Class18: Pertussis Mini Project

Jessica Gao (PID:A16939806)

Pertussis, also known as the whopping cough is a deadly lung infection caused by the bacteria B. Pertussis

The CDC tracks Pertussis causes around the U.S. https://tinyurl.com/pertussiscdc

We can “scrape” this data using the R **datapasta** package.

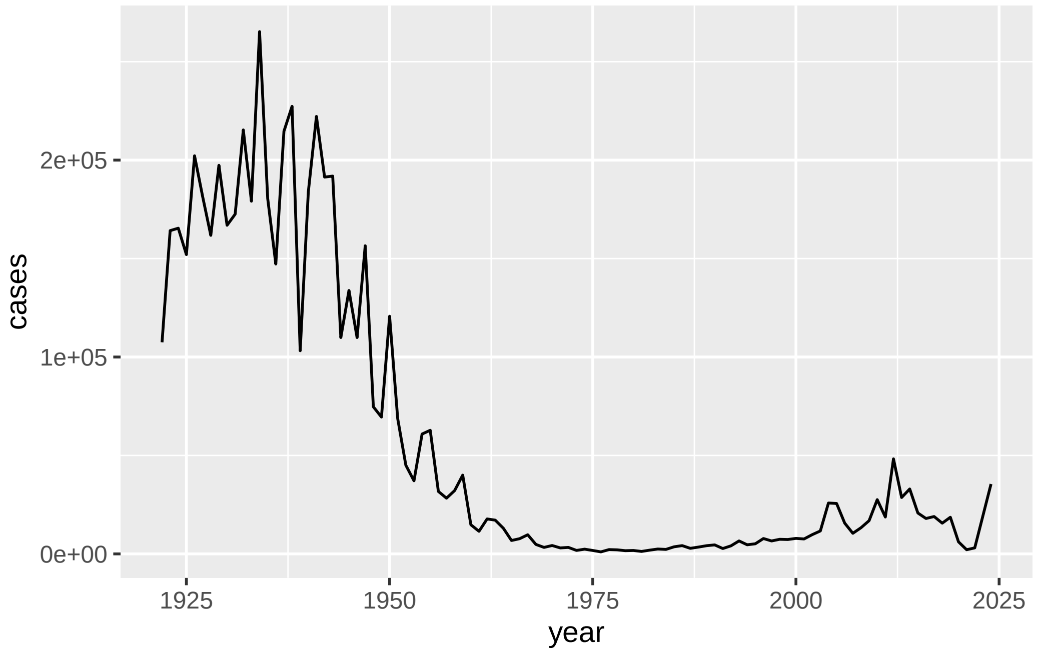
> Q1 With the help of the R “addin” package datapasta assign the CDC pertussis case number data to a data frame called cdc and use ggplot to make a plot of cases numbers over time.

```
head(cdc)
```

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

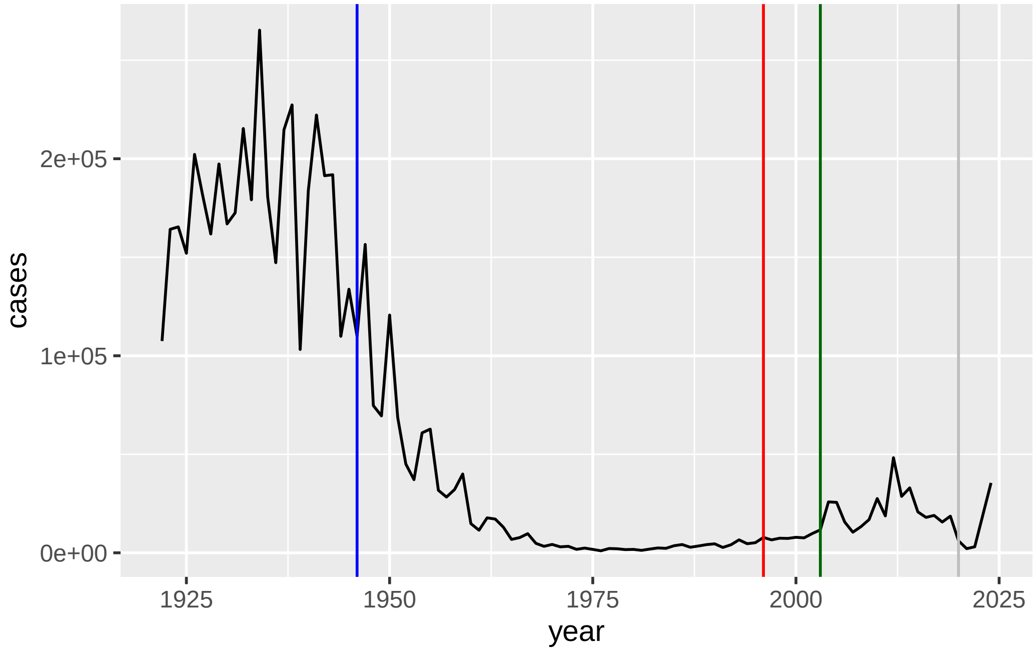
> Q1. With the help of the R “addin” package datapasta assign the CDC pertussis case number data to a data frame called cdc and use ggplot to make a plot of cases numbers over time.

```
library(ggplot2)

ggplot(cdc)+
  aes(year,cases)+
  geom_line()
```



