Class 15: Pertussis Mini Project

Derek Chang (PID: A16942232)

Background

Pertussis (Whooping Cough) is a highly infectious disease caused by *B. Pertussis*

The CDC tracked cases per year, let's take a closer look at this data:

CDC data

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

```
library(datapasta)
```

```
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),
         No..Reported.Pertussis.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)
       )
```

```
library(ggplot2)
```

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.

```
baseplot <- ggplot(cdc, aes(Year, No..Reported.Pertussis.Cases)) + geom_line() + geom_point()
```

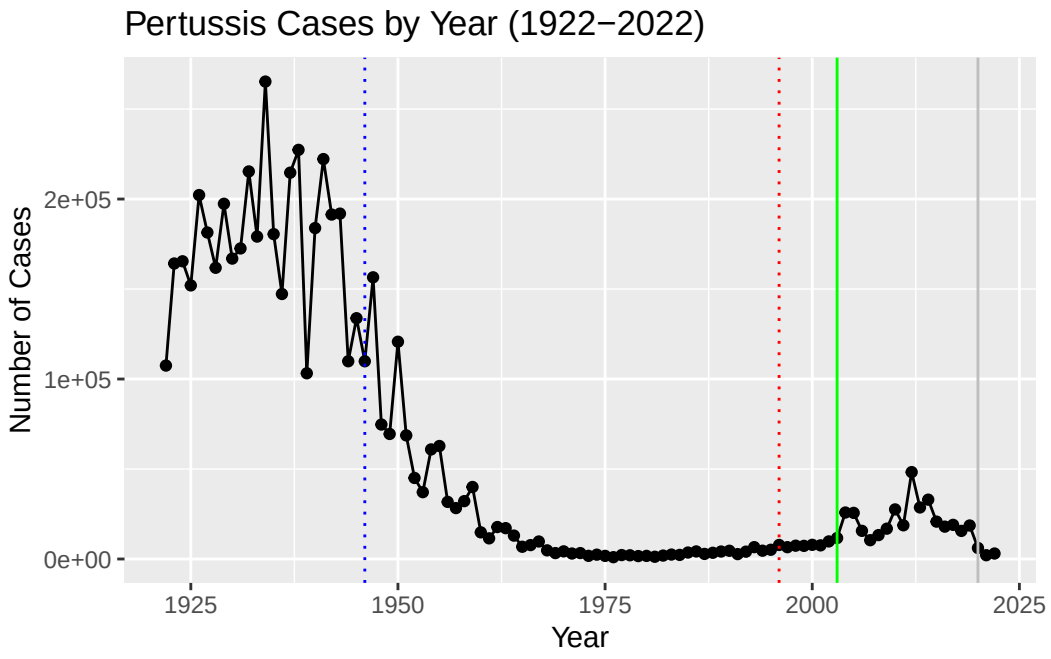
Q2. Using the ggplot geom_vline() function add lines to your previous plot for the 1946 introduction of the wP vaccine and the 1996 switch to aP vaccine (see example in the hint below). What do you notice? Add some landmark developments as annotation to our plot. We include the first whole cell (wP) vaccine roll-out in 1946 and the switch to acellular (aP) vaccine roll-out in 1996.

```
baseplot + geom_vline(xintercept = 1946, col = "blue", linetype = "dotted",) + geom_vline(xi
  geom_vline(xintercept = 2020, col = "gray") +
  geom_vline(xintercept = 2003, col = "green") +
  geom_text(aes(x = 1998, y = 1, label = "aP"), col = "red", vjust = -28) +
  geom_text(aes(x = 1948, y = 1, label = "wP"), col = "blue", vjust = -28)
```

```
Warning in geom_text(aes(x = 1998, y = 1, label = "aP"), col = "red", vjust = -28): All aestl
```

```
i Please consider using `annotate()` or provide this layer with data containing
  a single row.

Warning in geom_text(aes(x = 1948, y = 1, label = "wP"), col = "blue", vjust = -28): All aest
i Please consider using `annotate()` or provide this layer with data containing
  a single row.
```



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

We went from ~200,000 cases pre wP vaccine to ~1000 cases in 1976. The US switched to the aP vaccine in 1995. We start to see a big increase in 2004 to ~ 26,000 cases. We see a increase after the aP vaccine due to vaccine rates, bacterial evolution, and the aP vaccine might not give as strong of a immunity to the bacteria, their immunity can wane after a couple of years.

