Class 18: Pertussis Mini Project

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

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

There is interesting data to look at here, but it's not in an excel or csv file to download. We need to scrape the data using the **datapasta** pacakge. https://github.com/MilesMcBain/datapasta

> 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.

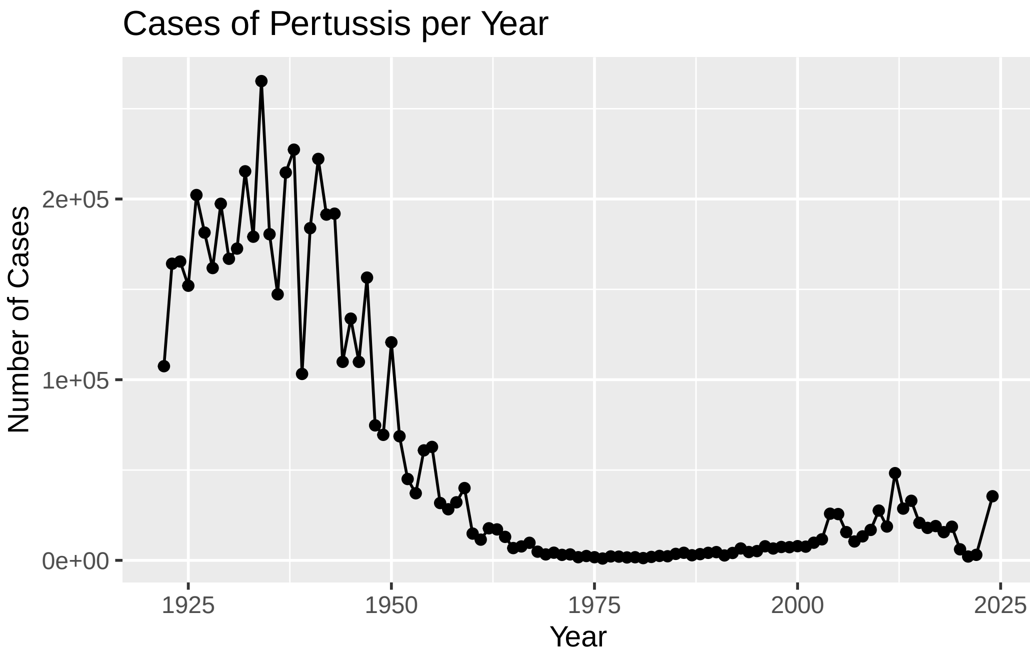
```
head(cdc)
```

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

Let's plot the new data

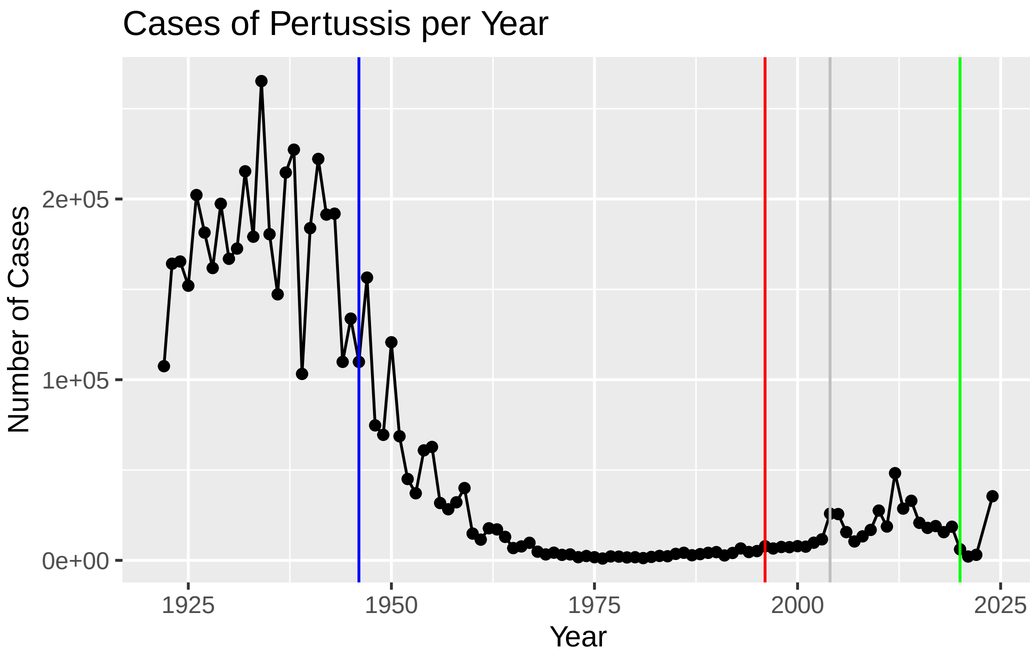
```
library(ggplot2)

ggplot(cdc, aes(year, cases))+
  geom_point() +
  geom_line() +
  ylab("Number of Cases")+
  xlab("Year")+
  ggtitle("Cases of Pertussis per Year")
```



