# Class 19: Pertussis and the CMI-PB Project

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Pertussis is a severe lung infection also known as a whooping cough.

We will begin by investigating the number of Pertussis cases per year in the US

This data is avaliable on the CDC website here

## 1. Investigating pertussis cases by year

### 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.

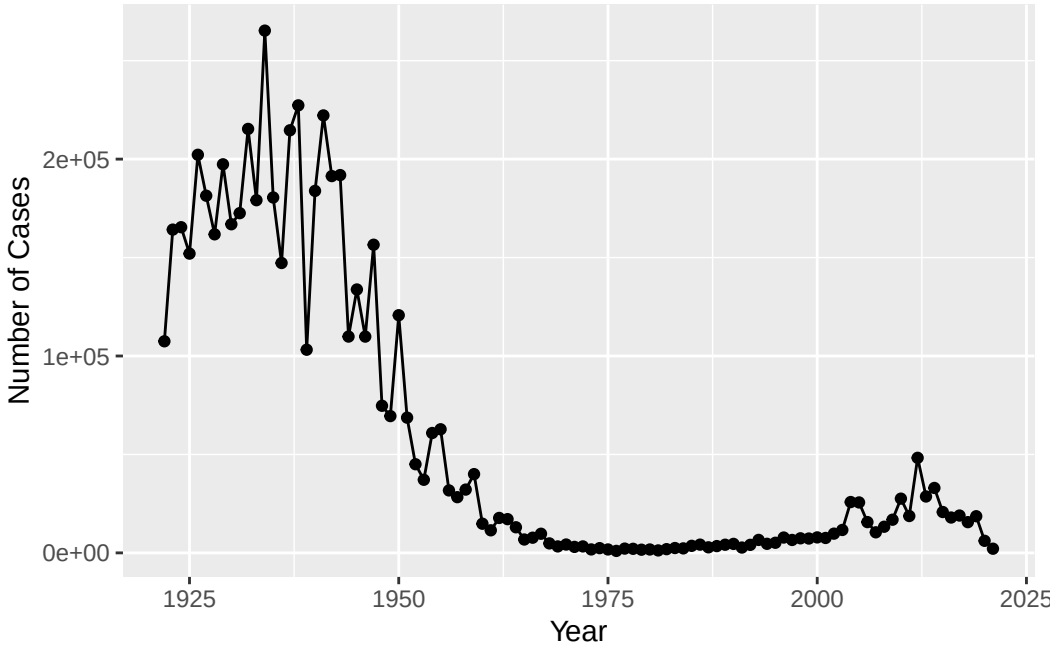
Let's have a look at this data.frame

```
head(cdc)
```

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

Make a plot of cases by year

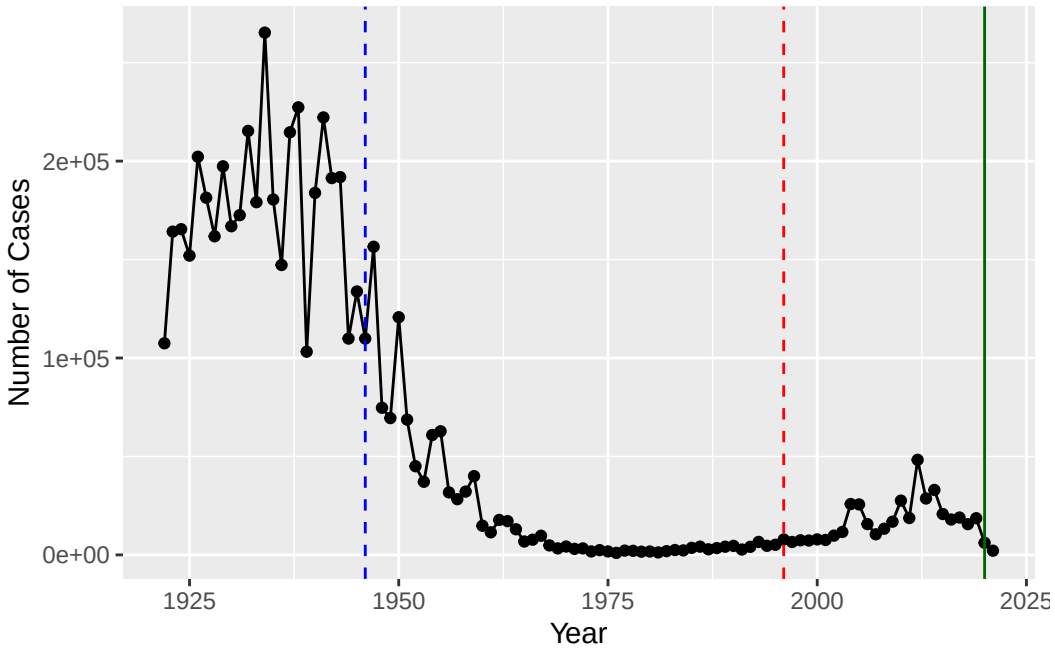
```
library(ggplot2)

ggplot(cdc, aes(year, cases)) + geom_point() + geom_line() + labs(x="Year", y="Number of C
```




