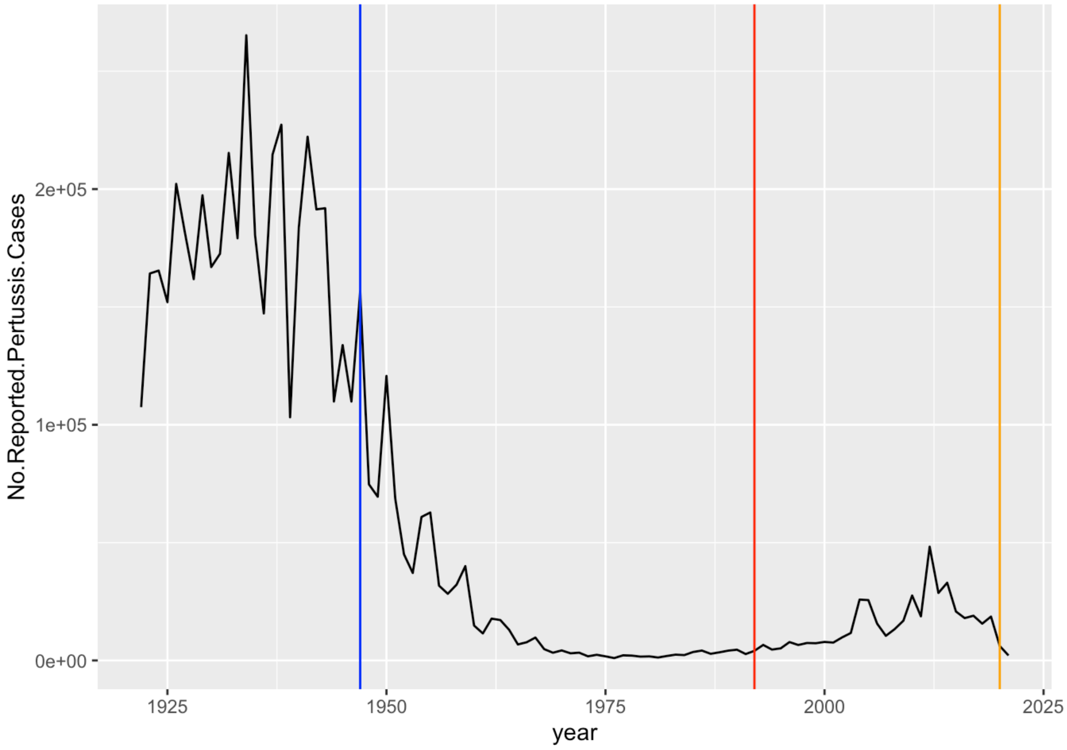
```
  year No.Reported.Pertussis.Cases
1 1922                      107473
2 1923                      164191
3 1924                      165418
4 1925                      152003
5 1926                      202210
6 1927                      181411
```

I want a plot of cases per year with ggplot

```
library(ggplot2)
```

> 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?

```
ggplot(cdc) +
aes(year, No.Reported.Pertussis.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?

There is an increase most likely due to COVID and comorbidities that could contribute to decreased immunity. THere could also be 1) more sensitive PCR-based testing, 2) vaccination hesitancy 3) bacterial evolution (escape from vaccine immunity), 4) waning of immunity in adolescents originally primed as infants with the newer aP vaccine as compared to the older wP vaccine.

Access data from the CMI-PB project

This database(like many modern project) uses an APi to return JSOn format data.

We will use the R package jsonlite

```
library(jsonlite)

subject <- read_json("http://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
```

> q4How 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. What is the number of individuals by biological sex and race

```
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
```

```
subject$year_of_birth
```

```
  [1] "1986-01-01" "1968-01-01" "1983-01-01" "1988-01-01"
"1991-01-01"
  [6] "1988-01-01" "1981-01-01" "1985-01-01" "1996-01-01"
"1982-01-01"
 [11] "1986-01-01" "1982-01-01" "1997-01-01" "1993-01-01"
"1989-01-01"
 [16] "1987-01-01" "1980-01-01" "1997-01-01" "1994-01-01"
"1981-01-01"
 [21] "1983-01-01" "1985-01-01" "1991-01-01" "1992-01-01"
"1988-01-01"
 [26] "1983-01-01" "1997-01-01" "1982-01-01" "1997-01-01"
"1988-01-01"
 [31] "1989-01-01" "1997-01-01" "1990-01-01" "1983-01-01"
"1991-01-01"
 [36] "1997-01-01" "1998-01-01" "1997-01-01" "1985-01-01"
"1994-01-01"
 [41] "1985-01-01" "1997-01-01" "1998-01-01" "1998-01-01"
"1997-01-01"
 [46] "1998-01-01" "1996-01-01" "1998-01-01" "1997-01-01"
"1997-01-01"
 [51] "1997-01-01" "1998-01-01" "1998-01-01" "1997-01-01"
```