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?

```
ggplot(cdc, aes(year, cases))+
  geom_point() +
  geom_line() +
  geom_vline(xintercept=1946,col="blue")+
  geom_vline(xintercept=1996,col="red")+
   geom_vline(xintercept=2004,col="gray")+
  geom_vline(xintercept=2020,col="green")+
  ylab("Number of Cases")+
  xlab("Year")+
  ggtitle("Cases of Pertussis per Year")
```



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 whole cell vaccine (blue line), then a rapid decline in cases following.There was a general hold of low values after the aP vaccine (red line), followed by a spike in 2004s. This could be a point where people began to mistrust vaccines and not get them as frequently or the vaccine could have been reformatted. There is a spike again following the green line after COVID19.

Infants who got the new vaccine are growing up and their immunity is waning and they need a new booster shot. It seems that something has to be different about the immune response to infection with the older wP vaccine versus the newer aP vaccine.

Computational Models of Immunity, Pertussis Booster Shot (CMI-PB)

The CMI-PB project aims to address this key question - what's different between aP and wP vaccinated individuals? This is called systems vaccinology. https://www.cmi-pb.org/

We can get all the data from this ongoing project via JSON API.For this we will use the **jsonlite** package.

```r
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 individual subjects are in this dataset?

```r
nrow(subject)
```

```
[1] 172
```

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

```r
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
```

This is not representative of the US population, but it's the best we have.

Let's 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`, and `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 the **dplyr** package.

```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 we can join our `ab_data` table to `meta`so we have all 3 sets of information in the same place.

```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
```

```r
dim(abdata)
```

```
[1] 61956    20
```

Q. How many different antibody isotypes are there is this dataset?

```r
length(abdata$isotype)
```

```
[1] 61956
```

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

```

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

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

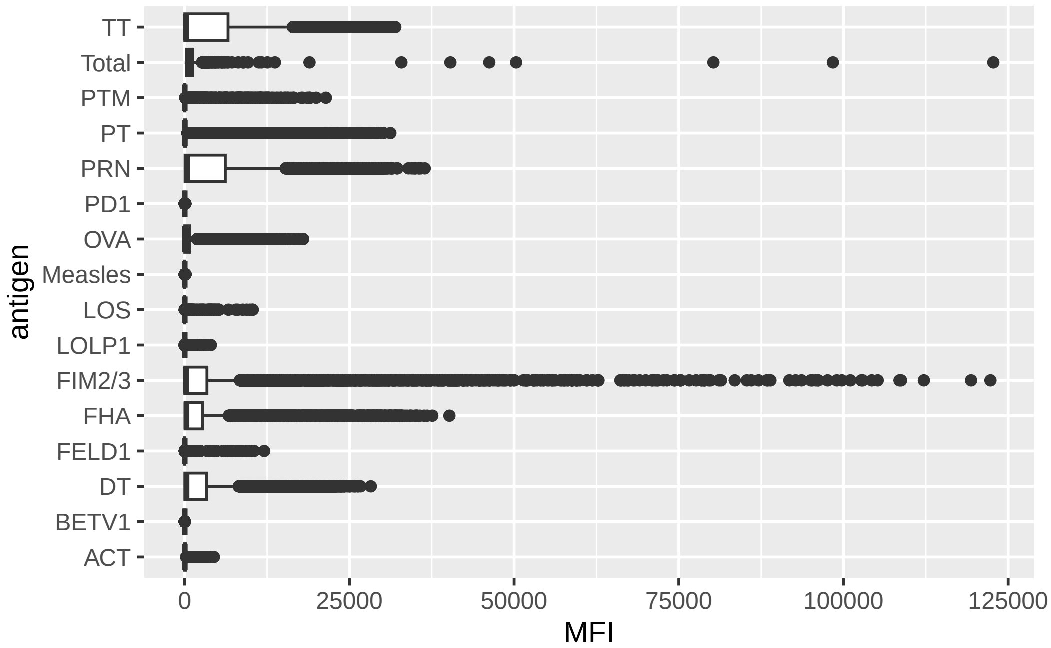
```

