Class 18: Pertussis Mini Project

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2025-03-06

Pertussis (a.k.a.) Whooping Cough is a deadly lung infection caused by the bacteria B. Pertussis.

The CDC tracks Pertussis cases around the US. At https://tinyurl.com/pertussiscdc

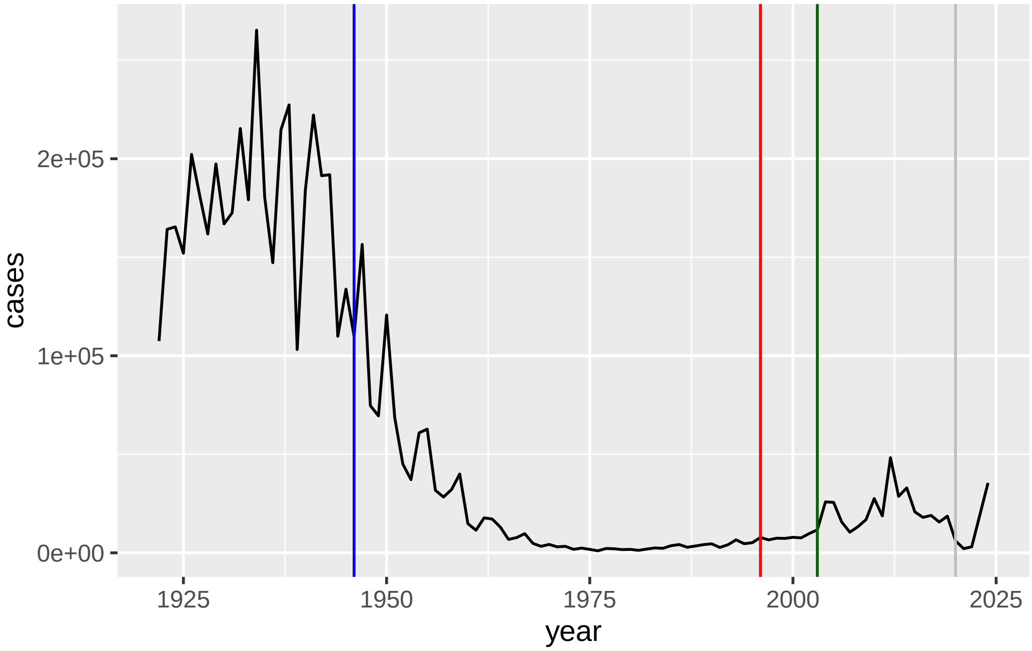
We can "scrape" this data using the R **datapasta** package.

```
head(cdc)
```

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

Q1, Q2.

```
library(ggplot2)

ggplot(cdc) +
  aes(year, cases) +
  geom_line() +
  geom_vline(xintercept = 1946, col="blue") +
  geom_vline(xintercept = 1996, col="red") +
  geom_vline(xintercept = 2020, col="gray") +
  geom_vline(xintercept = 2003, col="darkgreen")
```



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

There were high case numbers before the first wP (whole-cell) vaccine roll out in 1946 then a rapid decline in case numbers until 2004 when we have our first large-scale outbreak of pertussis again, not long after the switch to aP vaccine. This could be due to people being more skeptical of vaccination, but it is unclear what the difference is between people that have gotten the wP vs. aP vaccines. There is a notable COVID related dip and recent rapid rise.

Q. What is different about the immune response to infection if you had an older wP vaccine vs the newer aP vaccine?

Computational Models of Immunity - Pertussis Boost (CMI-PB)

The CMI-PB project aims to address this key question: what is different between aP and wP individuals?

We can get all the data from this ongoing project via JSON API calls For this we will use the **jsonlite** package. We can install with: `install.packages("jsonlite")`

```
library(jsonlite)
subject <- read_json("https://www.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" are in this data set?

```r
nrow(subject)
```

```
[1] 172
```

> Q4. How many wP and aP primed individuals are in this dataset?

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

```

aP wP 
87 85 
```

> Q5. How many male/female are there?

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

```

Female   Male 
   112     60 
```

> Q6. What is the breakdown of race and biological sex?