## 2. A tale of two vaccines (wP & aP)

**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, cases)) +
  geom_point() +
  geom_line() +
  labs(x="Year", y="Number of Cases") +
  geom_vline(xintercept = 1946, linetype = "dashed", col = "blue") +
  geom_vline(xintercept = 1996, linetype = "dashed", col = "red") +
  geom_vline(xintercept=2020, linetype="solid", col="darkgreen")
```




There seems to be a rise in cases several years after the aP vaccine, with ups and downs observed after that.

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

After the introduction of the aP vaccine, cases seem to rise after several years. The aP vaccine does not have as long of a protection period, causing older kids who were vaccinated to carry the disease.

## 3. Exploring CMI-PB data

Why is this vaccine-preventable disease on the upswing? The CMI-PB project aims to answer this question.

The CMI-PB project makes its data avaliable via "API-endpoint" that return JSON format. We will use the 'jsonlite' package to access this data. The main function in this package is called 'read_json()'.

```
library(jsonlite)
# Subject table
subject <- read_json("http://cmi-pb.org/api/subject", simplifyVector = TRUE)
specimen <- read_json("http://cmi-pb.org/api/specimen", simplifyVector = TRUE)
titer <- read_json("http://cmi-pb.org/api/v4/plasma_ab_titer", 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
```

```
head(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
```

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

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

```
aP wP
60 58
```

60 aP, 58 wP

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

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

```
Female   Male
    79     39
```

79 females, 39 males

### 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
```

There are much more white participants represented in the population than any other group.

## Side-Note: Working with dates

```
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 beco
```

```
today()
```

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

```
time_length(today()-mdy("6-26-2002"), "years")
```

```
[1] 21.44559
```

Add the age of each subject to the subject table

```
subject$age <- ymd(subject$date_of_boost) - ymd(subject$year_of_birth)
subject$age_years <- time_length(subject$age, "years")
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_years
1    1986-01-01    2016-09-12 2020_dataset 11212 days  30.69678
2    1968-01-01    2019-01-28 2020_dataset 18655 days  51.07461
3    1983-01-01    2016-10-10 2020_dataset 12336 days  33.77413
4    1988-01-01    2016-08-29 2020_dataset 10468 days  28.65982
5    1991-01-01    2016-08-29 2020_dataset  9372 days  25.65914
6    1988-01-01    2016-10-10 2020_dataset 10510 days  28.77481
```

**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?**

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

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

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
     19      20      20      21      21      28
```

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

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

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
     23      26      29      31      34      51
```

They are not significantly different.

