Class 15: Mini Project Investigating Pertussis Resurgence

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Background

Pertussis, a.k.a whooping cough, is a highly infectious lung disease caused by the bacteria *B. Pertussis*

The CDC tracks pertussis cases numbers per year. Let's have a closer look at this data.

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.

```
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,
```

```r
    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
  )
)
```

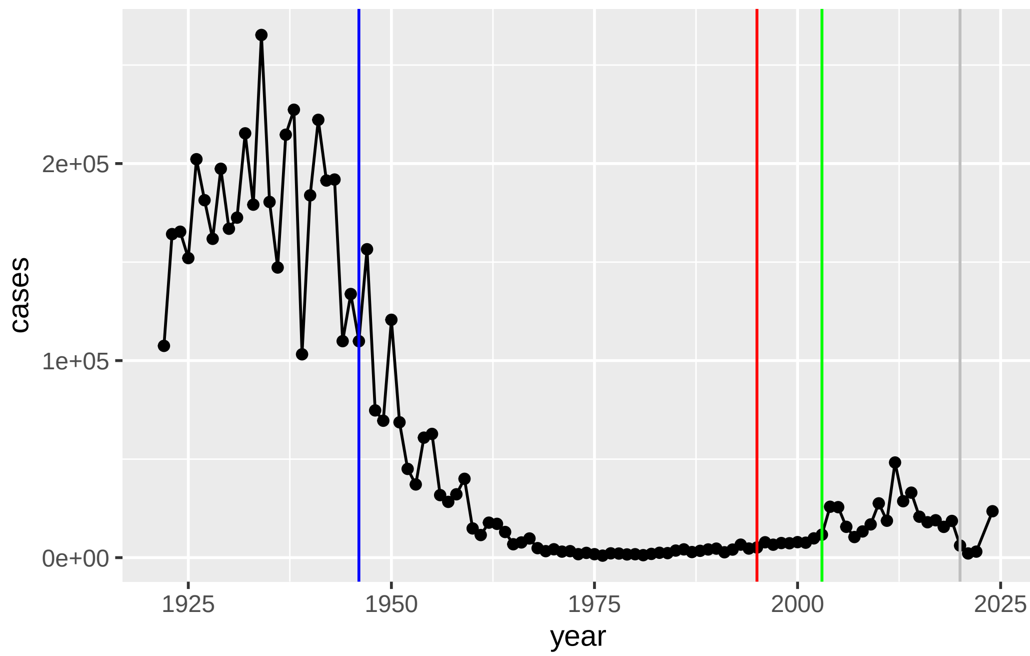
```r
library(ggplot2)
baseplot <-  ggplot(cdc) +
    aes(year, cases) +
    geom_point() +
    geom_line()
```

> 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?

Add some landmarks developments as annotation to our plot. We include the first whole-cell (wP) vaccine roll-out in 1940.

Let's add the switch to acellular vaccine (aP) in 1996.

```r
baseplot +
  geom_vline(xintercept = 1946, col="blue") +
  geom_vline(xintercept = 1995, col="red") +
  geom_vline(xintercept = 2020, col="gray") +
  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?

We went from ~200,000 cases pre wP vaccine to ~1000 cases in 1976. The US switched to the aP vaccine in 1955. We start to see a big increase in 2004 to ~26,000 cases.

There is a ~10 year 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?

CMI-PB

The CMI-PB (computational models of Immunity Pertussis Boost) makes available lots 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 make all their data freely availanble via JSON format tables from their database.

Let's read the first one of these tables:

```
library(jsonlite)

subject <- read_json("http://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
```

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

```
nrow(subject)
```

```
[1] 172
```

```
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 U.S. population?

No!

Now 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)
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 '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
```

```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 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
```

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(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
  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
```