```
"1997-01-01"
 [56] "1997-01-01" "1996-01-01" "1997-01-01" "1997-01-01"
"1997-01-01"
 [61] "1987-01-01" "1993-01-01" "1995-01-01" "1993-01-01"
"1990-01-01"
 [66] "1976-01-01" "1972-01-01" "1972-01-01" "1990-01-01"
"1998-01-01"
 [71] "1998-01-01" "1991-01-01" "1995-01-01" "1995-01-01"
"1998-01-01"
 [76] "1998-01-01" "1988-01-01" "1993-01-01" "1987-01-01"
"1992-01-01"
 [81] "1993-01-01" "1998-01-01" "1999-01-01" "1997-01-01"
"2000-01-01"
 [86] "1998-01-01" "2000-01-01" "2000-01-01" "1997-01-01"
"1999-01-01"
 [91] "1998-01-01" "2000-01-01" "1996-01-01" "1999-01-01"
"1998-01-01"
 [96] "2000-01-01" "1986-01-01" "1993-01-01" "1999-01-01"
"2001-01-01"
[101] "2003-01-01" "2003-01-01" "1994-01-01" "1989-01-01"
"1994-01-01"
[106] "1996-01-01" "1998-01-01" "1995-01-01" "1989-01-01"
"1997-01-01"
[111] "1996-01-01" "1996-01-01" "1996-01-01" "1990-01-01"
"2002-01-01"
[116] "2000-01-01" "1994-01-01" "1998-01-01"
```

#Side-Note: Working with dates

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

> Q7 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?

```r
library(lubridate)
```

```

Attaching package: 'lubridate'

The following objects are masked from 'package:base':
    date, intersect, setdiff, union
```

```
today()
```

```
[1] "2024-03-07"
```

```
today() - ymd("2002-01-01")
```

```
Time difference of 8101 days
```

```
today() - mdy("5-15-2002")
```

```
Time difference of 7967 days
```

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

```
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
```

So what is the age of everyone on our dataset.

```
time_length(today() - mdy("5-15-2002"), "years")
```

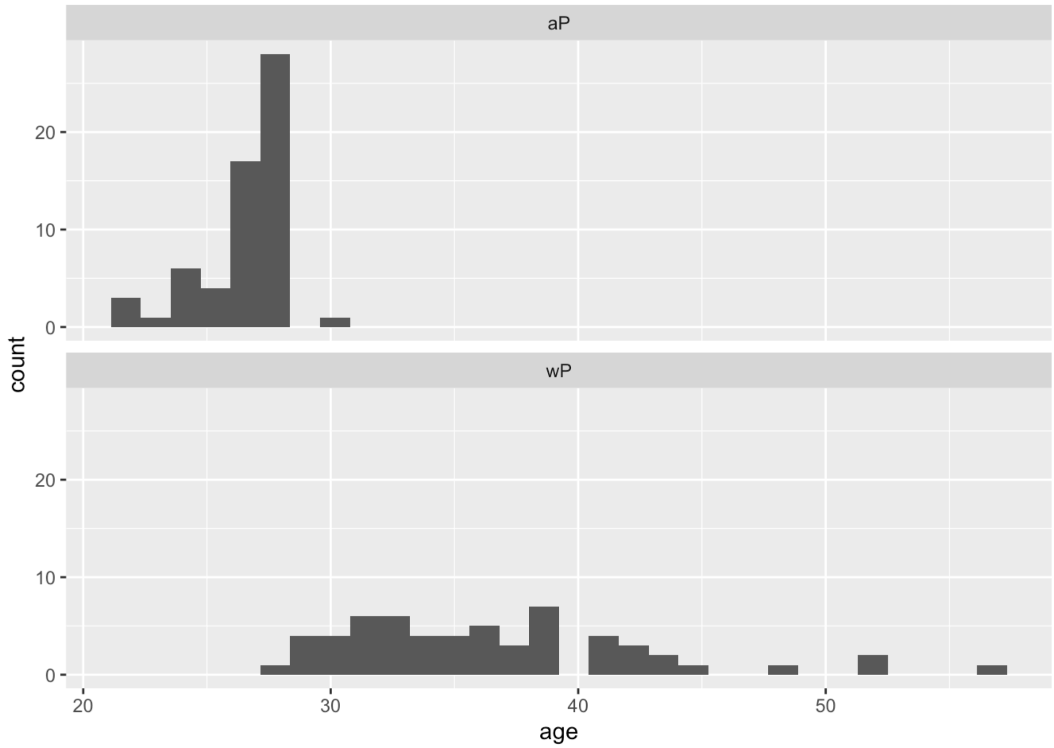
```
[1] 21.81246
```

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

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