There is a ~10 year lag from aP rollout to increasing case numbers. This holds true of other countries like japan.

Key Question: Why does the aP vaccine's induced immunity wane faster than that of the wP vaccine?

CMI-PB

The CMI-PB (Computational Models of Immunity Pertussis Boost) makes available lost of data about the immune response to Pertussis booster vaccination.

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

CMI-PB makes all their data freely available via JSON format tables from their databases.

Let's read the first one of these tables:

```
library(jsonlite)

subject <- read_json("https://www.cmi-pb.org/api/v5/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 subjects are there 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
```

There are 87 aP and 85 wP subjects in the dataset.

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

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

```
Female   Male
   112     60
```

112 Female and 60 Male subjects.

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

```
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
```

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

No, this is not representative, it represents more of the UCSD student population.

Let's get more data from CMI-PB, this time about specimens collected

```
specimen <- read_json("http://cmi-pb.org/api/v5/specimen",
          simplifyVector = TRUE)
```

Now we can join these two tables `subject` and `specimen` Using a Dplyr *_Join() function to make one new 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:

```
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 specimen_id
1    1986-01-01    2016-09-12 2020_dataset           1
2    1986-01-01    2016-09-12 2020_dataset           2
```

```
3    1986-01-01    2016-09-12 2020_dataset           3
4    1986-01-01    2016-09-12 2020_dataset           4
5    1986-01-01    2016-09-12 2020_dataset           5
6    1986-01-01    2016-09-12 2020_dataset           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 from CMI-PB

```
titer <- read_json("https://www.cmi-pb.org/api/v5/plasma_ab_titer",
                   simplifyVector = TRUE)
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
```

One more join to do of `meta` and `abdata`to associate all the metadata about the individual and their race, biological sex and infincy vaccination status together with Antibody levels.

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.

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

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

```
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
  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
1     1
2     1
3     1
```

```
4     1
5     1
6     1
```

```
dim(ab)
```

```
[1] 52576    20
```

Q. How many Ab measurements do we have?

```
nrow(ab)
```

```
[1] 52576
```

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

How many isotypes

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

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

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

```
table(ab$dataset)
```

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

There are 4 different datasets, the most recent dataset of 2023 only has 5670 rows as the database is still ongoing.

There are 4 IgG subtypes

How many Antigens?

```
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
```

Let's focus in on IgG - one of the main antibody types responsive to bacteria or viral infections.

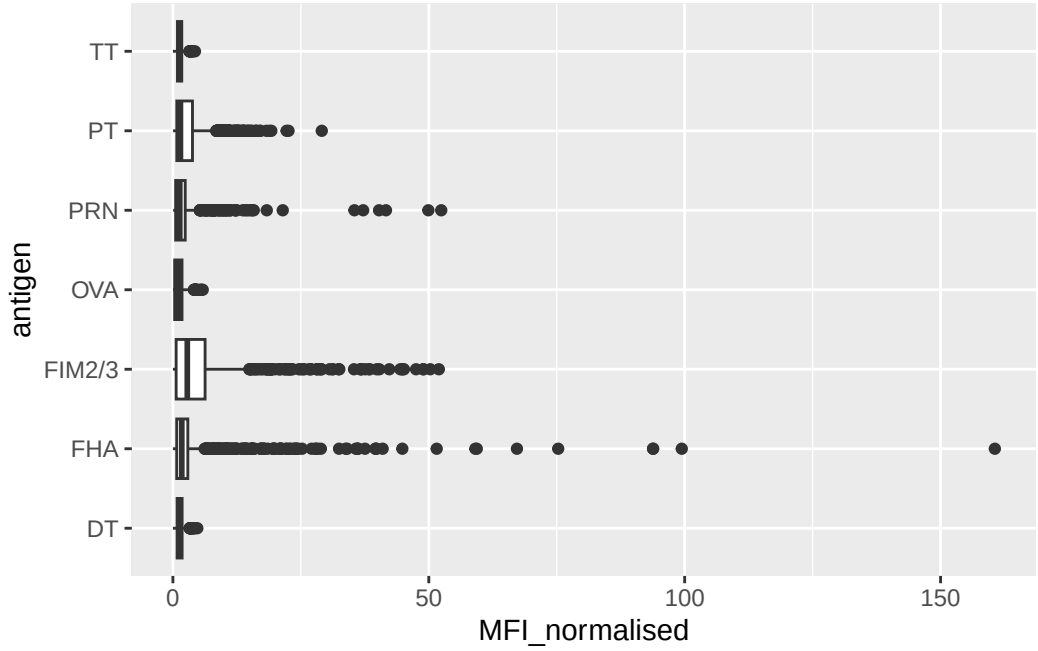
```
igg <- filter(ab, isotype == "IgG")
head(igg)
```