> Q. How many Ab measurements do we have?

```r
nrow(ab)
```

```
[1] 52576
```

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 
```

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

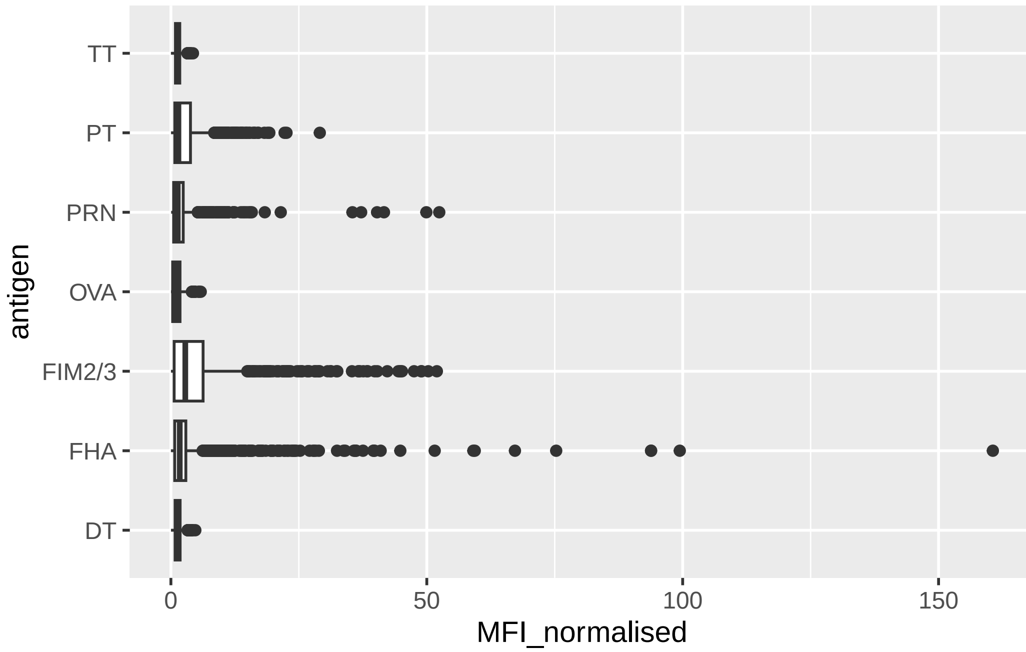
```r
igg <- filter(ab, isotype=="IgG")
head(igg)
```

