Class18: Pertussis mini project

Yiyu

Table of contents

Pertussis (aka whooping cough) is a serious lung infection caused by the bacteria *B. Pertussis.*

The CDC tracks Pertussis case numbers and we can fin dthis data here: http://tinyurl.com/pertussiscdc

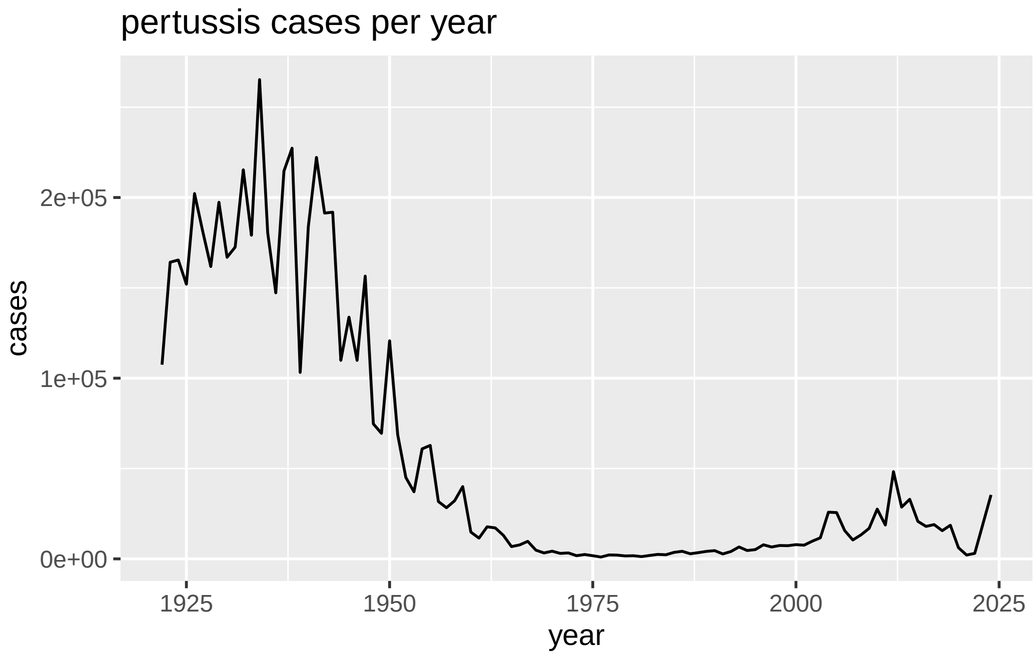
We can "scrape" this data using the **datapasta** package. Download updated package from github and install in R console.

```
head(cdc)
```

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

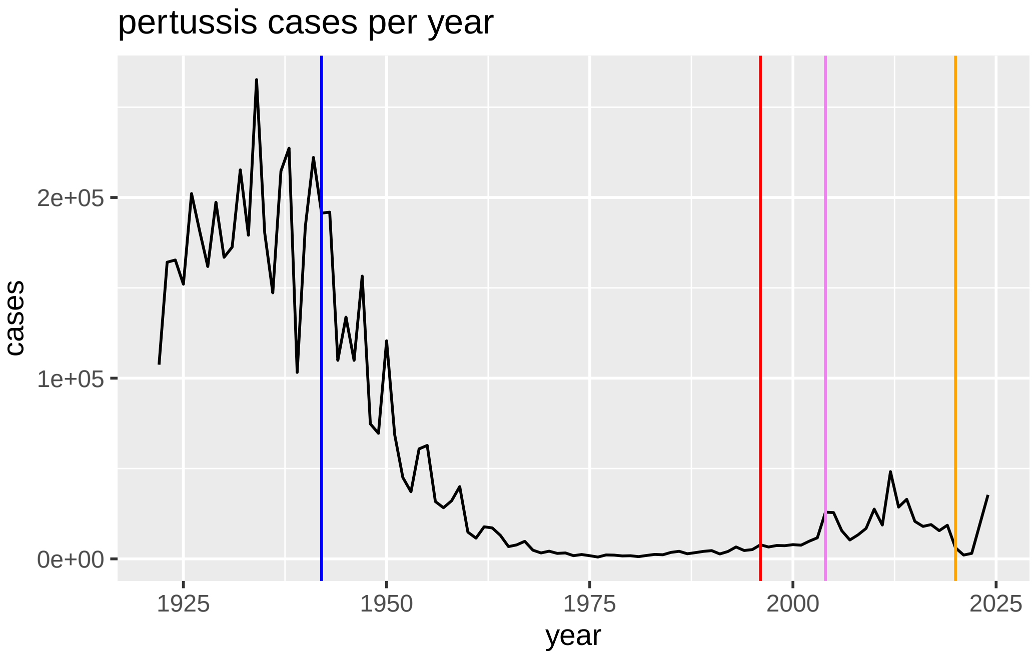
> Q1. Make a plot of pertussis cases per year using ggplot.

```
library(ggplot2)
ggplot(cdc) +
  aes(year, cases) +
  labs(title = "pertussis cases per year") +
  geom_line()
```