```
  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
  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
1     1
2     1
3     1
4     1
5     1
6     1
```

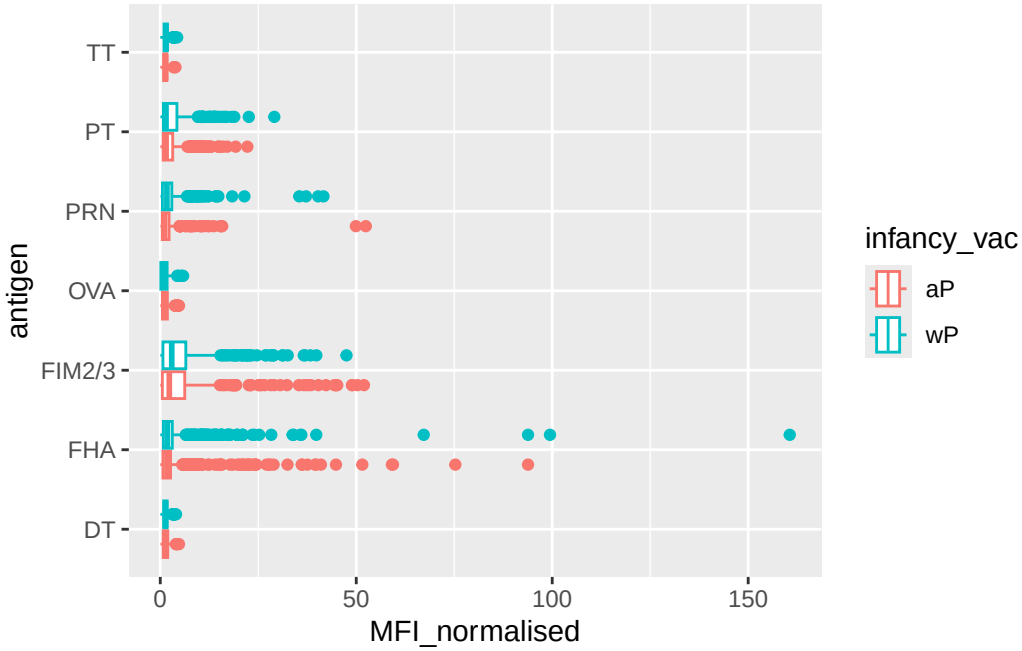
Make a plot of MFI (Main Fluorescence Intensity) - a measure of how much is detected for each antigen.

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

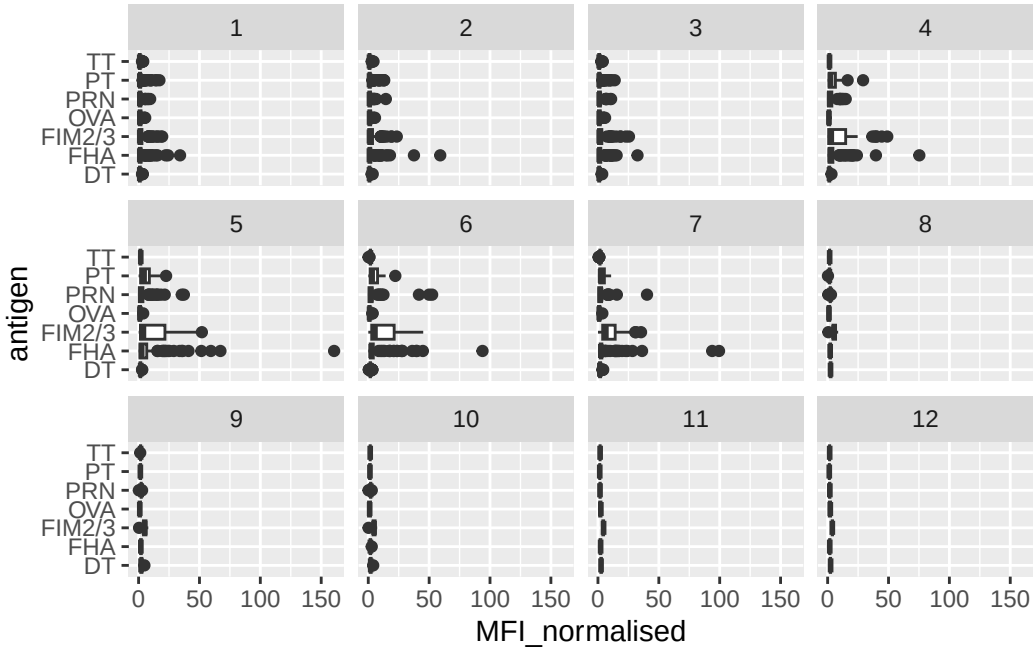


Let's color by aP/wP infancy_vac

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




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