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

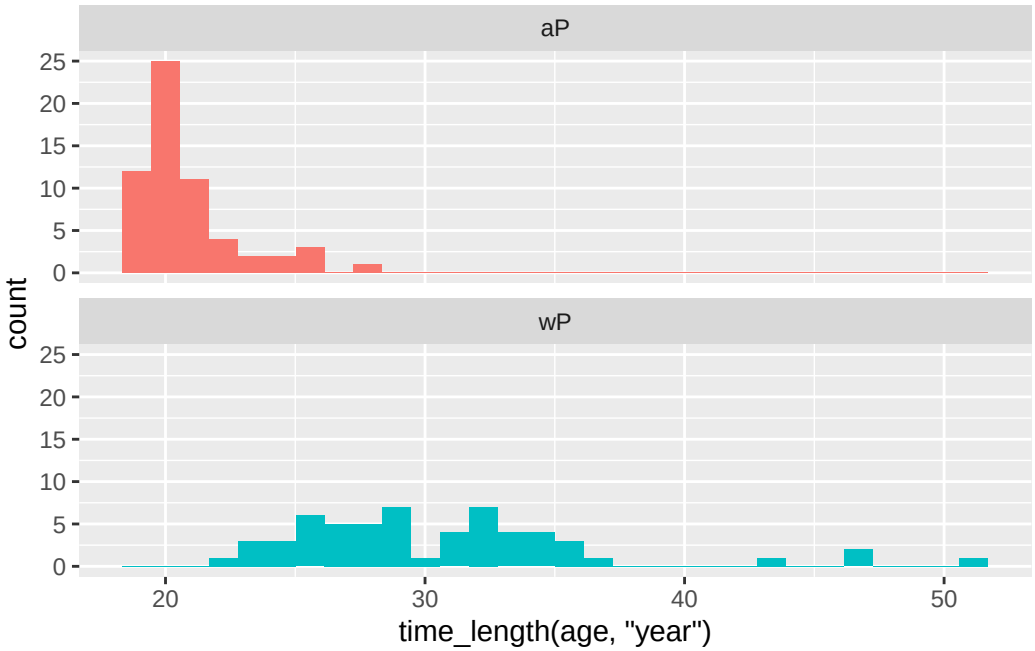
```
head(subject$age_years)
```

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

### Q9. With the help of a faceted boxplot (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)
```

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




They have a good amount of overlap, so are probably not significantly different.

## Merge or join tables

### 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:

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

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

```
dim(meta)
```

```
[1] 939  15
```

```
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_years
1 11212 days  30.69678
2 11212 days  30.69678
3 11212 days  30.69678
4 11212 days  30.69678
5 11212 days  30.69678
6 11212 days  30.69678
```

**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.**

Antibody measurments in blood

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

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

```
dim(abdata)
```

```
[1] 41810    22
```

```
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_years
1 11212 days  30.69678
2 11212 days  30.69678
3 11212 days  30.69678
4 11212 days  30.69678
5 11212 days  30.69678
6 11212 days  30.69678
```

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

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

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

Let's focus on one of these IgG

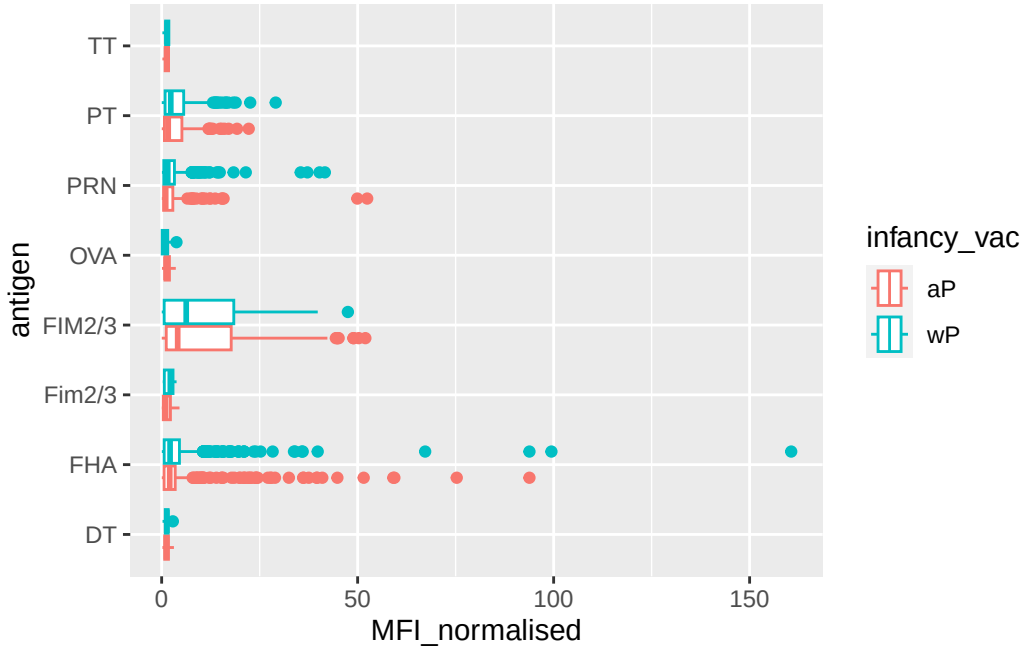
```
igg <- abdata %>% filter(isotype == "IgG")
head(igg)
```

