Class 15

Sophia Wang (A16838155)

##Background Pertussis, aka whooping cough, is a highly infections lung disease cuased by the bacteria *B. Pertussis*.

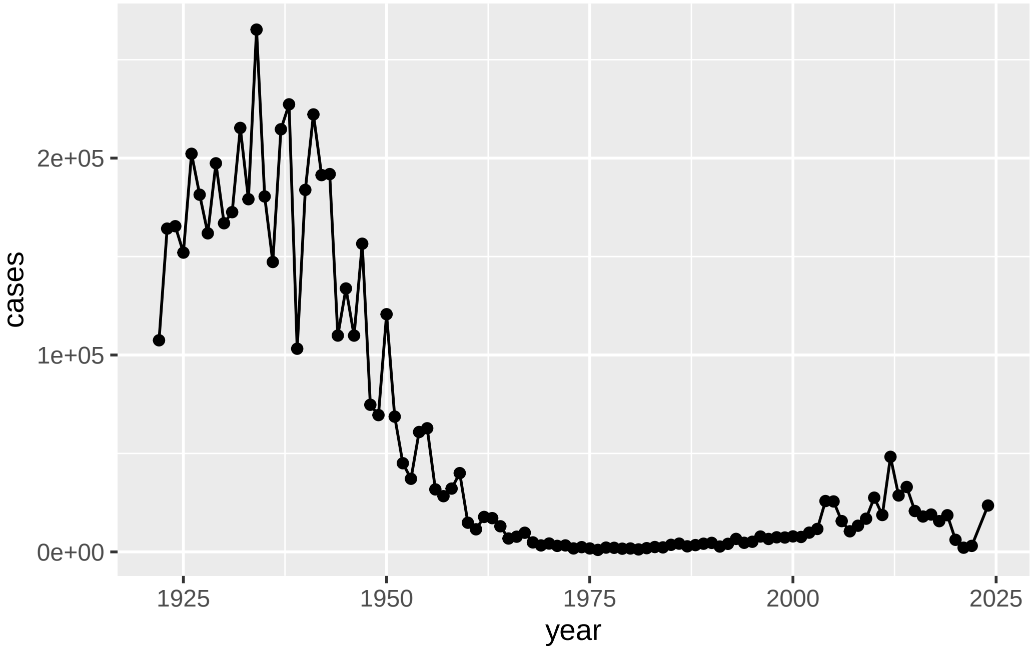
CDC data

We will use the **datapasta** R package to scrape this data into R.

> 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.

```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,2022L,2024L),
       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,
                                        6124,2116,3044,23544)
     )
```

```
library(ggplot2)
baseplot<-ggplot(cdc)+
  aes(year, cases)+
  geom_point()+
  geom_line()
baseplot
```



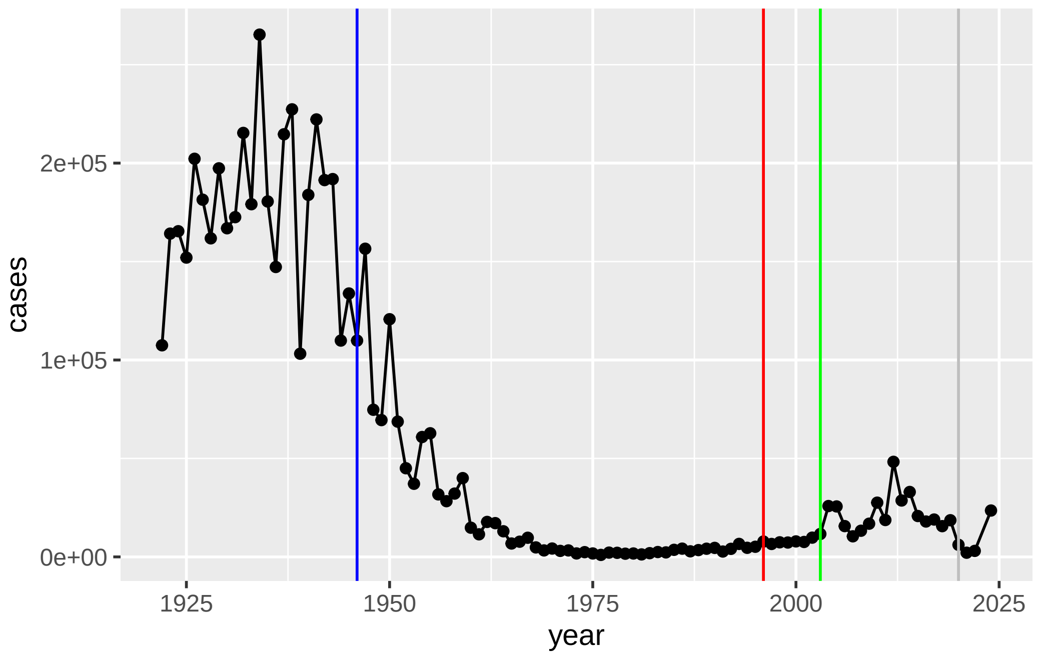
Add some landmark developments as annotation to our plot. We include the first whole-cell (wP) vaccine roll-out in 1946.