    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 
```

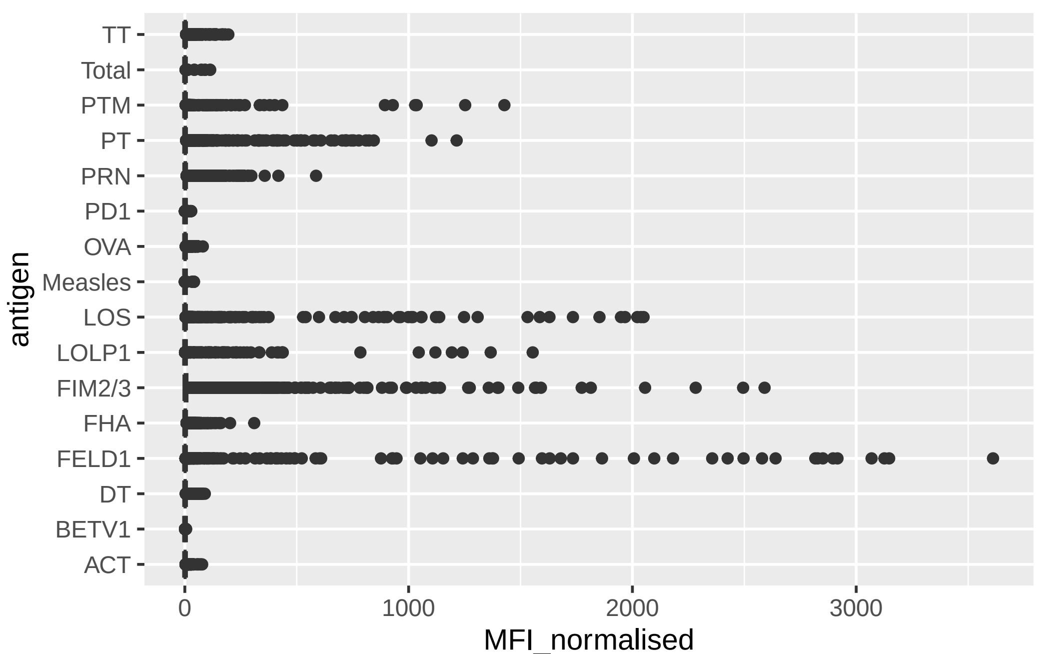
I want a plot of antigen levels across the whole dataset.

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

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



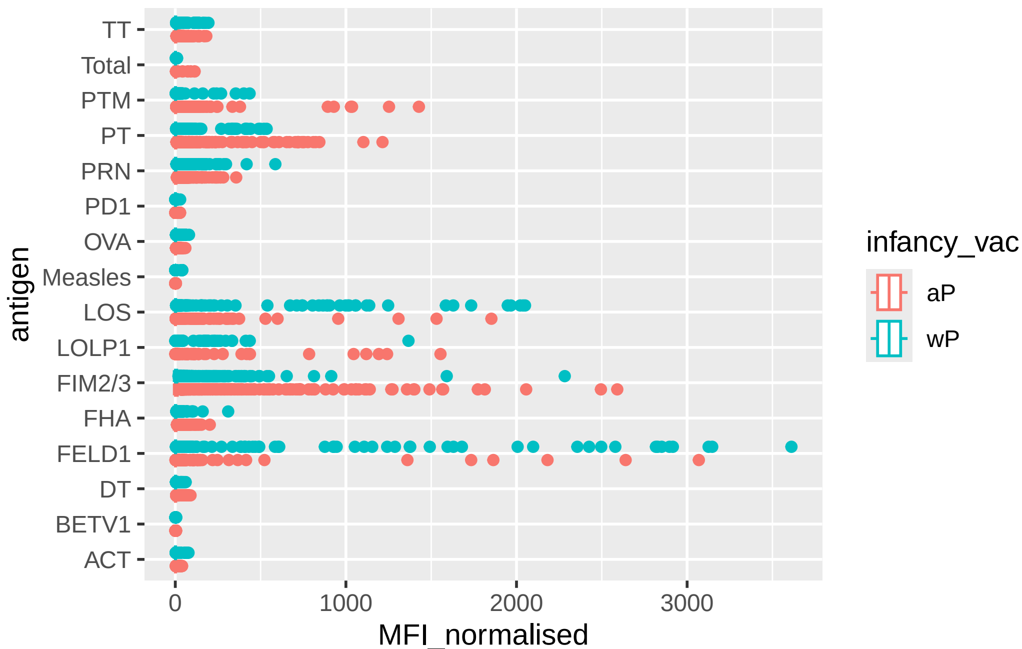