```
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
```

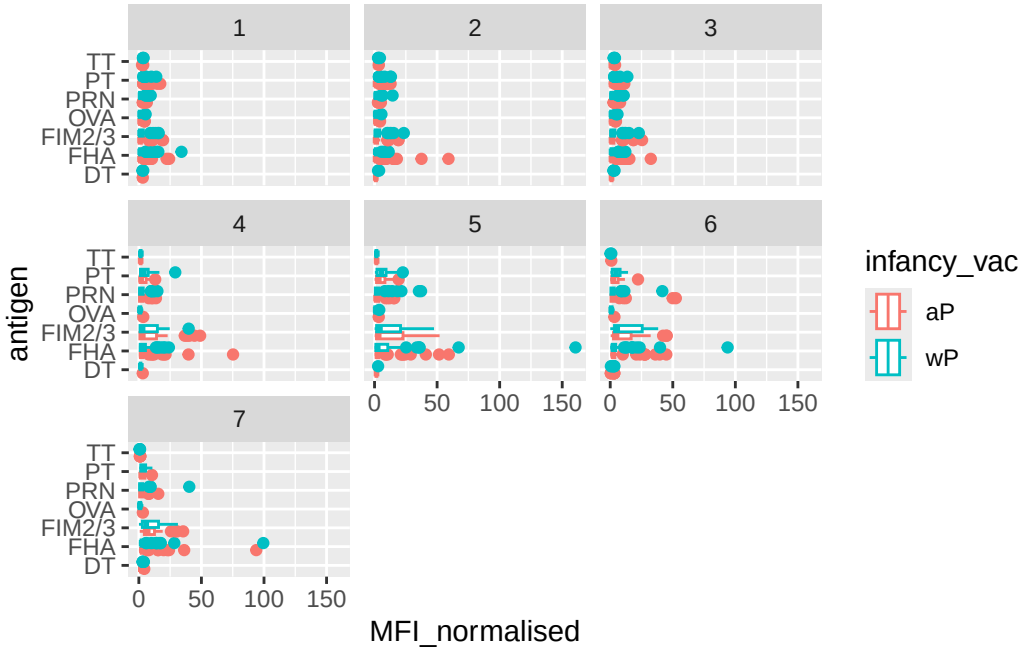
We don't have all the data for all 12 visits. Visits 8 onwards will be excluded.