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=1946, col="blue")+
  geom_vline(xintercept=1996, col="red")+
  geom_vline(xintercept=2020, col="gray")+
  geom_vline(xintercept=2003, col="darkgreen")
```



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

There were high cases numbers before the first wP(whole-cell) vaccine roll out in 1946 then a rapid decline in case numbers until 2004 when we have our first large-scale outbreaks of pertussis again. There is also a notable COVID-19 related dip and recent rapid rise.

So the question is what is different about the immune response to the infection if you had a older version wP vaccine versus the newer aP vaccine.

##CMI-PB (Computational Models of Immunity Pertussis Boost)

The CMI-PB project aims to address this key question: what is the different between aP and wP individuals.

We can get all the data from this ongoing project via JSON API calls. For this we will use the **jsonlite** package

```
library(jsonlite)
```

```
Warning: package 'jsonlite' was built under R version 4.4.3
```

```
subject <- read_json("https://www.cmi-pb.org/api/v5_1/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
```

> Q. How many individuals "subjects" are in this dataset?

```
nrow(subject)
```

```
[1] 172
```

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

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

```

aP wP 
87 85 
```

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

```
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…)?

```
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
```

Working with dates

```
library(lubridate)
```

```

Attaching package: 'lubridate'

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

    date, intersect, setdiff, union
```

> 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$age <- today() - ymd(subject$year_of_birth)
```

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

round( summary( time_length( ap$age, "years" ) ) )
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max. 
     22      26      27      27      28      34 
```

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

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max. 
     22      32      34      36      39      57 
```

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

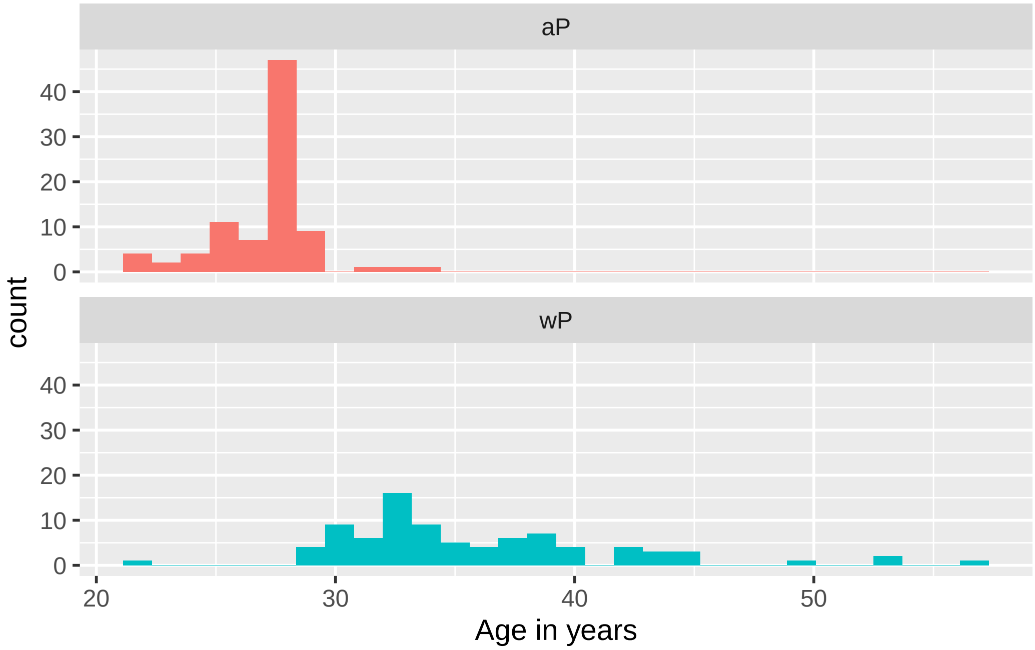
```
int <- ymd(subject$date_of_boost) - ymd(subject$year_of_birth)
age_at_boost <- time_length(int, "year")
head(age_at_boost)
```

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

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`.
```



```
# Or use wilcox.test()
x <- t.test(time_length( wp$age, "years" ),
       time_length( ap$age, "years" ))

x$p.value
```

```
[1] 2.372101e-23
```