Lets add the switch to acellular vaccine (aP) in 1996.

> 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?

We went from around 200,000 cases pre wP vaccine to around 1000 cases in 1976. The US switched to the aP vaccine in 1996. We start to see a big increase in 2004 to around 26,000 cases. The number of cases decreased after the introduction of wP vaccine, while the number of cases increased after the introduction of aP vaccine.

```
baseplot+
  geom_vline(xintercept=1946,col="blue")+
  geom_vline(xintercept=1996,col="red")+
  geom_vline(xintercept=2020,col="grey")+
  geom_vline(xintercept = 2003,col="green")
```



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

The number of cases increased after the introductin of the aP vaccine. One possible explanation for the observed trend is the vaccine conspiracy going on at that time that caused people to avoid getting vaccinated.

The is a ~10year lag from aP roll out to increasing case numbers. This holds true of other countires like Japan, UK, etc.

Key question: Why does aP vaccine induced immunity wane faster than that of the wP vaccine.

##CMI-PB

The CMI-PB (computational models of immunity pertusis boost) makes available lost of data about the immune response to Pertussis boost vaccination.

Critically, it tracks wP and aP individuals over time to see their immune response changes.

CMI-PB make all their data freely available via JSON format tables from their database.

Lets read the first one of these tabels:

```
library(jsonlite)
subject <- read_json("http://cmi-pb.org/api/v5/subject",simplifyVector = T)
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
```

Q. How many subjects are there in this dataset?

```r
nrow(subject)
```

```
[1] 172
```

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

```r
sum(subject$infancy_vac=="aP")
```

```
[1] 87
```

```r
sum(subject$infancy_vac=="wP")
```

```
[1] 85
```

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

```

aP wP 
87 85 
```

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

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

```
Female   Male 
   112     60 
```

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

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

```
                                           
                                            Female Male
  American Indian/Alaska Native                  0    1
  Asian                                         32   12
  Black or African American                      2    3
  More Than One Race                            15    4
  Native Hawaiian or Other Pacific Islander      1    1
  Unknown or Not Reported                       14    7
  White                                         48   32
```

> 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?

Average age of wP individuals is 35.5 years, and the average age of aP individuals is 26.8 years. They are significantly different.

```r
library(lubridate)
```

```

Attaching package: 'lubridate'

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

    date, intersect, setdiff, union
```

```r
subject$age <- today() - ymd(subject$year_of_birth)
time_length(mean(subject[subject$infancy_vac=="wP","age"]),"years")
```

```
[1] 35.53038
```

```
time_length(mean(subject[subject$infancy_vac=="aP","age"]),"years")
```

```
[1] 26.77967
```

> 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
```

> Q. Does this do a good job of representing the US populus?

No.

Lets get more data from CMI-PB, this time about the specimens collected.

```
specimen <- read_json("http://cmi-pb.org/api/v5/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
```

Now we can join (merge) these two tables `subject` and `specimen` to make one new `metat` table with the combined data.

> 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:

```r
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
```

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

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

```r
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 14202 days           1
2    1986-01-01    2016-09-12 2020_dataset 14202 days           2
3    1986-01-01    2016-09-12 2020_dataset 14202 days           3
4    1986-01-01    2016-09-12 2020_dataset 14202 days           4
5    1986-01-01    2016-09-12 2020_dataset 14202 days           5
6    1986-01-01    2016-09-12 2020_dataset 14202 days           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 read an “experiment data” table CMI-PB

> 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.

```
abdata <- read_json("http://cmi-pb.org/api/v5/plasma_ab_titer",simplifyVector = T)
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
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 join to do of `meta` and `abdata` to assoiate all the metadata about the individual and their race, biological sex and infincy vaccination status together with Antibody levels…

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

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

```r
head(ab)
```

```
  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 14202 days                           -3                             0
2 14202 days                           -3                             0
3 14202 days                           -3                             0
4 14202 days                           -3                             0
5 14202 days                           -3                             0
6 14202 days                           -3                             0
  specimen_type visit
1         Blood     1
2         Blood     1
3         Blood     1
4         Blood     1
5         Blood     1
6         Blood     1
```

How many Ab measurements do we have?