```
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
```

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

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

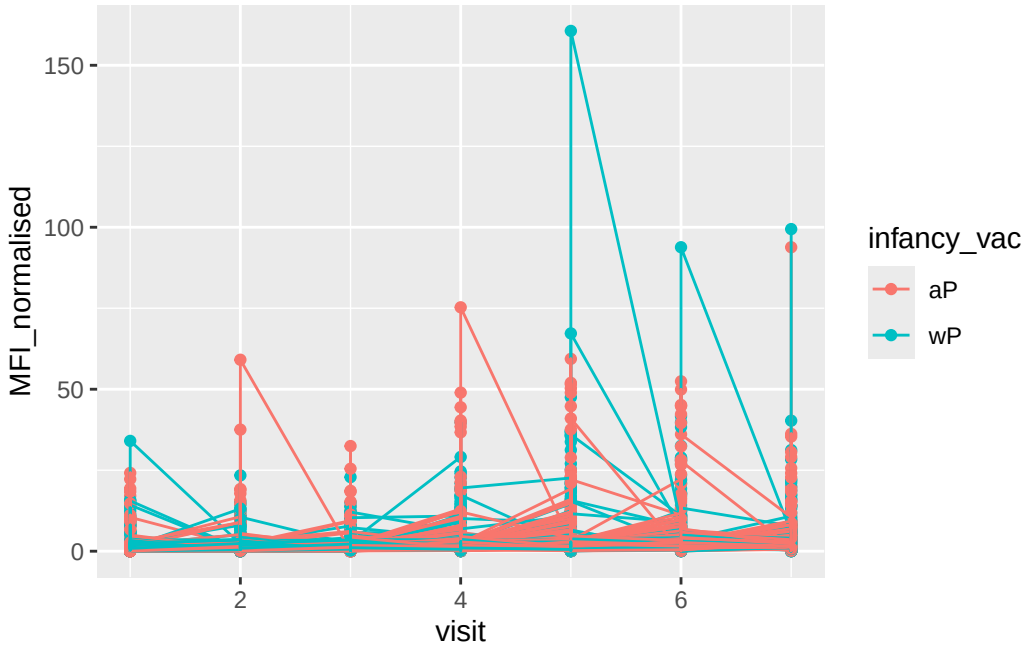


Q14. What antigens show differences in the level of IgG antibody titers recognizing them over time? Why these and not others?

Fim2/3, PT, PRN seem to show differences in the level of IgG antibody titers recognizing them over time. This might be because these antigens could be potentially important antigens that cause whooping cough, and they could be widely used in aB and wB vaccines, as well as differences in antigenic variation.

Let's try a different plot to see if there's a difference between aP and wP. First start with PT (pertussis Toxin) and plot visit or time on the X-axis, and the MFI_normalized on the Y axis.

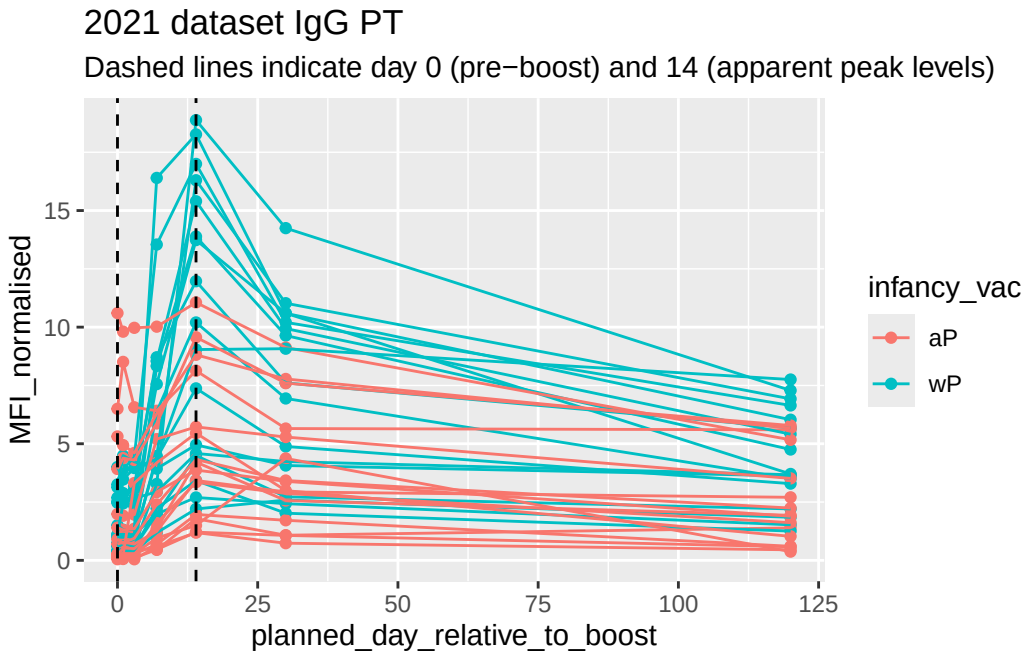
```
ggplot(igg_7) +
  aes(visit, MFI_normalised, group = subject_id, col = infancy_vac) +
  geom_point() +
  geom_line()
```




```
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)")
```



Let's Finish here for today. We are beginning to see some interesting differences between aP and wP individuals. There is likely lots of interesting things to find in this dataset.