Lab 15

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Background

Pertussis, aka whopping cough, is a highly infections lunch disease caused by the bacteria *B. Pertussis*. The CDC tracks pertussis cases numbers per year. Lets have a close look at this data. [CDC data] (https://www.cdc.gov/pertussis/php/surveillance/pertussis-cases-by-year.html?CDC_AAref_Val=https://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html)

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

1. Investigating pertussis cases by year

```
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)
)
```

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
library(ggplot2)

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

Add some developmental landmarks as annotation. We include first whole-cell(wP) vaccine roll-out in 1946. Let's add the switch to acellular (aP) vaccine 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?

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

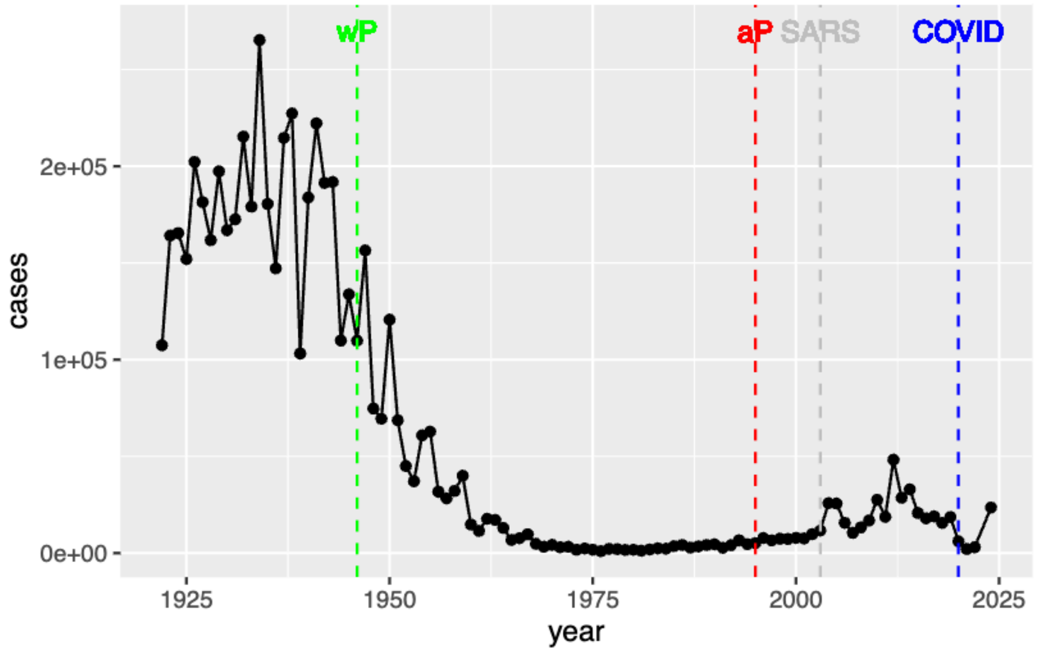
2. A tale of two vaccines (wP & aP)

cases started to reappear except for the covid time (around 2020)

```r
baseplot +
  geom_vline(xintercept = 1946, col = "green",linetype = "dashed")+
  geom_text(aes(x = 1946, y = 270000), label = "wP", color = "green")+
  geom_vline(xintercept = 1995, col = "red", linetype = "dashed")+
  geom_text(aes(x = 1995, y = 270000), label = "aP", color = "red")+
  geom_vline(xintercept = 2020, col = "blue", linetype = "dashed")+
  geom_text(aes(x = 2020, y = 270000), label = "COVID", color = "blue")+
  geom_vline(xintercept = 2003, col = "grey", linetype = "dashed")+
  geom_text(aes(x = 2003, y = 270000), label = "SARS", color = "grey")
```

```
Warning in geom_text(aes(x = 1946, y = 270000), label = "wP", color = "green"): All aesthetic
i Please consider using `annotate()` or provide this layer with data containing
  a single row.

Warning in geom_text(aes(x = 1995, y = 270000), label = "aP", color = "red"): All aesthetics
i Please consider using `annotate()` or provide this layer with data containing
  a single row.

Warning in geom_text(aes(x = 2020, y = 270000), label = "COVID", color = "blue"): All aesthet
i Please consider using `annotate()` or provide this layer with data containing
  a single row.
```

```
Warning in geom_text(aes(x = 2003, y = 270000), label = "SARS", color = "grey"): All aesthet
i Please consider using `annotate()` or provide this layer with data containing
  a single row.
```



We went from ~200,000 cases per 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. The resurge after 2000 might due to the hesitation to take vaccine.