Obtain more data from CMI-PB

```
specimen <- read_json("https://www.cmi-pb.org/api/v5_1/specimen",
                      simplifyVector = TRUE)
ab_data <- read_json("https://www.cmi-pb.org/api/v5_1/plasma_ab_titer",
                     simplifyVector = TRUE)
```

```
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
```

```r
head(ab_data)
```

```
  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
```

I now have three tables of data from CMI-PB: ‘subject,’ ‘specimen,’ and ‘ab_data.’ I need to join these tables so I will have all tge info I need to work with.

For this we will use the ‘inner_joint()’ function from the **dplyr** packages.

> 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)

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 14311 days           1
2    1986-01-01    2016-09-12 2020_dataset 14311 days           2
3    1986-01-01    2016-09-12 2020_dataset 14311 days           3
4    1986-01-01    2016-09-12 2020_dataset 14311 days           4
5    1986-01-01    2016-09-12 2020_dataset 14311 days           5
6    1986-01-01    2016-09-12 2020_dataset 14311 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
```

```r
dim(subject)
```

```
[1] 172   9
```

```r
dim(specimen)
```

```
[1] 1503    6
```

```r
dim(meta)
```

```
[1] 1503   14
```

```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 14311 days           1
2    1986-01-01    2016-09-12 2020_dataset 14311 days           2
3    1986-01-01    2016-09-12 2020_dataset 14311 days           3
4    1986-01-01    2016-09-12 2020_dataset 14311 days           4
5    1986-01-01    2016-09-12 2020_dataset 14311 days           5
6    1986-01-01    2016-09-12 2020_dataset 14311 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
```

> 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 join our ‘ab_data’ table to ‘meta’ so we have all the info we need about antibody levels.

```r
abdata <- inner_join(meta, ab_data)
```

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

```r
head(abdata)
```

```
  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 14311 days           1
2    1986-01-01    2016-09-12 2020_dataset 14311 days           1
3    1986-01-01    2016-09-12 2020_dataset 14311 days           1
4    1986-01-01    2016-09-12 2020_dataset 14311 days           1
5    1986-01-01    2016-09-12 2020_dataset 14311 days           1
6    1986-01-01    2016-09-12 2020_dataset 14311 days           1
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -3                             0         Blood
2                           -3                             0         Blood
3                           -3                             0         Blood
4                           -3                             0         Blood
5                           -3                             0         Blood
6                           -3                             0         Blood
  visit isotype is_antigen_specific antigen        MFI MFI_normalised  unit
1     1     IgE               FALSE   Total 1110.21154       2.493425 UG/ML
2     1     IgE               FALSE   Total 2708.91616       2.493425 IU/ML
3     1     IgG                TRUE      PT   68.56614       3.736992 IU/ML
4     1     IgG                TRUE     PRN  332.12718       2.602350 IU/ML
5     1     IgG                TRUE     FHA 1887.12263      34.050956 IU/ML
6     1     IgE                TRUE     ACT    0.10000       1.000000 IU/ML
  lower_limit_of_detection
1                 2.096133
2                29.170000
3                 0.530000
4                 6.205949
5                 4.679535
6                 2.816431
```

> Q11. How many specimens (i.e. entries in abdata) do we have for each isotype? Q. How many different antibody isotypes are there in this dataset?