```
  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_years
1 11212 days  30.69678
2 11212 days  30.69678
3 11212 days  30.69678
4 12336 days  33.77413
5 12336 days  33.77413
6 12336 days  33.77413
```

Box plot of MFI_normamised vs antigen

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




```
head(igg)
```

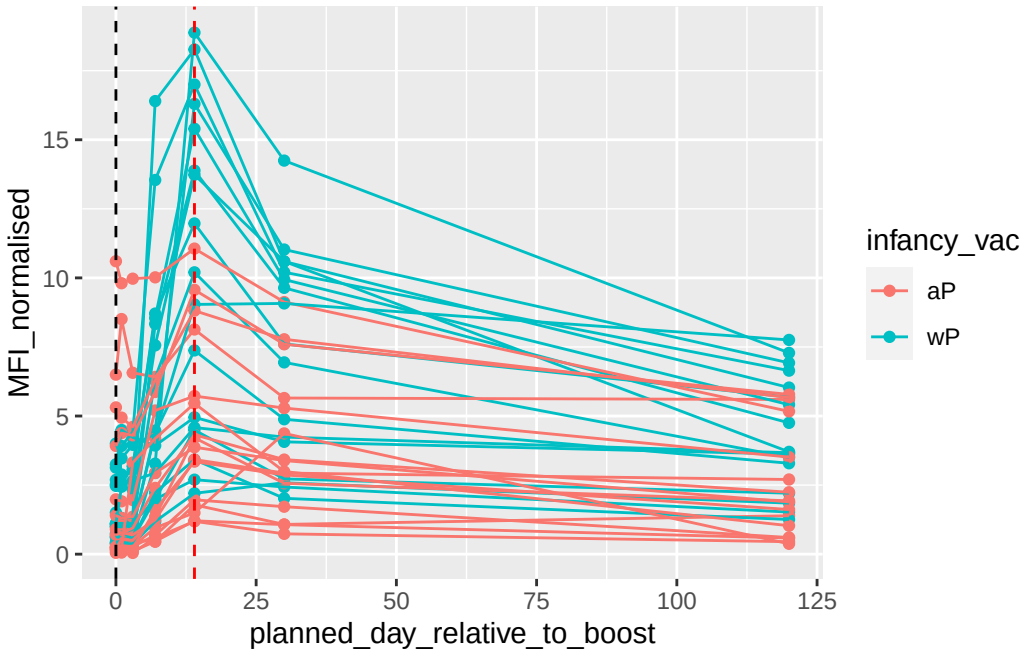
```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgG                TRUE      PT   68.56614       3.736992
2           1     IgG                TRUE     PRN  332.12718       2.602350
3           1     IgG                TRUE     FHA 1887.12263      34.050956
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_years
1 11212 days  30.69678
2 11212 days  30.69678
3 11212 days  30.69678
4 12336 days  33.77413
5 12336 days  33.77413
6 12336 days  33.77413
```

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=s
  geom_point() +
  geom_line()+
  geom_vline(xintercept=0, linetype="dashed", col="black")+
  geom_vline(xintercept=14, linetype="dashed", col="red")
```