```
library(ggplot2)
ggplot(subject) +
aes(age) +
  facet_wrap(vars(infancy_vac), nrow=2) +
  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", simplif
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 of our metadata

```
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
```

```
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
```

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

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:

> Q.10

```
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

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

```

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

> Q12

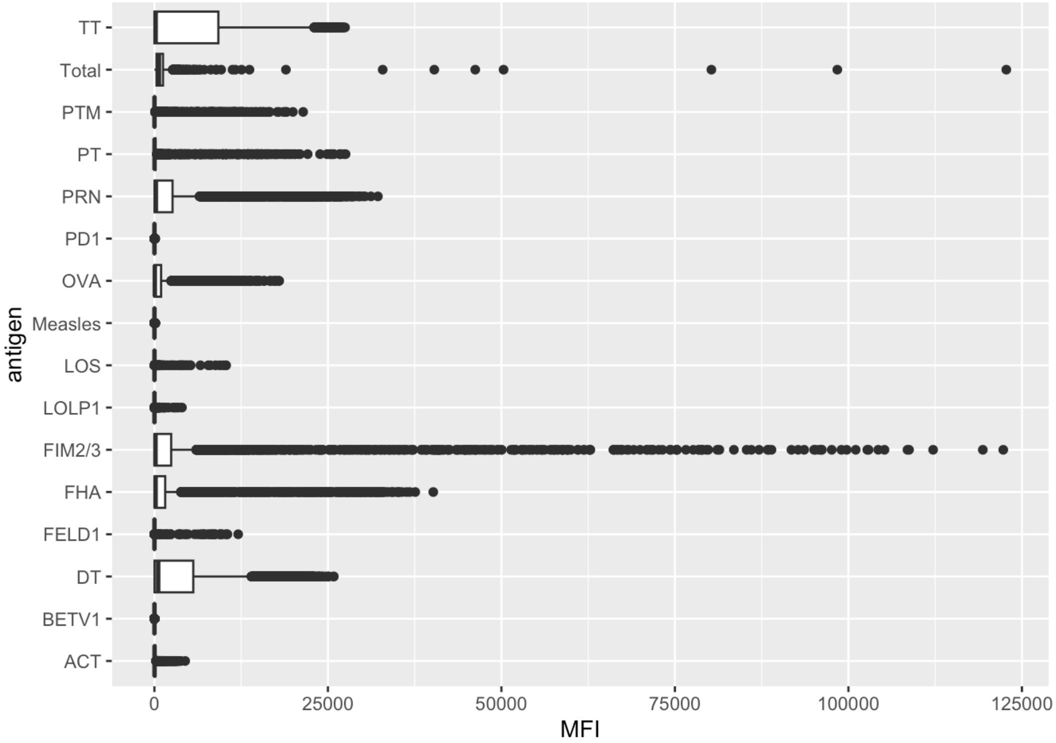
```
table(abdata$antigen)
```

```

    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 
```

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

```
Warning: Removed 1 row containing non-finite outside the scale
range
(`stat_boxplot()`).
```



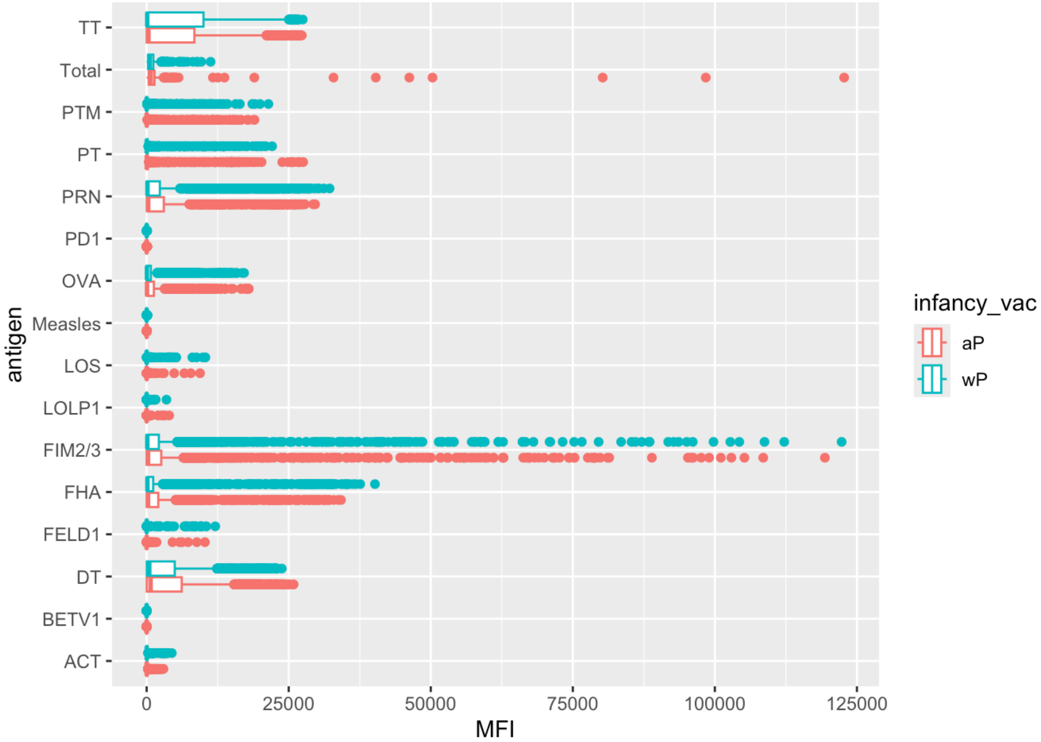
> Q13. Complete the following code to make a summary boxplot of Ab titer levels (MFI) for all antigens:

why are certain antigens and not others very variable in their detection levels here?

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

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

```
Warning: Removed 1 row containing non-finite outside the scale
range
(`stat_boxplot()`).
```



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

You can use the CMI-PB website search functionality and Terminology Browser (under development) to find out about each antigen. Note that this is still work in progress.

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 
```

Lets focus in on just the 2021 dataset

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

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

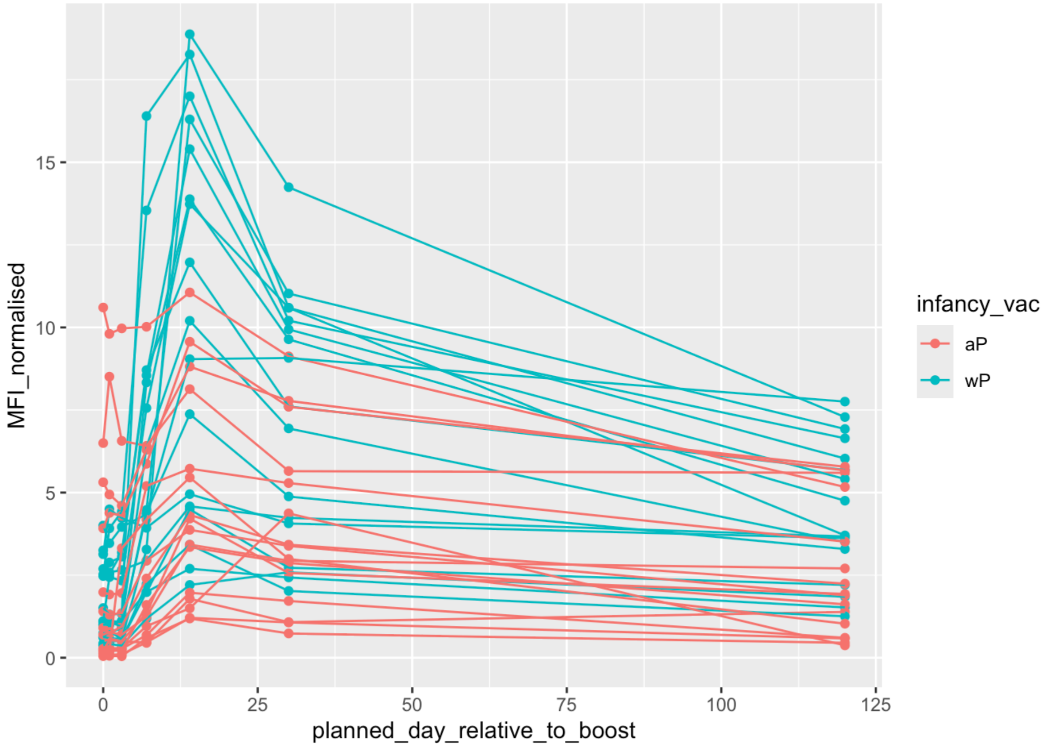
Focus on PT antigen IgG levels

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

plot of days(time) relative to boost vs MFI leves

> 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).

```
ggplot(pt.21)+
    aes(x=planned_day_relative_to_boost,
        y=MFI_normalised,
        col=infancy_vac,
        group=subject_id) +
    geom_point() +
    geom_line()
```



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

PT levels clearly rise over time and far exceed those of OVA. They also appear to peak at visit 5 and then decline. This trend appears similar for wP and aP subjects.

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

Yes I do see differences in an increased MFI values in the beginning planned day to relative boost. ```