Q2. Let's add key milestones of the DTP (wP) vaccine roll out in 1942 and switch to the new aP vaccine in 1996. We can use `geom_vline()` to add vertical line for these. Booster shots started in 2004, while covid quarantine began in 2020.

```
ggplot(cdc) +
  aes(year, cases) +
  labs(title = "pertussis cases per year") +
  geom_line() +
  geom_vline(xintercept = 1942, col = "blue") +
  geom_vline(xintercept = 1996, col = "red") +
  geom_vline(xintercept = 2004, col = "violet") +
  geom_vline(xintercept = 2020, col= "orange")
```



There were high case numbers pre 1946 (before the wP vaccine), then relatively rapid decrease in cases post wP vaccine. The case numbers remained low throughout the 1970s until 2004 when the first widespread outbreak occurred again.

In 1996 there was a switch from the wP vaccine to the aP vaccine, and soon after in 2004 there was an increase in Pertussis cases in adolescents.

Mounting evidence indicates that the aP vaccine induced immunity wanes faster than the older wP vaccine.

Computational Models of Immunity Pertussis Boost

One of the main goals of this project is to determine what is different in the immune repsonse between wP and aP primed individuals.

Using the booster vaccine as a proxy for ineffection

All data is available here https://www.cmi-pb.org/ in JSON format. We can use the **jsonlite** package to read this data into R.

```
library(jsonlite)
```

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

```r
subject <- read_json("http://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”

```r
nrow(subject)
```

```
[1] 172
```

> Q. How many aP and wP subjects are there?

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

```

aP wP 
87 85 
```

> Q. Male/Female numbers

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

```

Female   Male 
   112     60 
```

Q. Breakdown of biological sex and race?

```
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 look to be representitive of the US population at large?

NO. This is not representative of the US population at large, it is biased.

Let's read some more CMI-PB data

```
specimen <- read_json("http://cmi-pb.org/api/v5_1/specimen",
                      simplifyVector = TRUE)
titer <- read_json("http://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(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
```

To use this data we need to "join" the various tables to find all the information I need to know about a particular measurement.

```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
dim(meta)
```

```
[1] 1503   13
```

```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 we can join `meta` with `titer` data.

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

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

```
head(ab_data)
```

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

> Q. How many different antibody isotypes are we measuring?

```r
table(ab_data$isotype)
```

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

> Q. How many antigens?