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

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

3. Exploring CMI-PB data

The CMI_PB (Computational Models of Immunity PErtussis Boost) makes avaibable lots of data about 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 database.

Lets read the first one of these tables

```r
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 in this file?

```r
nrow(subject)
```

```
[1] 172
```

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

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

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

It's not.

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

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

> 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 can join these two tables `subject` and `specimen` to make one new `meta` table with the combined data.

```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
```

```
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

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

> 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.

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

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

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

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

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

```

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

```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?

much more than the previous dataset

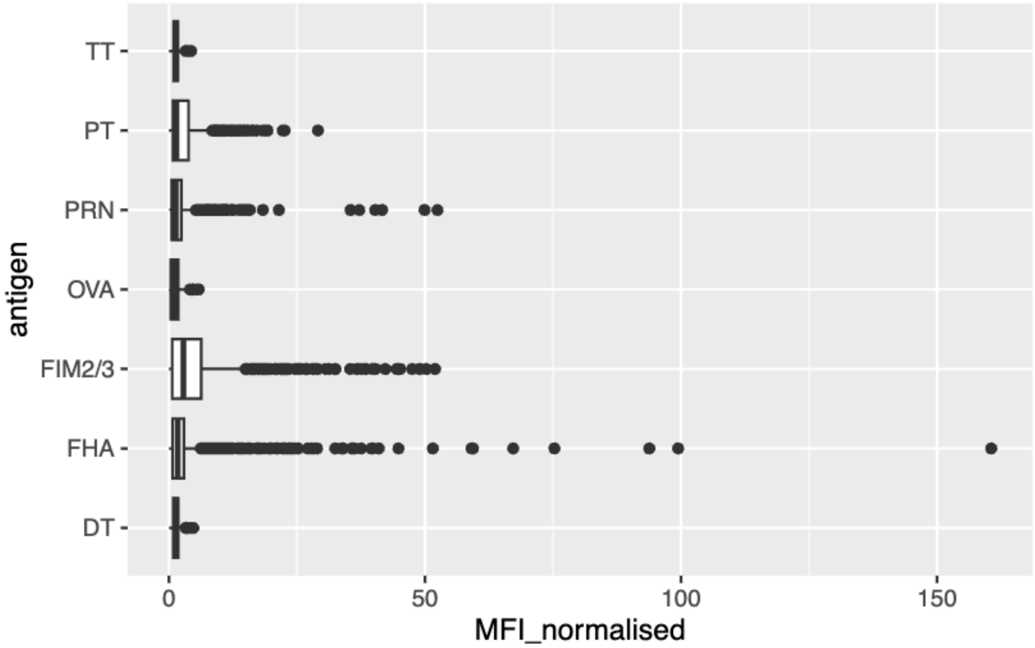
4. Examine IgG Ab titer levels

Let's focus on IgG- one of the main antibody types responsie to bacteria or virial infections