```r
length(abdata$isotype)
```

```
[1] 61956
```

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

```

  IgE   IgG  IgG1  IgG2  IgG3  IgG4 
 6698  7265 11993 12000 12000 12000 
```

> 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 2023_dataset 
       31520         8085         7301        15050 
```

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

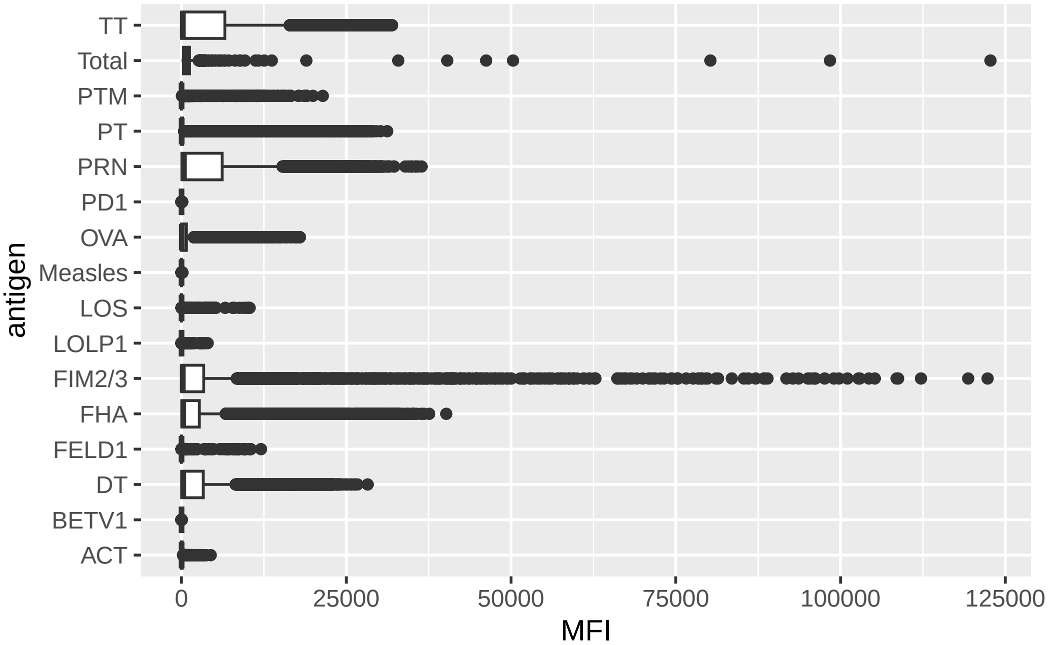
```

    ACT   BETV1      DT   FELD1     FHA  FIM2/3   LOLP1     LOS Measles     OVA 
   1970    1970    6318    1970    6712    6318    1970    1970    1970    6318 
    PD1     PRN      PT     PTM   Total      TT 
   1970    6712    6712    1970     788    6318 
```

I want a plot of antigen levels across the whole dataset.

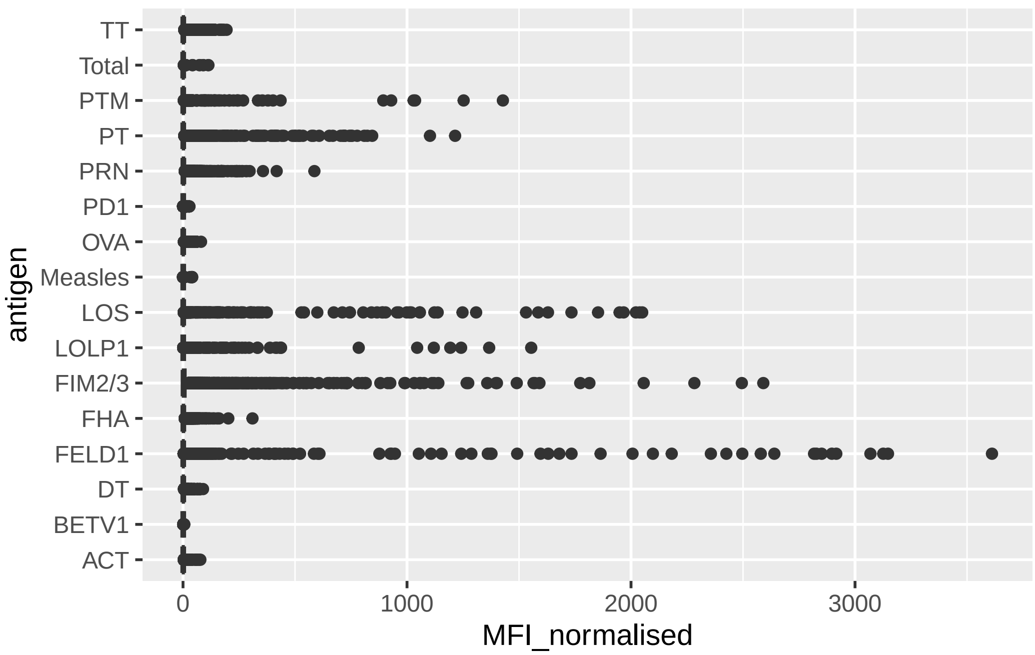
> Q13. Complete the following code to make a summary boxplot of Ab titer levels (MFI) for all antigens:

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

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



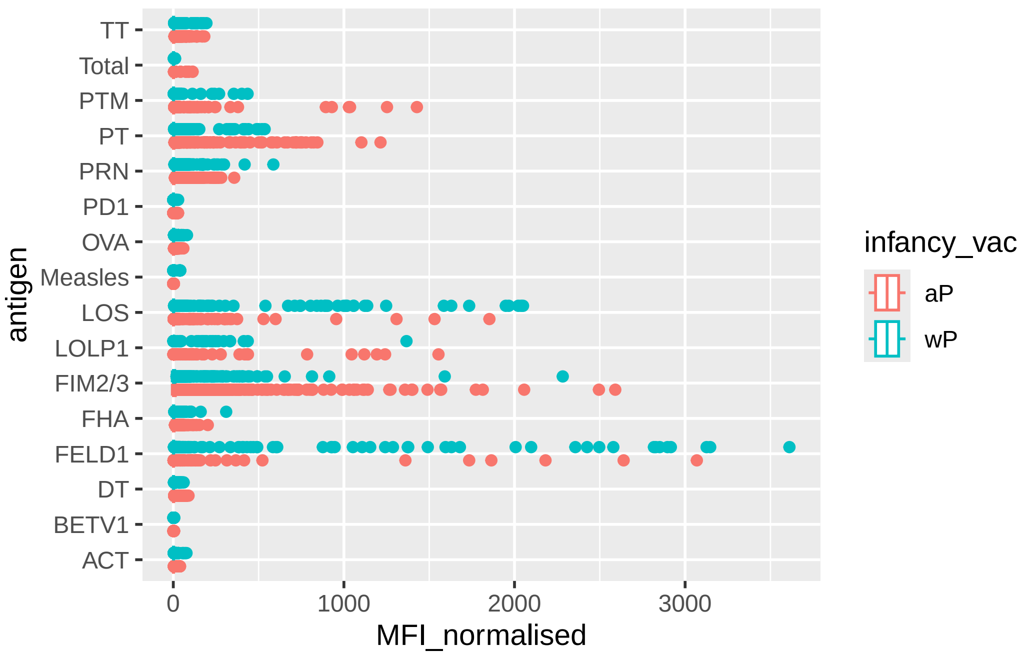
```r
ggplot(abdata)+
  aes(MFI_normalised, antigen)+
  geom_boxplot()
```



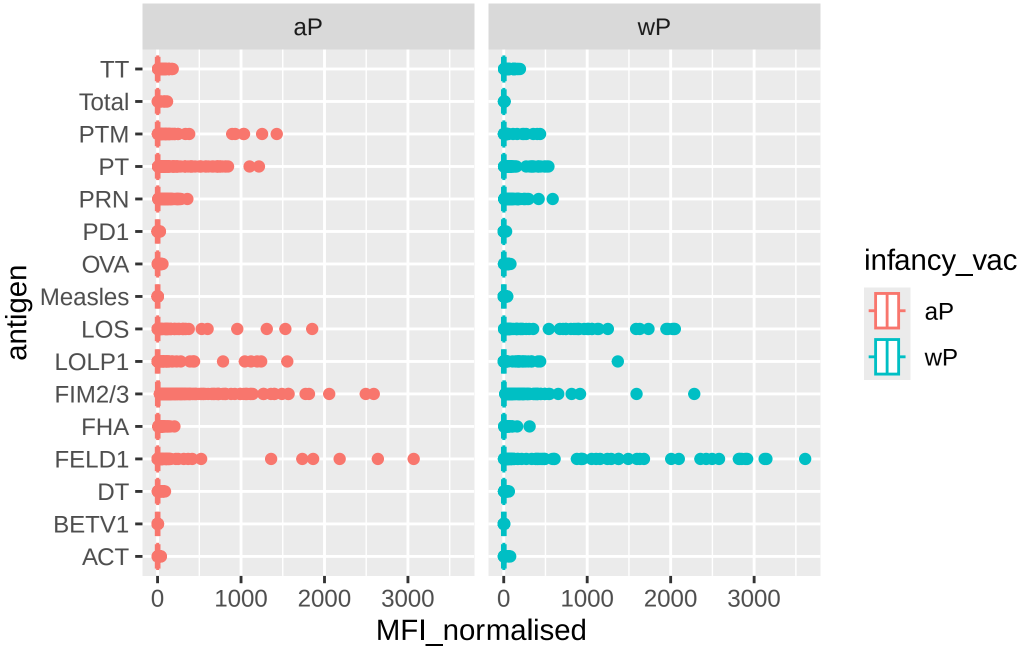
Q. Are there differences at this whole-dataset level between aP and wP?