```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
```

This is not representative of the US population but it is the biggest dataset of its type so let's see what we can learn.

Obtain more data from CMI-PB:

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

```r
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(ab_data)
```

```
  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
```

I now have 3 tables of data from CMI-PB: `subject`, `specimen`, `ab_data`. I need to "join" these tables so I will have all the info I need to work with.

For this we will use the `inner_join()` function from **dplyr** package.

> 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:

```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
```

```r
dim(subject)
```

```
[1] 172   8
```

```r
dim(specimen)
```

```
[1] 1503    6
```

```r
dim(meta)
```

```
[1] 1503   13
```

> 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.

Now we can join our `ab_data` table to `meta` so we have all the info we need about antibody levels.

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

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

```r
head(abdata)
```

```
  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
```

> Q11. How many different antibody isotypes are there in this dataset? How many specimens (i.e. entries in abdata) do we have for each isotype?

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

```

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

> 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(abdata$dataset)
```

```

2020_dataset 2021_dataset 2022_dataset 2023_dataset 
       31520         8085         7301        15050 
```

The most "recent" dataset (2023) has double the number of rows of the previous year.

```
table(abdata$antigen)
```

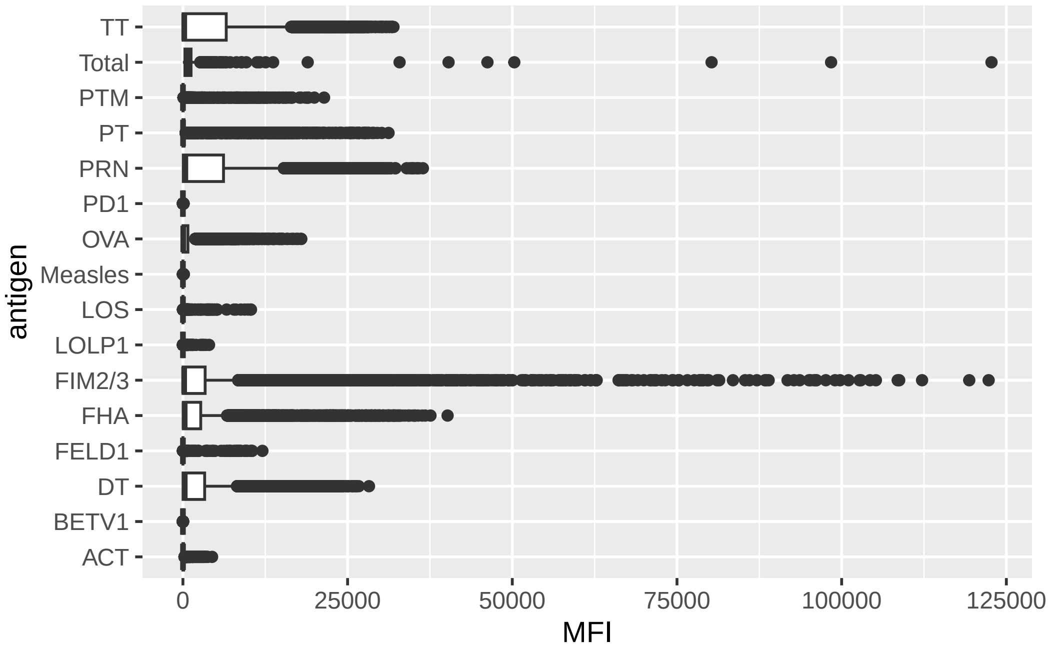
```

    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 
```

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

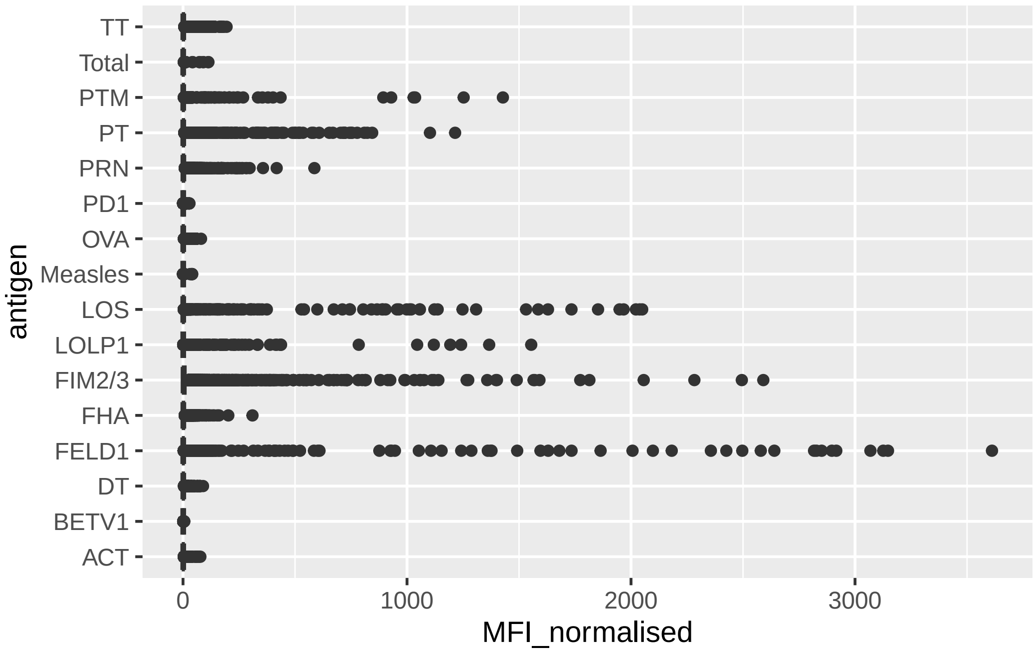
I want a plot of antigen levels across the whole dataset.

```
ggplot(abdata) +
  aes(MFI, antigen) +
  geom_boxplot()
```

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



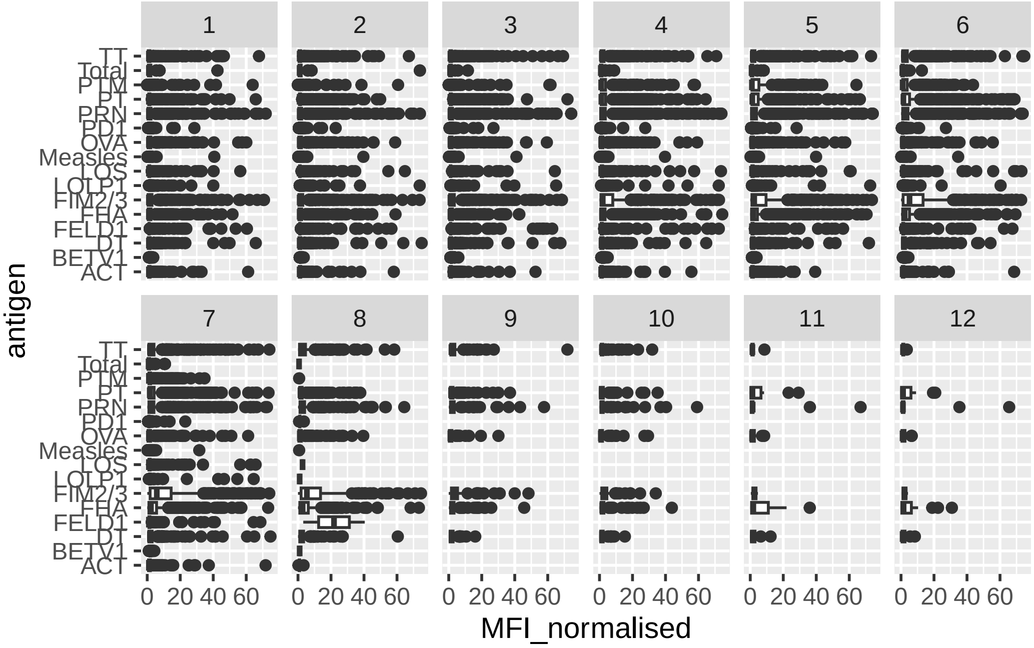
```
ggplot(abdata) +
  aes(MFI_normalised, antigen) +
  geom_boxplot()
```



Antigens like FIM2/3, PT, FELD1 have quite a large range of values. Others like Measles don't show much activity.