```r
table(ab_data$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 
```

> Q. Let's look at antigen levels over the whole dataset?

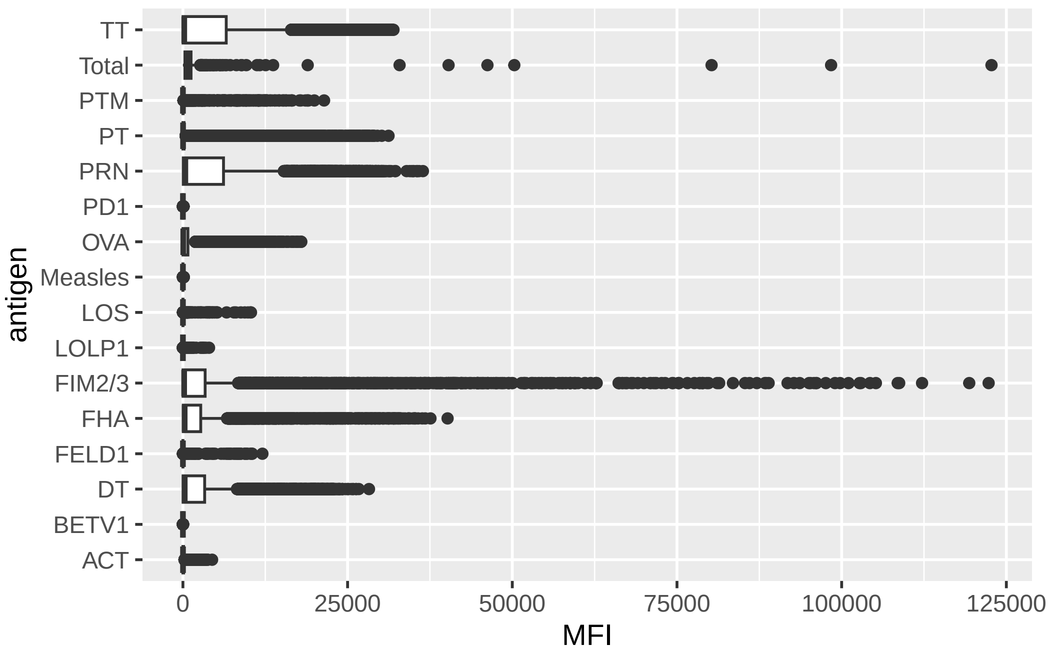
```r
dim(ab_data)
```

```
[1] 61956    20
```

Let's look at a boxplot of antigen levels

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

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

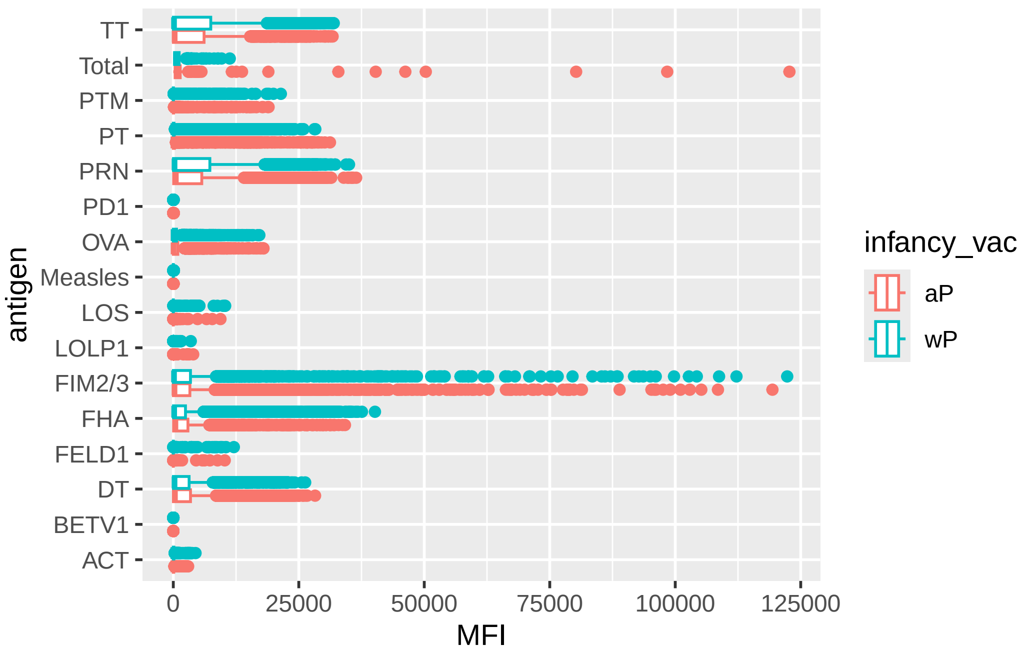


Q. Break this plot down by aP or wP.

We can use coloring `col=` by `infancy_vac`.