Antigens like FIM2/3, PT, FELD1 have quite a large range of values. Others like Measels don't show much activity. These ones that has large range values are in the wP vaccines.

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



```
ggplot(abdata)+
  aes(MFI_normalised, antigen, col=infancy_vac)+
  geom_boxplot()+
  facet_wrap(~infancy_vac)
```



Examine IgG Ab titer levels

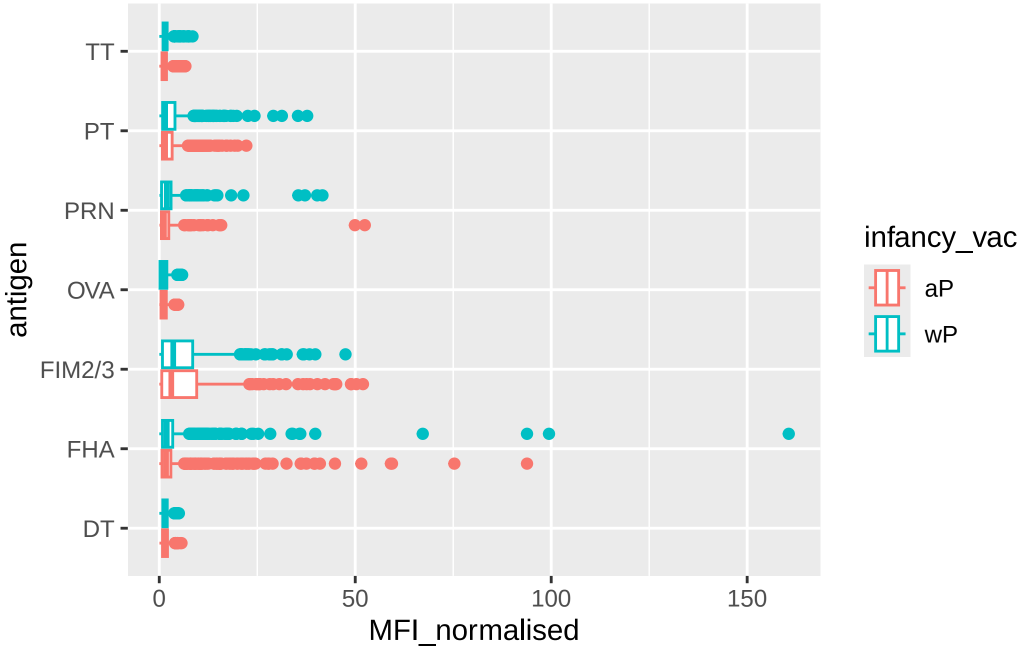
For this I need to select out just isotype IgG.