```r
nrow(ab)
```

```
[1] 52576
```

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

How many isotypes

```r
table(ab$isotype)
```

```

  IgE   IgG  IgG1  IgG2  IgG3  IgG4 
 6698  5389 10117 10124 10124 10124 
```

How many antigens?

```r
table(ab$antigen)
```

```

    ACT   BETV1      DT   FELD1     FHA  FIM2/3   LOLP1     LOS Measles     OVA 
   1970    1970    4978    1970    5372    4978    1970    1970    1970    4978 
    PD1     PRN      PT     PTM   Total      TT 
   1970    5372    5372    1970     788    4978 
```

> 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(ab$dataset)
```

```

2020_dataset 2021_dataset 2022_dataset 2023_dataset 
       31520         8085         7301         5670 
```

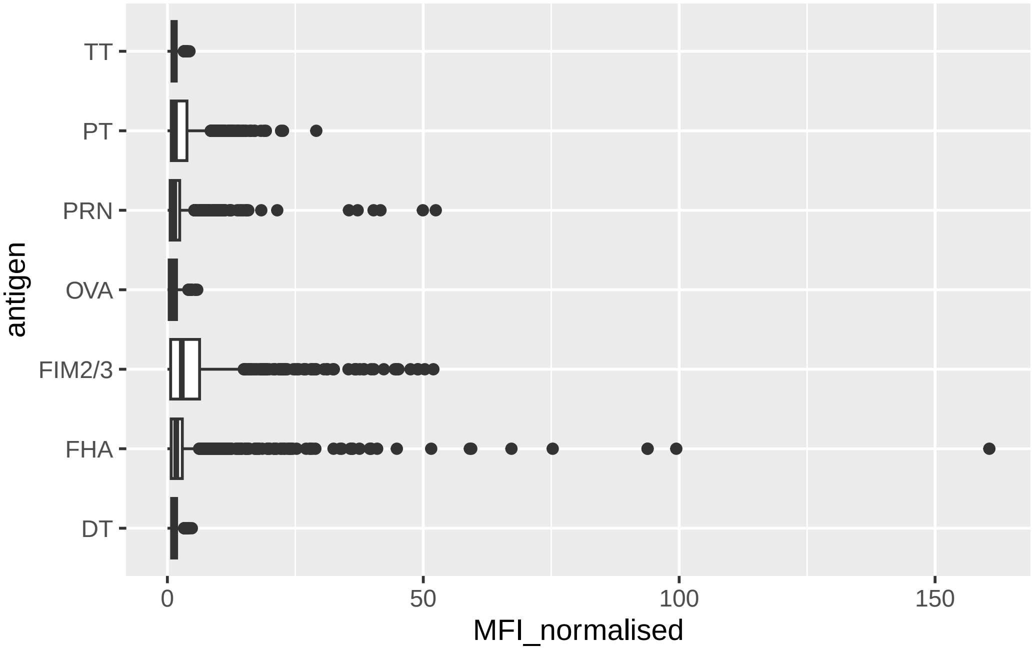
Lets focus in IgG-one of the main antibody types responsive to bacteria or viral infections

```r
igg <- filter(ab,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 infancy_vac biological_sex
1 IU/ML                 0.530000          1          wP         Female
2 IU/ML                 6.205949          1          wP         Female
3 IU/ML                 4.679535          1          wP         Female
4 IU/ML                 0.530000          3          wP         Female
5 IU/ML                 6.205949          3          wP         Female
6 IU/ML                 4.679535          3          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 actual_day_relative_to_boost planned_day_relative_to_boost
1 14202 days                           -3                             0
2 14202 days                           -3                             0
3 14202 days                           -3                             0
4 15298 days                           -3                             0
5 15298 days                           -3                             0
6 15298 days                           -3                             0
  specimen_type visit
1         Blood     1
2         Blood     1
3         Blood     1
4         Blood     1
5         Blood     1
6         Blood     1
```