```
  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
  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
```

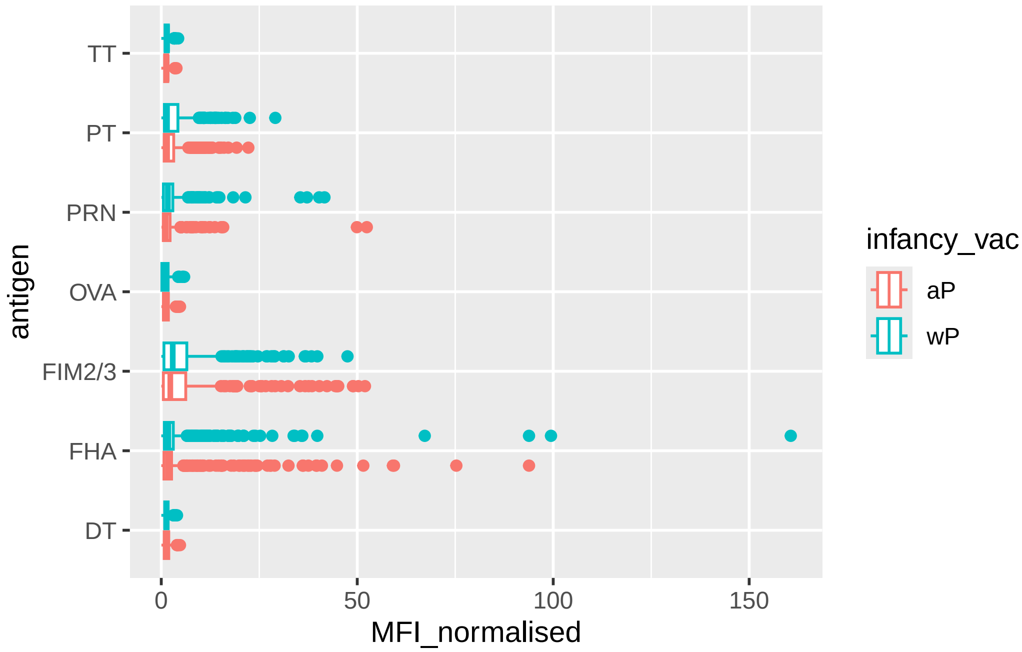
Make a first plot of MFI (Mean Fluroscence Intensity- measure of how much is detected) for each antigen.

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

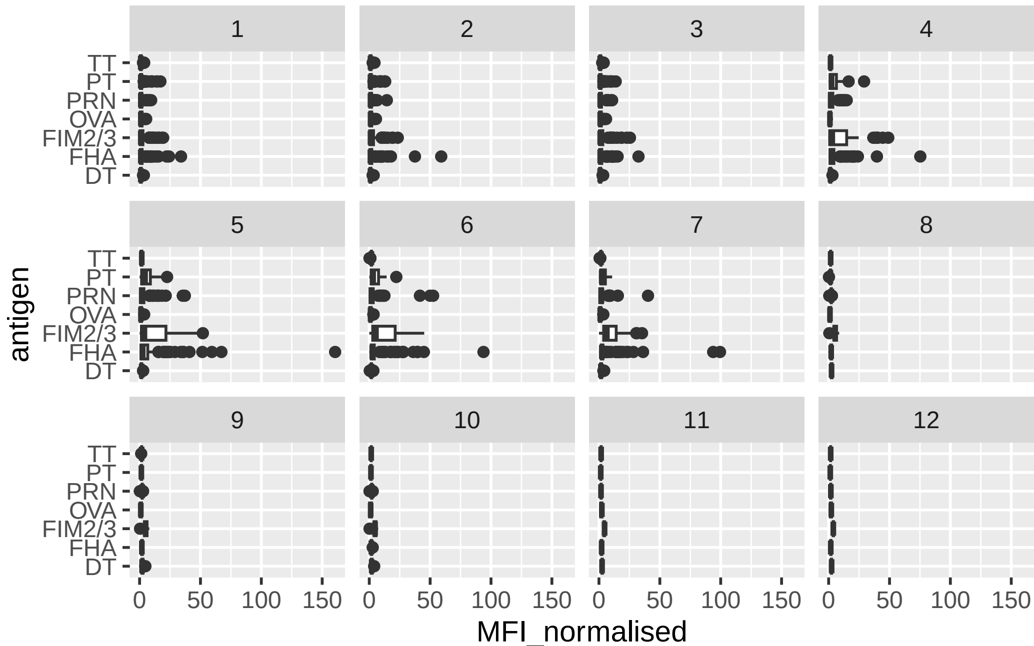


Let's color by aP/wP infancy_vac

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




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




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

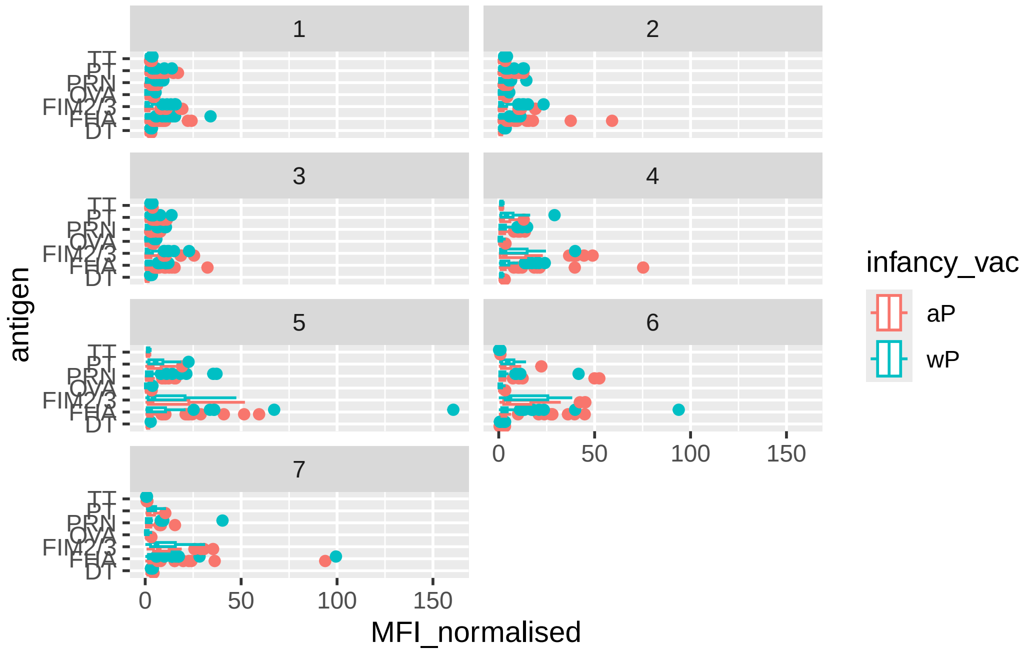
```

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

Looks like we don't have data yet for all the subjects in terms of visits 8 onwards. So lets exclude these.