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

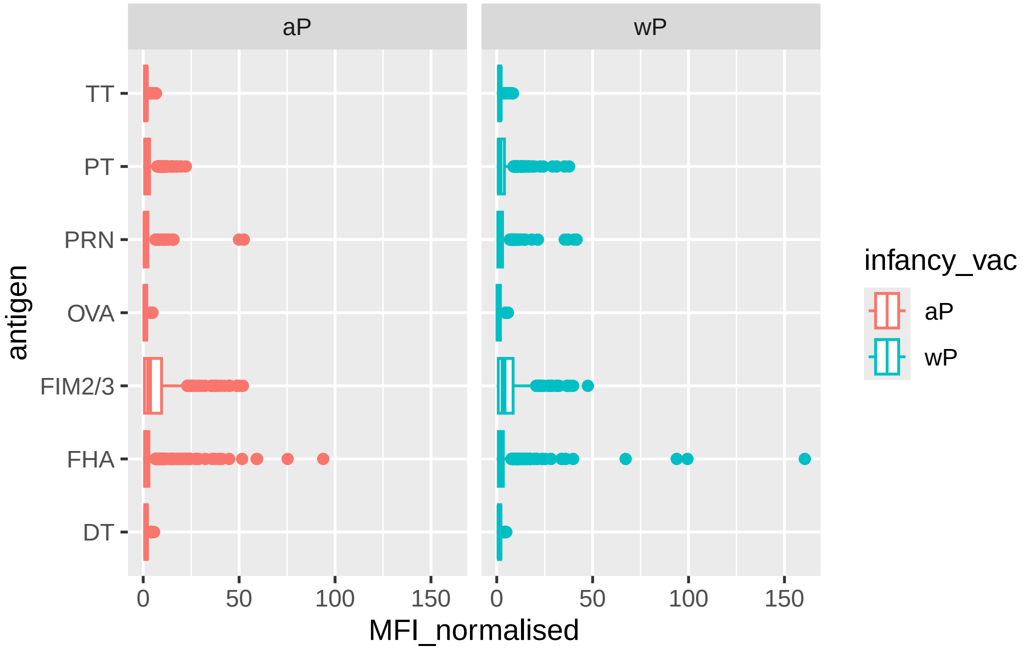
```
  subject_id infancy_vac biological_sex              ethnicity  race
1          1          wP         Female Not Hispanic or Latino White
2          1          wP         Female Not Hispanic or Latino White
3          1          wP         Female Not Hispanic or Latino White
4          1          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 14311 days           1
2    1986-01-01    2016-09-12 2020_dataset 14311 days           1
3    1986-01-01    2016-09-12 2020_dataset 14311 days           1
4    1986-01-01    2016-09-12 2020_dataset 14311 days           2
5    1986-01-01    2016-09-12 2020_dataset 14311 days           2
6    1986-01-01    2016-09-12 2020_dataset 14311 days           2
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
```

```
1                            -3                              0         Blood
2                            -3                              0         Blood
3                            -3                              0         Blood
4                             1                              1         Blood
5                             1                              1         Blood
6                             1                              1         Blood
  visit isotype is_antigen_specific antigen        MFI MFI_normalised  unit
1     1     IgG                TRUE      PT   68.56614       3.736992 IU/ML
2     1     IgG                TRUE     PRN  332.12718       2.602350 IU/ML
3     1     IgG                TRUE     FHA 1887.12263      34.050956 IU/ML
4     2     IgG                TRUE      PT   41.38442       2.255534 IU/ML
5     2     IgG                TRUE     PRN  174.89761       1.370393 IU/ML
6     2     IgG                TRUE     FHA  246.00957       4.438960 IU/ML
  lower_limit_of_detection
1                 0.530000
2                 6.205949
3                 4.679535
4                 0.530000
5                 6.205949
6                 4.679535
```

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



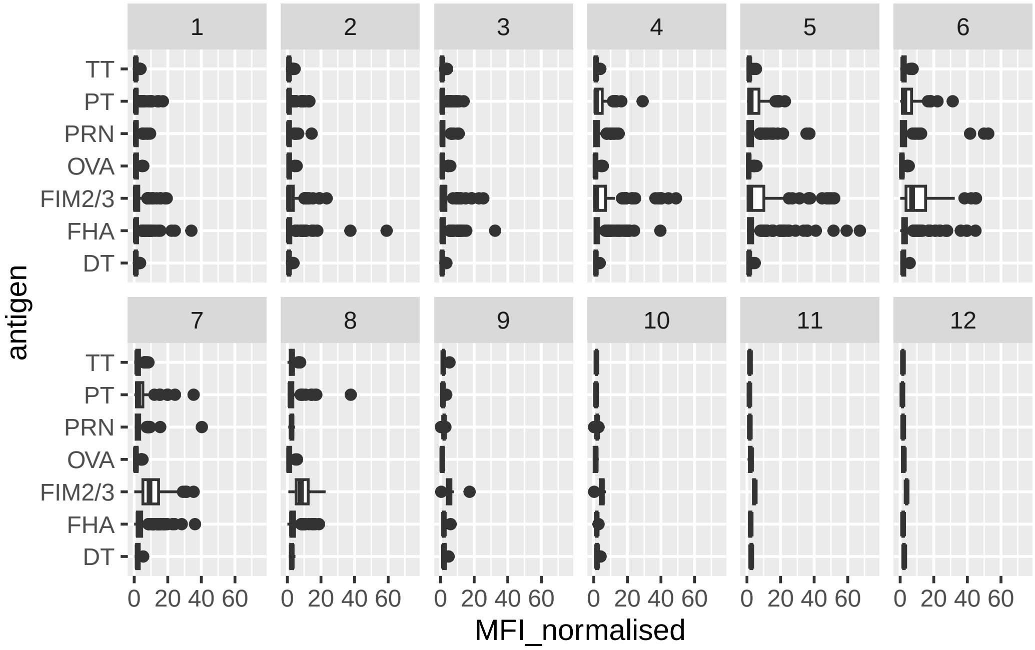
```
ggplot(igg)+
  aes(MFI_normalised, antigen, col=infancy_vac)+
  geom_boxplot()+
  facet_wrap(~infancy_vac)
```