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

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

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

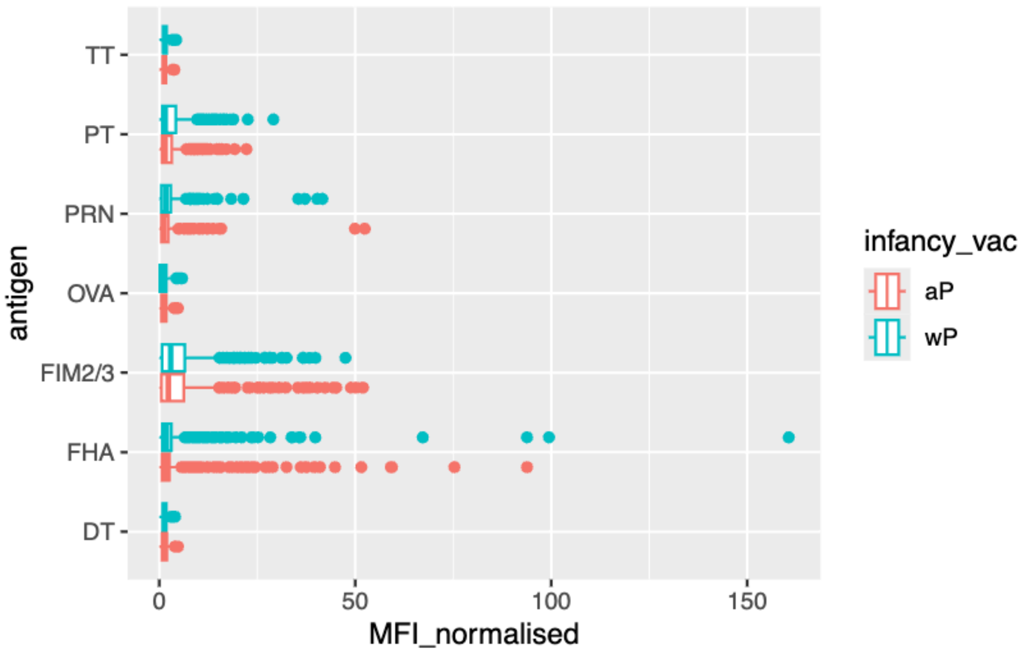


Q14. What antigens show differences in the level of IgG antibody titers recognizing them over time? Why these and not others?