```
ggplot(ab_data) +
  aes(MFI, antigen, col = infancy_vac) +
  geom_boxplot()
```

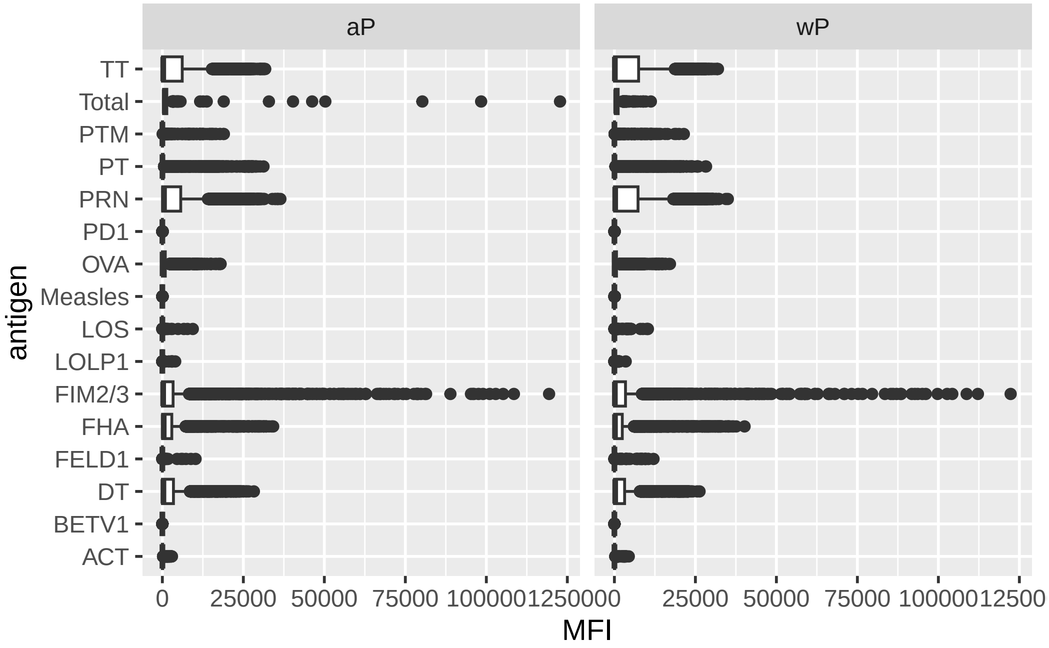
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Or we can `facet` the plot by `~infancy_vac`

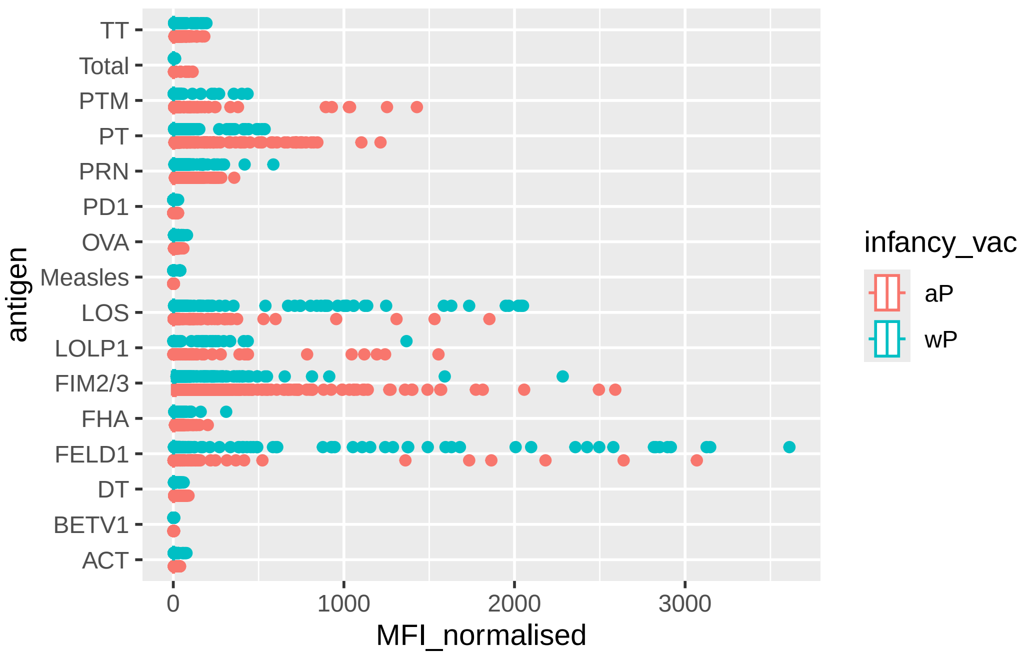
```
ggplot(ab_data) +
  aes(MFI, antigen) +
  geom_boxplot() +