```
ggplot(abdata) +
  aes(MFI_normalised, antigen) +
  geom_boxplot() +
  xlim(0,75) +
  facet_wrap(vars(visit), nrow=2)
```

```
Warning: Removed 983 rows containing non-finite outside the scale range
(`stat_boxplot()`).
```

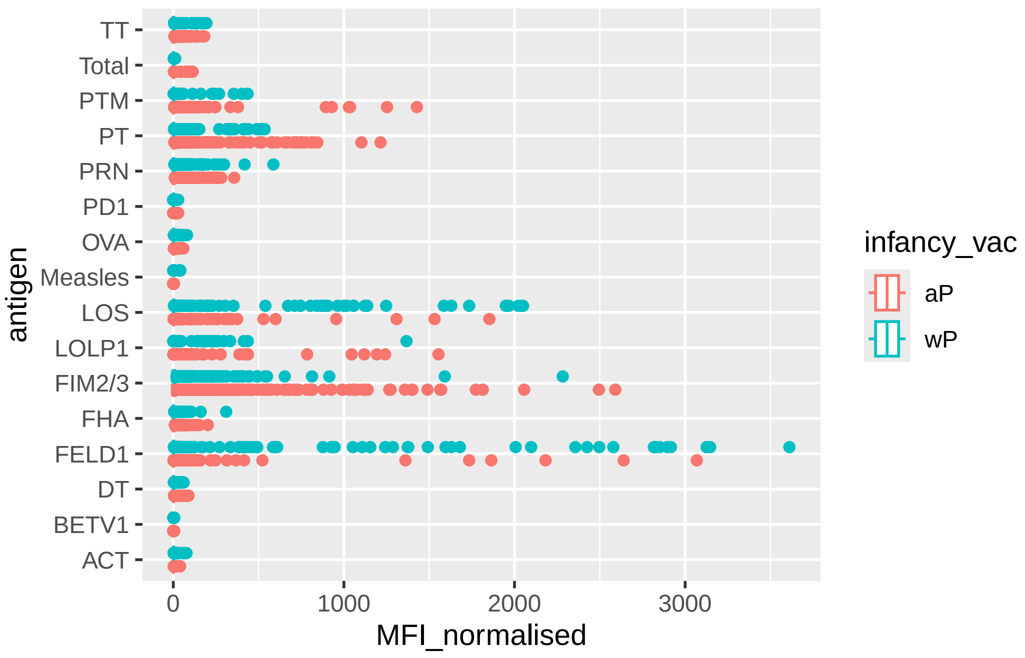


Q14. What antigens show differences in the level of IgG antibody titers recognizing them over time? Why these and not others?

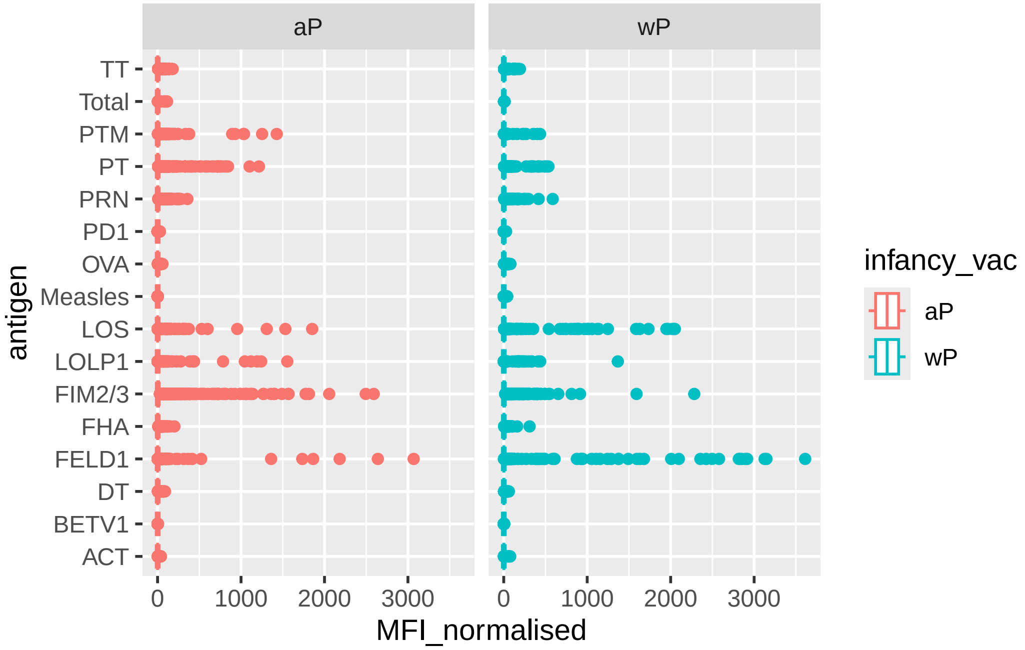
IgG antibodies against antigens like PT, PRN, FIM2/23, and FHA seem to decrease over