PT, FIM2/3

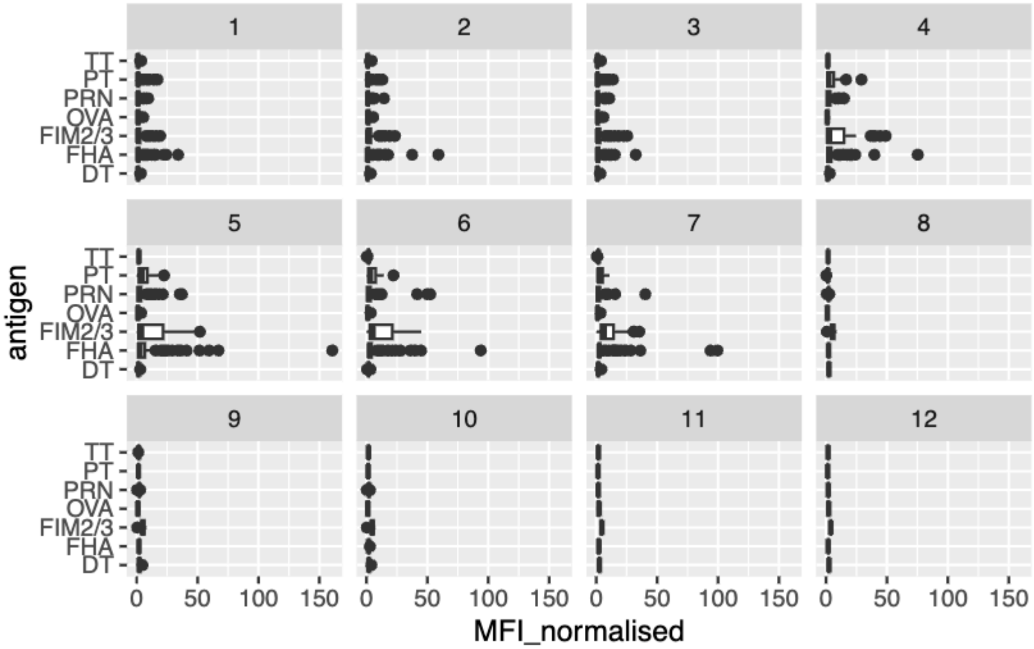
Let's color by aP/wP infancy_vac

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



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)
```



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

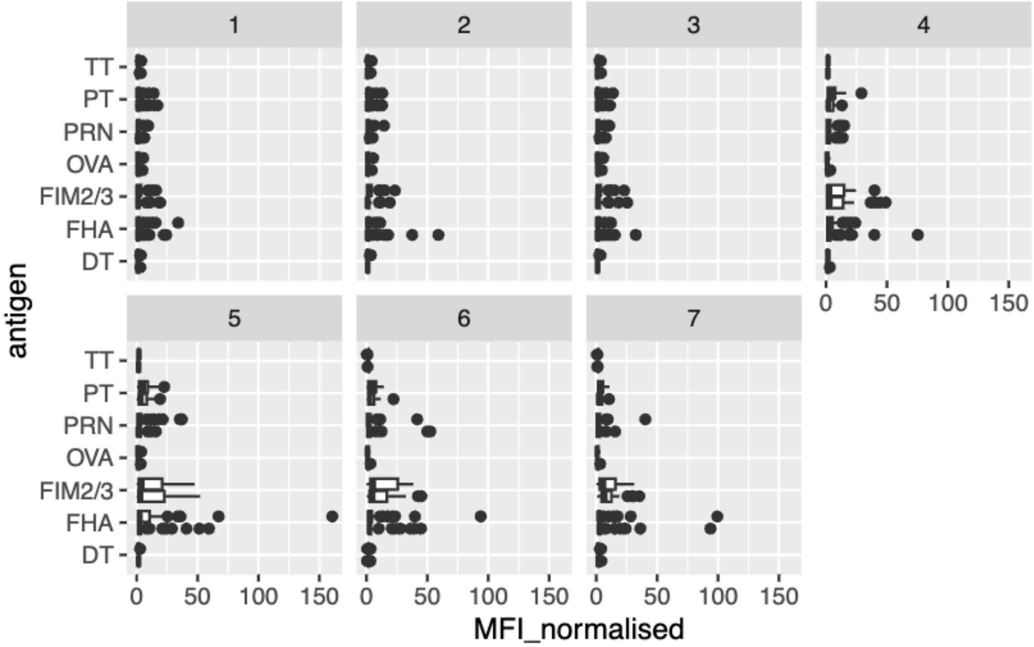
```

  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 don't have data yet for all subjects in terms of visit 8 onwards. So let's exclude them.

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

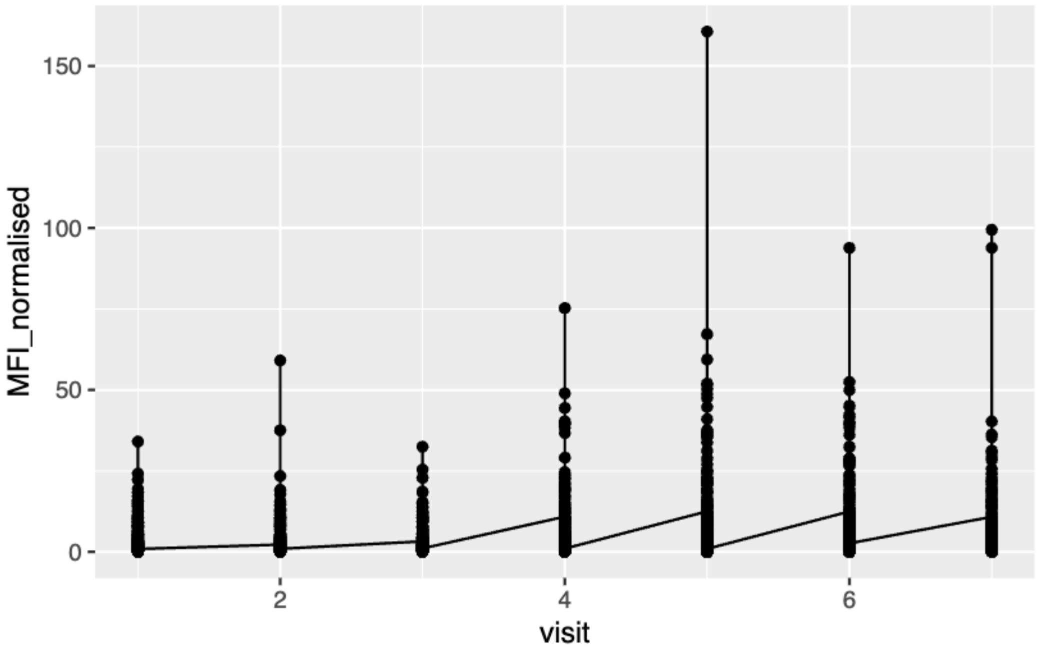
```

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