  facet_wrap(~infancy_vac)
```

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



Let's try using MFI_normalized instead of MFI

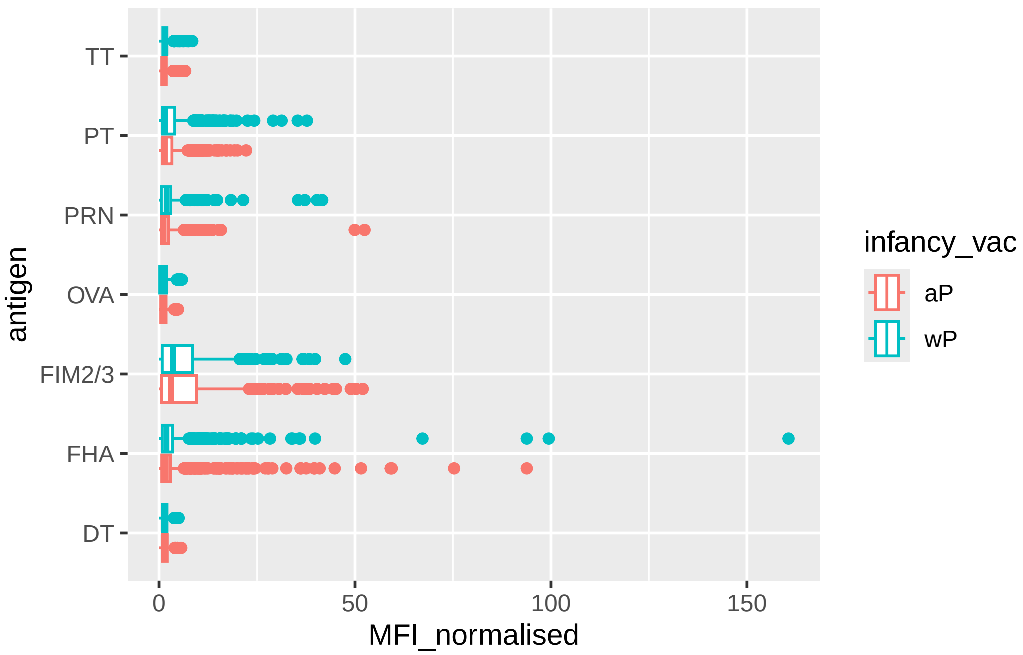
```
ggplot(ab_data) +
  aes(MFI_normalised, antigen, col = infancy_vac) +
  geom_boxplot()
```



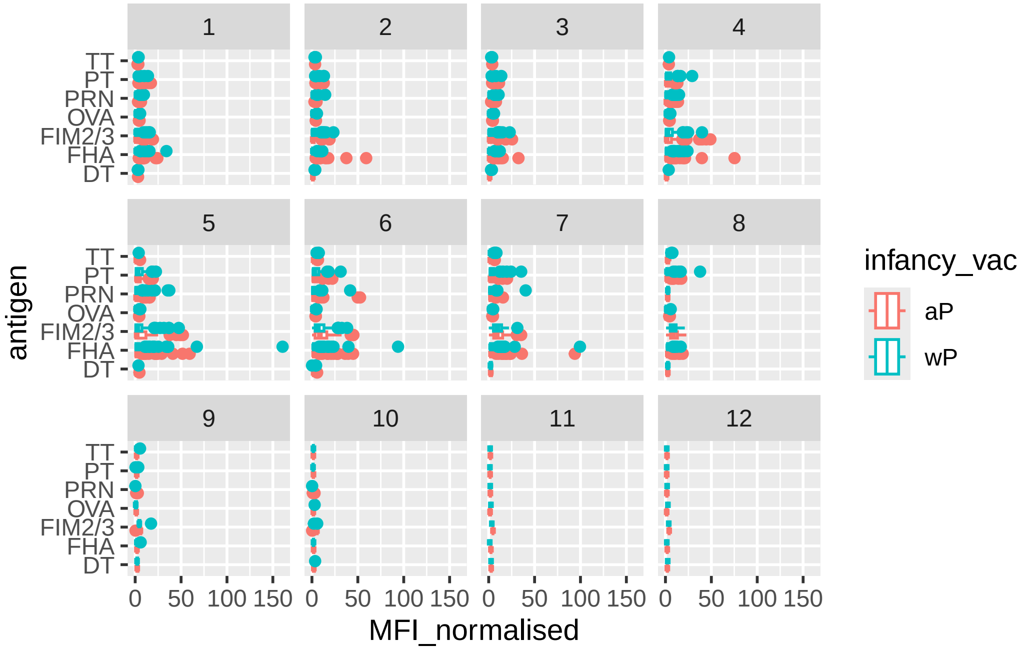
Let's focus on just IgG