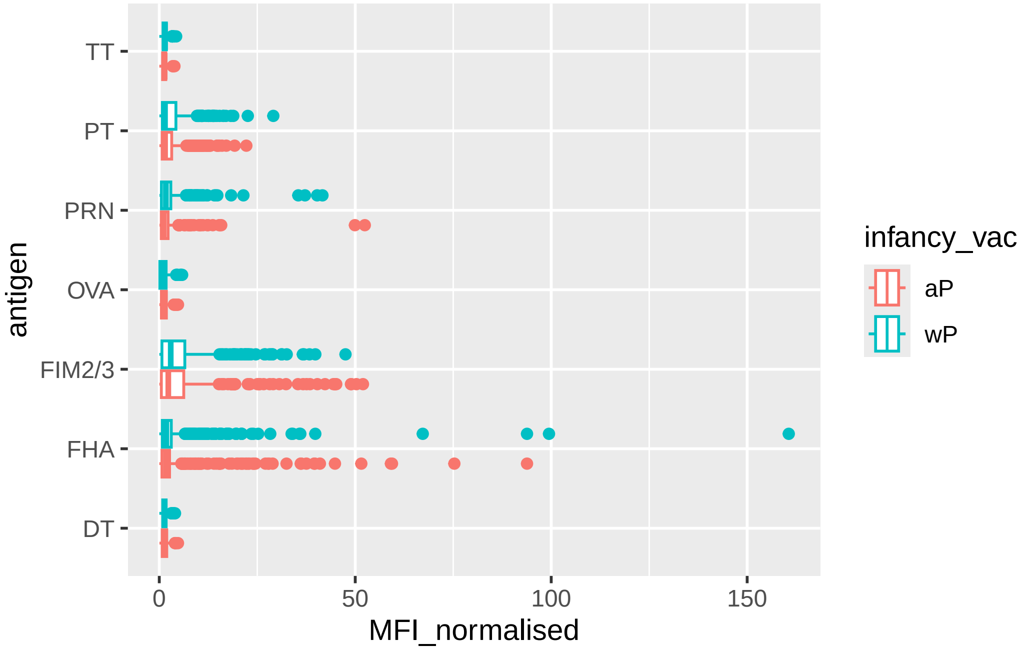
Make a first plot of MFI (Mean Fluorescence Intensity-a measure of much is detected) for each antigen.