**Q12. What do you notice about the number of visit 8 specimens compared to other visits?**

```
table(abdata$visit)
```

```
   1    2    3    4    5    6    7    8
6390 6460 6530 5900 5900 5475 5075   80
```

8 has very low visits compared to all others

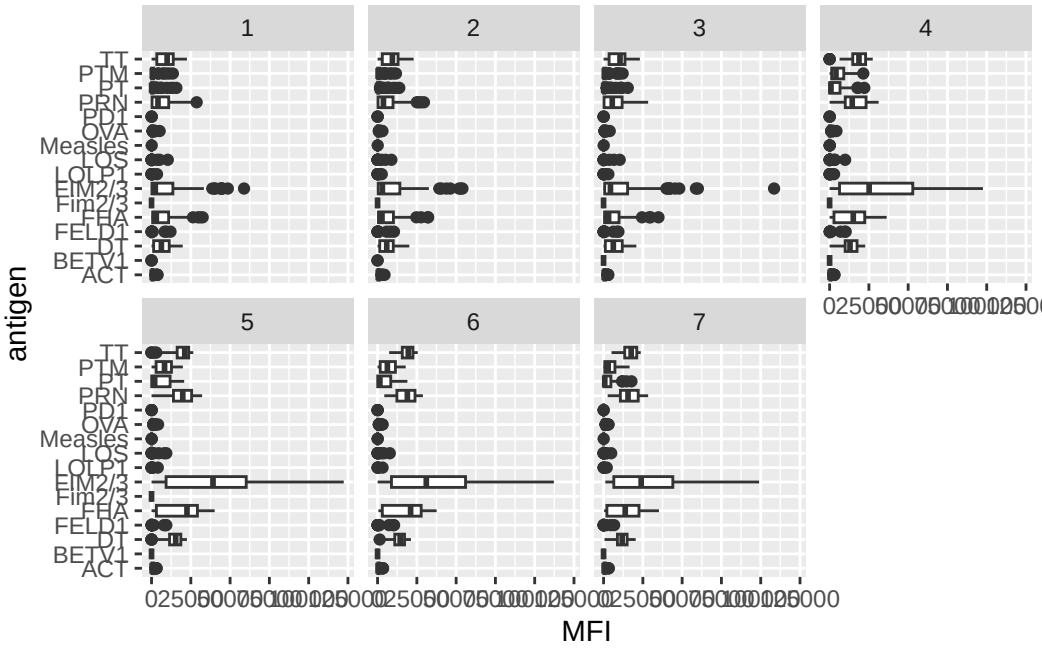
**Q13. Complete the following code to make a summary boxplot of Ab titer levels for all antigens:**

```
ig1 <- abdata %>% filter(isotype == "IgG1", visit!=8)
head(ig1)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1    IgG1                TRUE     ACT 274.355068      0.6928058
```

```
2           1    IgG1               TRUE     LOS  10.974026      2.1645083
3           1    IgG1               TRUE   FELD1   1.448796      0.8080941
4           1    IgG1               TRUE   BETV1   0.100000      1.0000000
5           1    IgG1               TRUE   LOLP1   0.100000      1.0000000
6           1    IgG1               TRUE Measles  36.277417      1.6638332
   unit lower_limit_of_detection subject_id actual_day_relative_to_boost
1 IU/ML                 3.848750          1                           -3
2 IU/ML                 4.357917          1                           -3
3 IU/ML                 2.699944          1                           -3
4 IU/ML                 1.734784          1                           -3
5 IU/ML                 2.550606          1                           -3
6 IU/ML                 4.438966          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_years
1 11212 days  30.69678
2 11212 days  30.69678
3 11212 days  30.69678
4 11212 days  30.69678
5 11212 days  30.69678
6 11212 days  30.69678
```

```r
ggplot(ig1)+
  aes(MFI, antigen)+
  geom_boxplot()+
  facet_wrap(vars(visit),nrow=2)
```


1
2
3
4
5
6
7
antigen
TT
PTM
PT
PRN
PD1
OVA
Measles
IQS
LQLP1
EIM2/3
Fim2/3
FHA
FELD1
DJ1
BETV1
ACT
MFI