```
igg <- ab_data |>
  filter(isotype == "IgG")

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



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

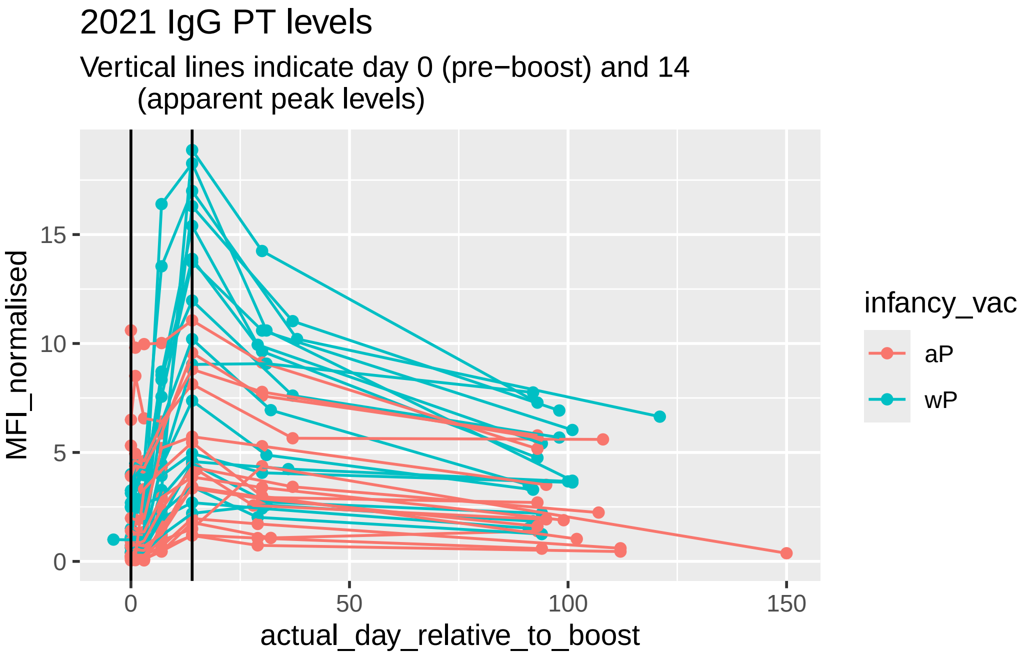


Let’s focus on PT (pertussis toxin) and igg levels over time. To do this we’ll filter to focus on one antigen “PT” and IgG levels in 2021 dataset.

```
pt_igg_2021 <- ab_data |>
      filter(isotype == "IgG", antigen == "PT", dataset == "2021_dataset")
```

A plot of `actual_day_relative_to_boost_` vs `MFI_normalised`

```
ggplot(pt_igg_2021) +
  aes(actual_day_relative_to_boost, MFI_normalised, col=infancy_vac,
      group = subject_id) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept = 14) +
  geom_vline(xintercept = 0) +
  labs(title = "2021 IgG PT levels",
       xlab = "Days relative to Boost",
       ylab = "MFI (normalized)",
       subtitle = "Vertical lines indicate day 0 (pre-boost) and 14
       (apparent peak levels)")
```



```r
library(lubridate)
```

```
Attaching package: 'lubridate'

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

    date, intersect, setdiff, union
```

```r
today () - mdy("04-23-2001")
```

```
Time difference of 8719 days
```

```r
time_length( today() - mdy("04-23-2001"), "years")
```

```
[1] 23.87132
```

```r
subject$age <- time_length(today() - ymd(subject$year_of_birth), "years")
```