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

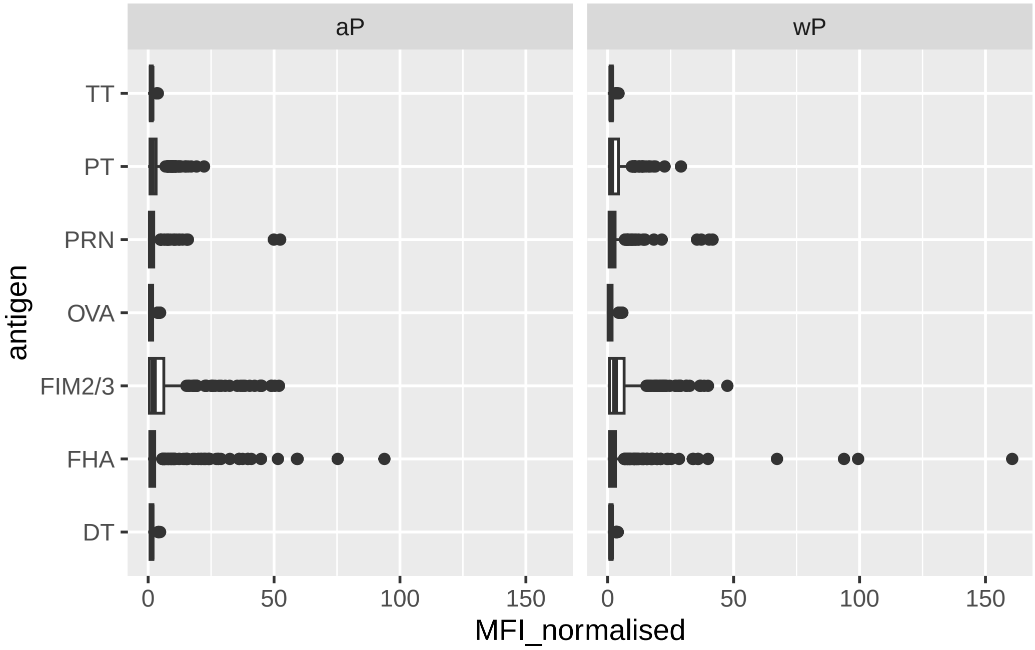


Lets color by aP/wP infancy_vac

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

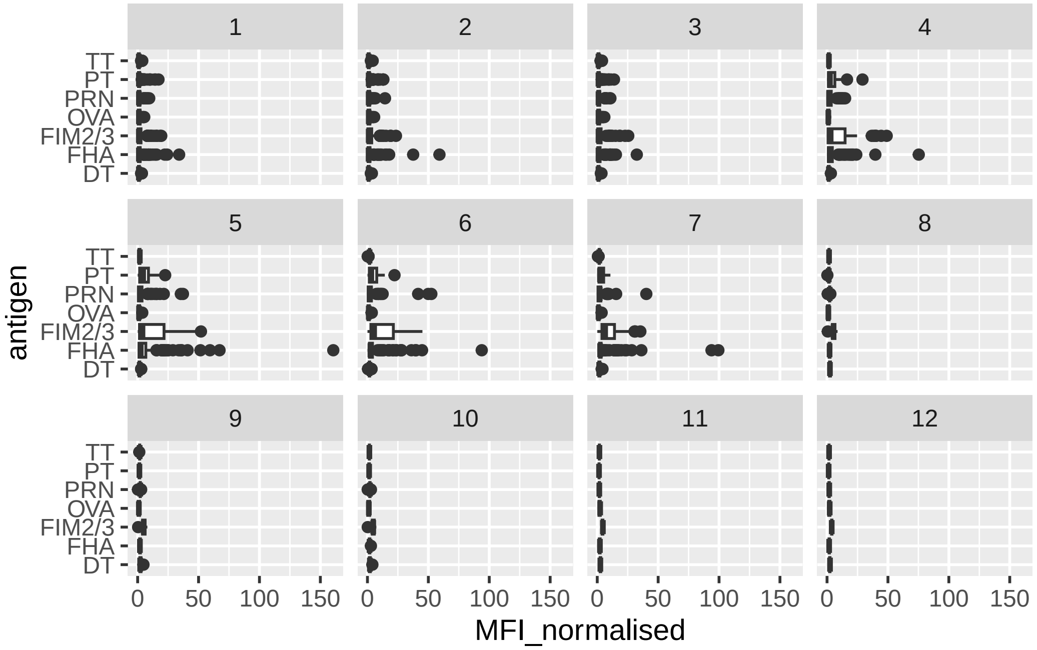


```
ggplot(igg)+
  aes(MFI_normalised, antigen)+
  geom_boxplot()+
  facet_wrap(~infancy_vac)
```



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

```
ggplot(igg)+
  aes(MFI_normalised, antigen)+
  geom_boxplot()+
  facet_wrap(~visit)
```



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

PT, PRN, FHA and FIM2/3. These proteins are thought to participate in the bacterial infection process and they are the components included in the acellular vaccine.

```
table(igg$visit)
```

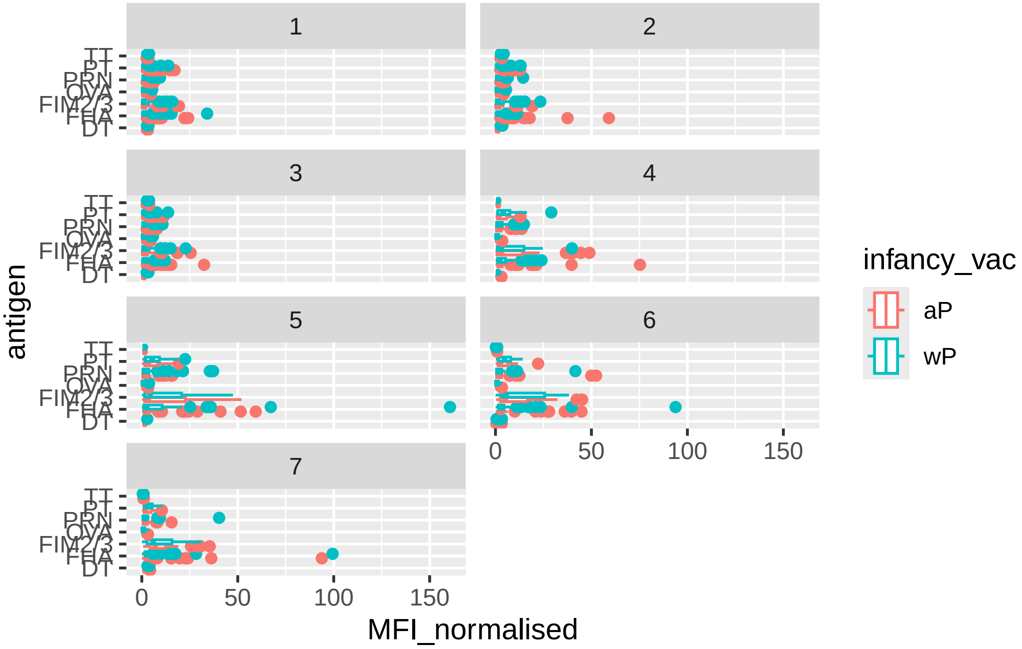
```
  1   2   3   4   5   6   7   8   9  10  11  12 
902 902 930 559 559 540 525 150 147 133  21  21 
```