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() +
    xlim(0,75) +
  facet_wrap(vars(visit), nrow=2)
```

```
Warning: Removed 5 rows containing non-finite outside the scale range
(`stat_boxplot()`).
```

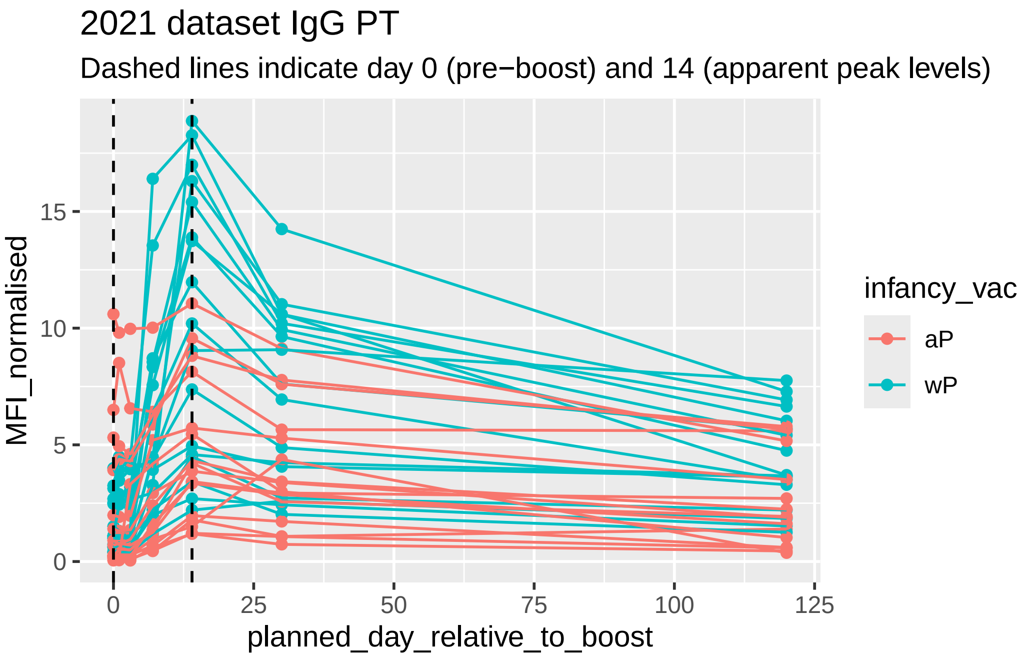


> Q14. What antigens show differences in the level of IgG antibody titers recognizing them over time? Why these and not others?

PT, FELD1, and FIM2/3 show differences in the level of IgG antibody titers, their MFI_normalised is much higher than the other antigens. This is because they are the antigens present within the vaccines to give immunity to the patient's body while the other antigens were used more as control groups and not within the vaccines.

Digging in further to look at the time course of IgG Isotype PT antigen levels across aP and wP individuals:

```r
##Filter to include 2021 data only
abdata.21 <- abdata |>  filter(dataset == "2021_dataset")
##Filter to look at IgG PT data only
pt.igg <- abdata.21 |>
  filter(isotype == "IgG",  antigen == "PT")
##Plotting and color by infancy_vac(wP vs aP)
  ggplot(pt.igg) +
    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)")
```


2021 dataset IgG PT
Dashed lines indicate day 0 (pre−boost) and 14 (apparent peak levels)
MFI_normalised
planned_day_relative_to_boost
infancy_vac
aP
wP