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

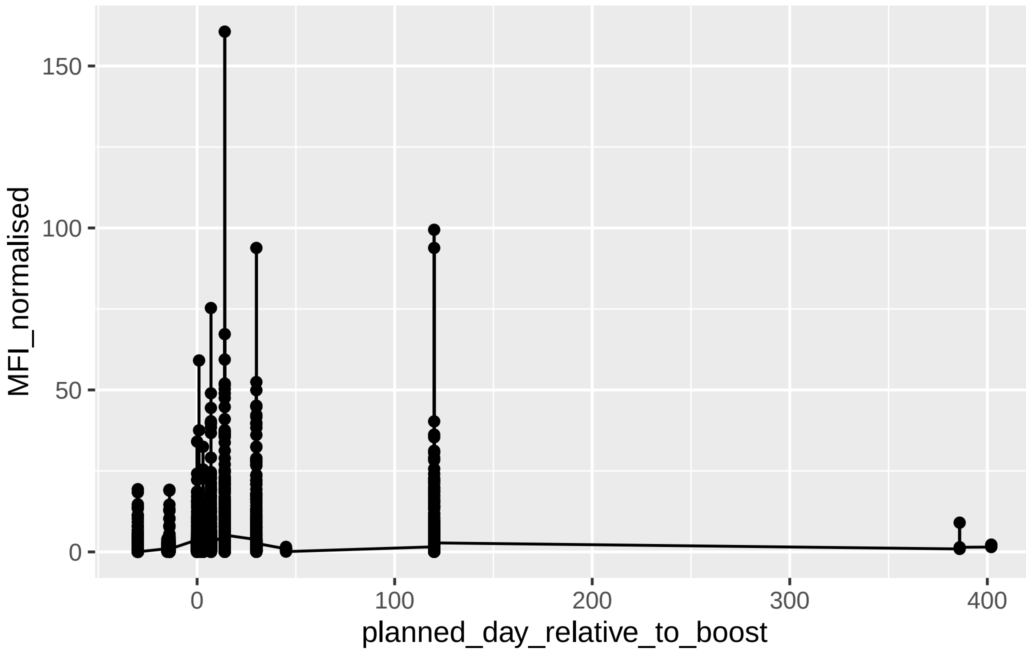
```

  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)
```

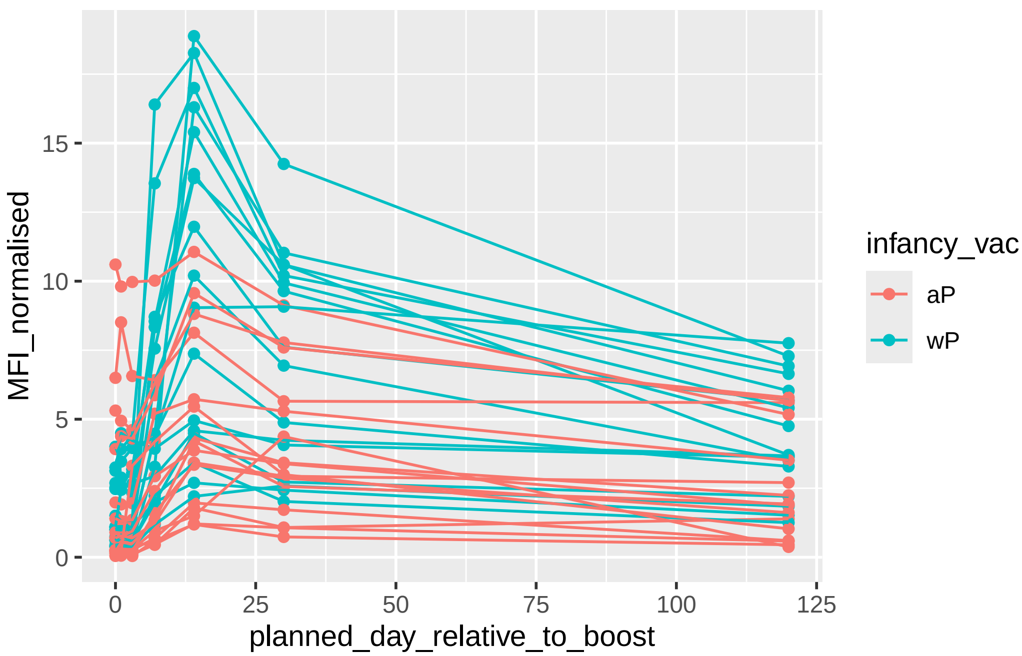


Let's try a different plot. First focus on one antigen, start with PT (pertussis toxin) and plot visit or time on the x-axis and MFI_normalized on the y-axis.

```
ggplot(igg_7) +
  aes(planned_day_relative_to_boost, 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()
```



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