time. This is because these are the antigens that are introduced in the aP and wP vaccines and the presence of IgG that detect them decrease over time.

Q. Are there differences at the whole-dataset level between aP and wP?

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



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



Examine IgG Ab titer levels

For this I need to select out just isotype IgG.

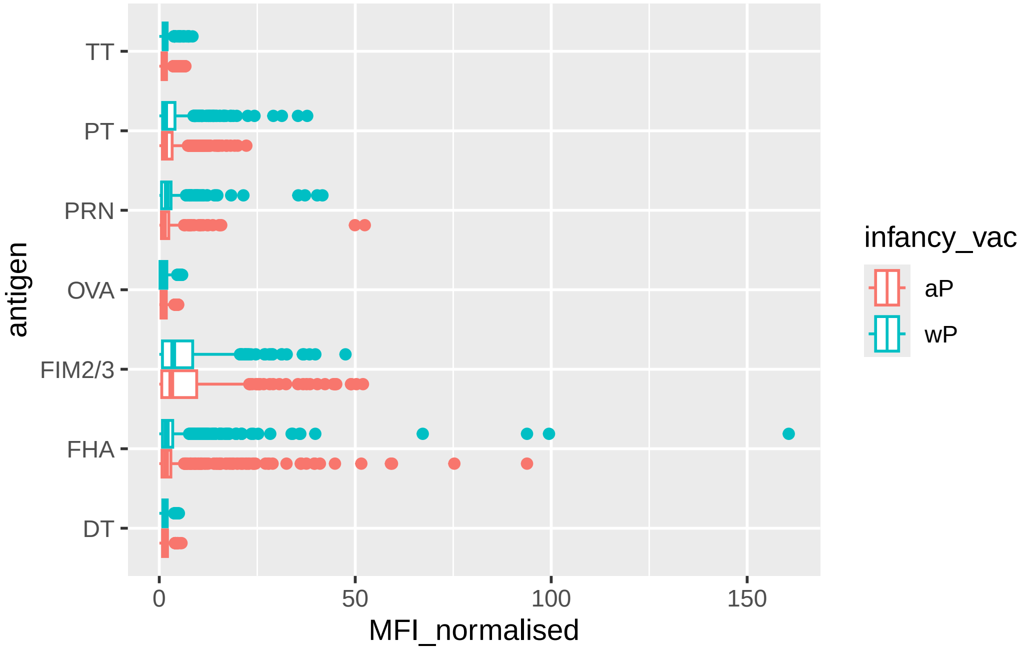
```
igg <- abdata %>%
  filter(isotype == "IgG")
head(igg)
```