Looks like we dont have data yet for all subjects in terms of visits 8 onwards. So lets exclude these.

```
igg_7 <- filter(igg,visit %in% 1:7)
table(igg_7$visit)
```

```
  1   2   3   4   5   6   7 
902 902 930 559 559 540 525 
```

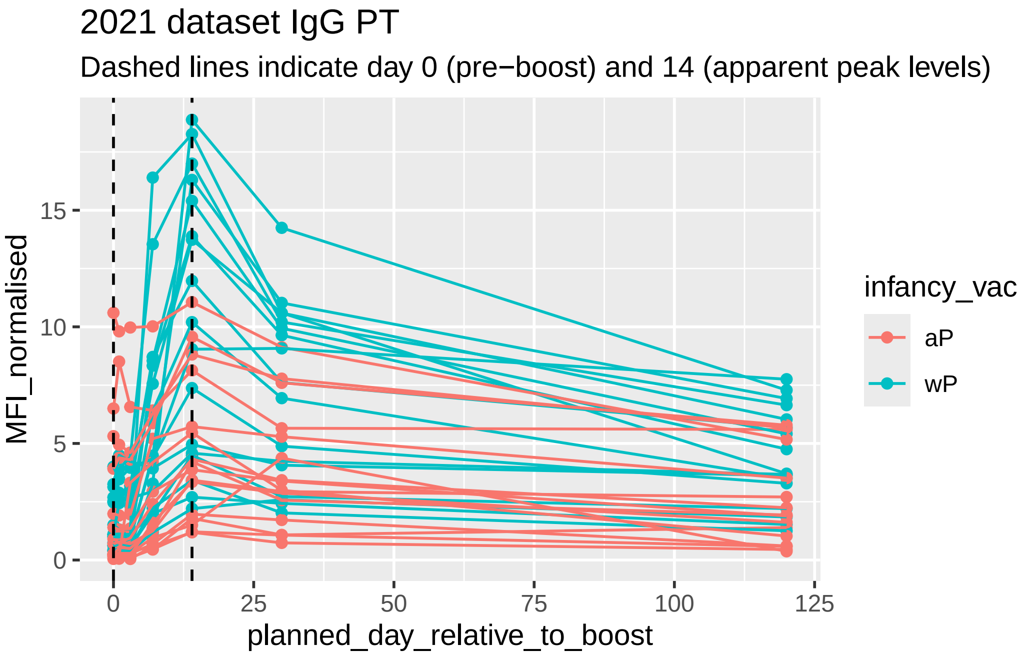
```
ggplot(igg_7)+
  aes(MFI_normalised, antigen,col=infancy_vac)+
  geom_boxplot()+
  facet_wrap(~visit,ncol=2)
```



Lets try a different plot. First focus on one antigen, start with PT (Pertussis Toxin) and plot visit or time on the x-axis and MFI_normalized on the y-axis.

```
abdata.21 <- ab %>% filter(dataset == "2021_dataset")

abdata.21 %>%
  filter(isotype == "IgG",  antigen == "PT") %>%
  ggplot() +
    aes(x=planned_day_relative_to_boost,
        y=MFI_normalised,
        col=infancy_vac,
        group=subject_id) +
    geom_point() +
    geom_line() +
    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)")
```



Lets finish here for today. We are beginning to see some interesting differences between aP and wP individuals. There is likely lots of other interesting thing to find in this dataset…