```r
ggplot(igg_7)+
  aes(MFI_normalised, antigen, cols = infancy_vac)+
  geom_boxplot()+
  facet_wrap(~visit, nrow = 2)
```

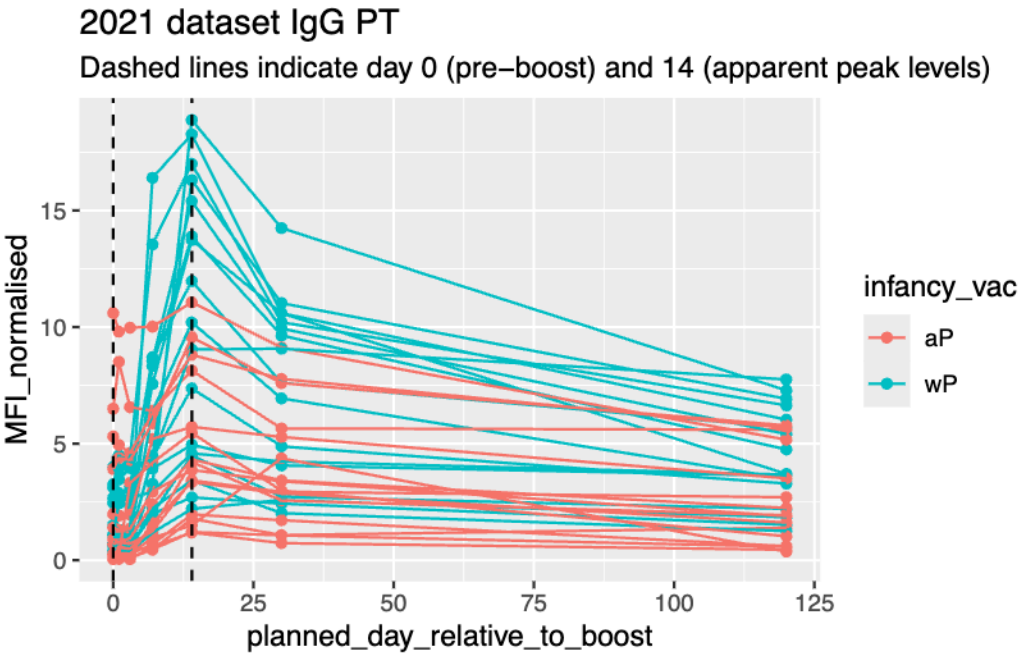


Lets try a different plot. First focus on one antigen, start with PT (Pertussis Toxin) and plot visit or time on the x-axis and MFI_normalised on the y-axis.

```
ggplot(igg_7)+
  aes(visit, MFI_normalised)+
  geom_point()+
  geom_line()
```

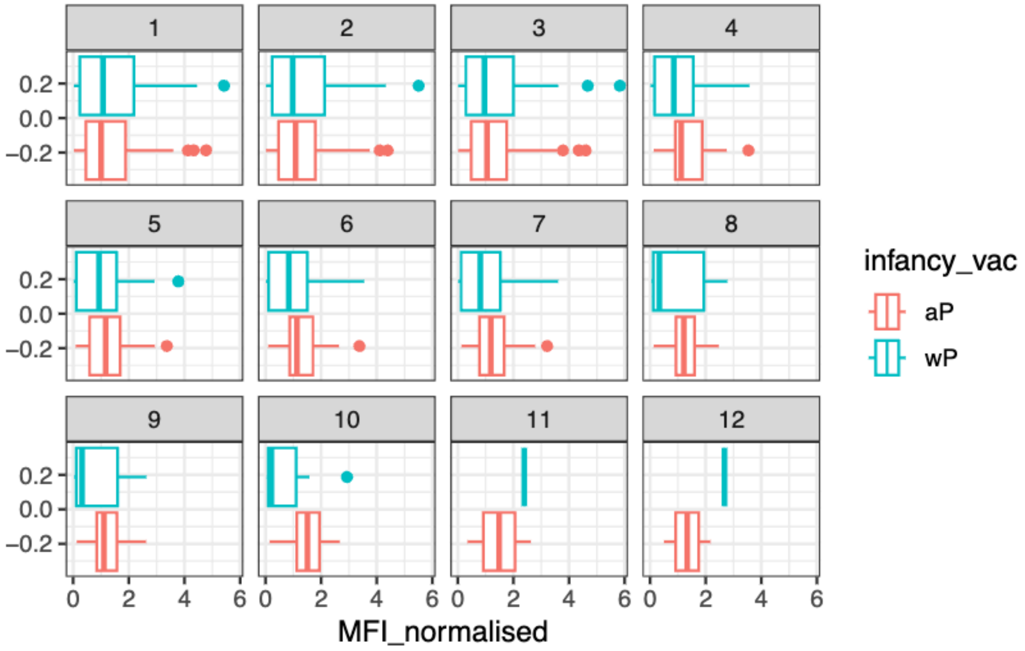