```
  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           2
5    1986-01-01    2016-09-12 2020_dataset           2
6    1986-01-01    2016-09-12 2020_dataset           2
```

```
  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                            1                             1         Blood
5                            1                             1         Blood
6                            1                             1         Blood
  visit isotype is_antigen_specific antigen        MFI MFI_normalised  unit
1     1     IgG                TRUE      PT   68.56614       3.736992 IU/ML
2     1     IgG                TRUE     PRN  332.12718       2.602350 IU/ML
3     1     IgG                TRUE     FHA 1887.12263      34.050956 IU/ML
4     2     IgG                TRUE      PT   41.38442       2.255534 IU/ML
5     2     IgG                TRUE     PRN  174.89761       1.370393 IU/ML
6     2     IgG                TRUE     FHA  246.00957       4.438960 IU/ML
  lower_limit_of_detection
1                 0.530000
2                 6.205949
3                 4.679535
4                 0.530000
5                 6.205949
6                 4.679535
```

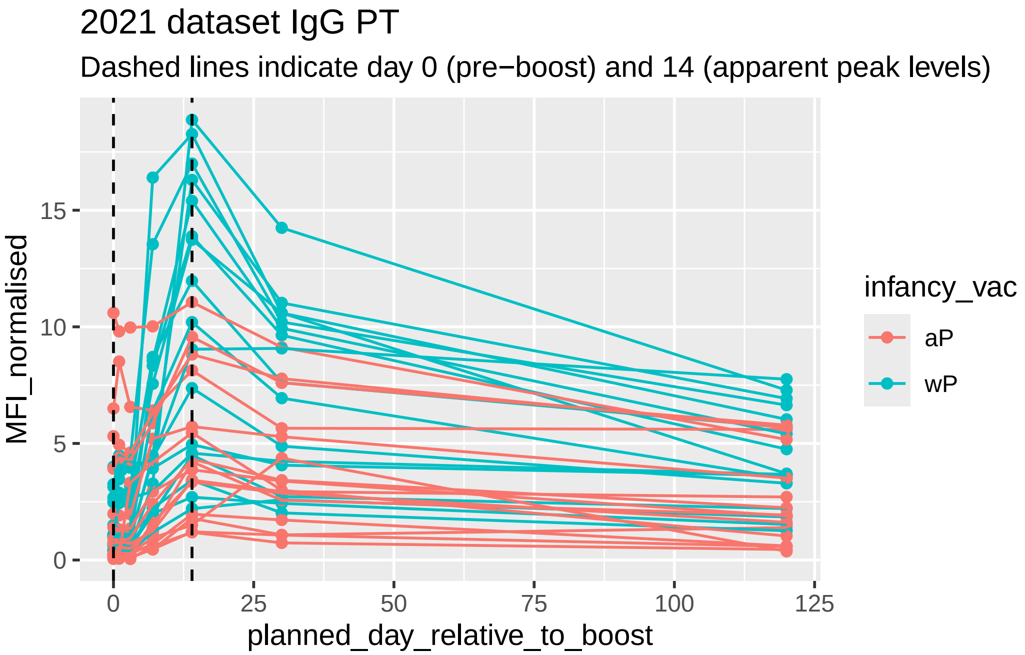
An overview boxplot:

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



Digging in further to look at the time course of IgG isotype PT antigen levels across aP and wP individuals:

```
abdata.21 <- abdata %>% filter(dataset == "2021_dataset") ## Filter to include 2021 data onl

abdata.21 %>% ## Filter to look at IgG PT data only
  filter(isotype == "IgG",  antigen == "PT") %>%
  ggplot() +   ## Plot
    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)")
```


2021 dataset IgG PT
Dashed lines indicate day 0 (pre−boost) and 14 (apparent peak levels)
MFI_normalised
15
10
5
0
0
25
50
75
100
125
planned_day_relative_to_boost
infancy_vac
aP
wP