```
abdata.21 <- ab %>% filter(dataset == "2021_dataset")

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)")
```

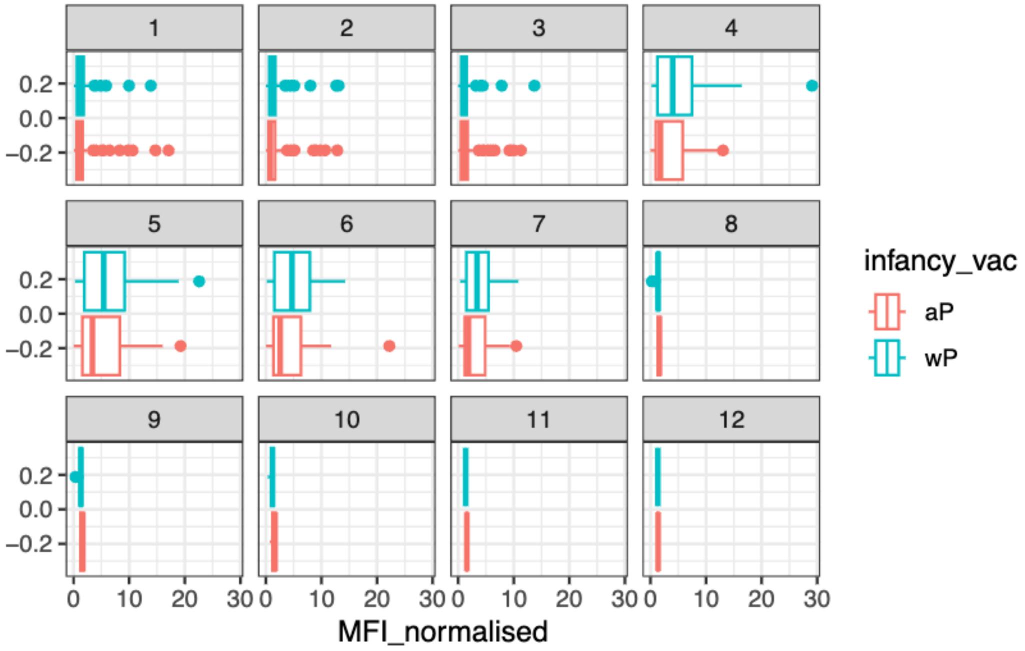


Q15. Filter to pull out only two specific antigens for analysis and create a boxplot for each. You can chose any you like. Below I picked a "control" antigen ("OVA", that is not in our vaccines) and a clear antigen of interest ("PT", Pertussis Toxin, one of the key virulence factors produced by the bacterium B. pertussis).

```
filter(igg, antigen=="OVA") %>%
  ggplot() +
  aes(MFI_normalised, col=infancy_vac) +
  geom_boxplot(show.legend = TRUE) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



```
filter(igg, antigen=="PT") %>%
  ggplot() +
  aes(MFI_normalised, col=infancy_vac) +
  geom_boxplot(show.legend = TRUE) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



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

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