```r
ggplot(abdata, aes(MFI_normalised, antigen))+
  geom_boxplot()
```



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

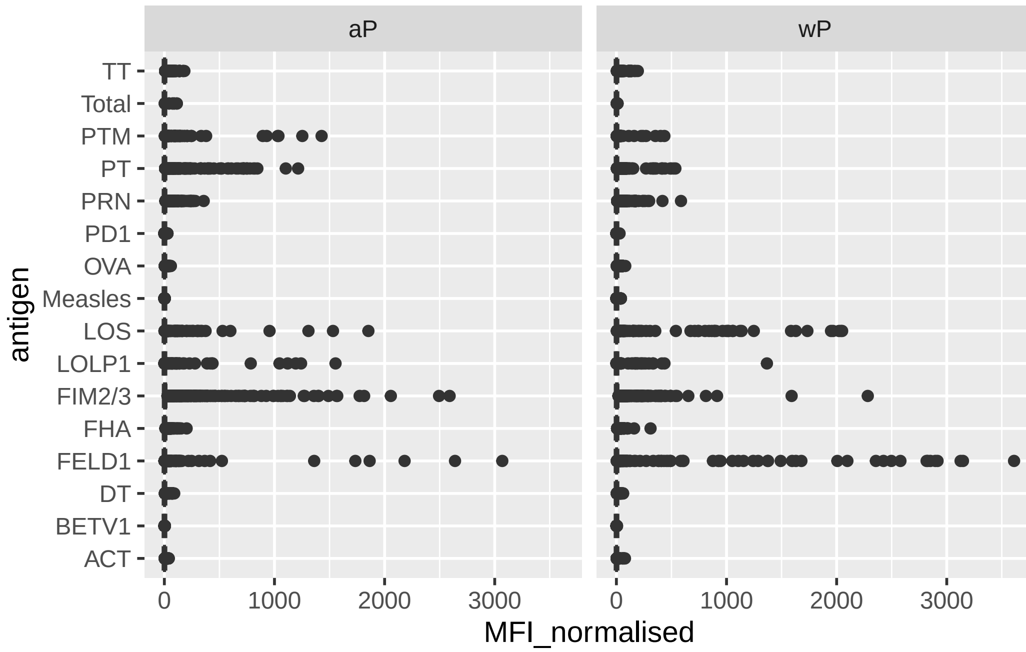
Q. Are there differences at this whole-data level between aP and wP?

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



This is a lot and we're looking at every antibody type.

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



Examine just IgG levels

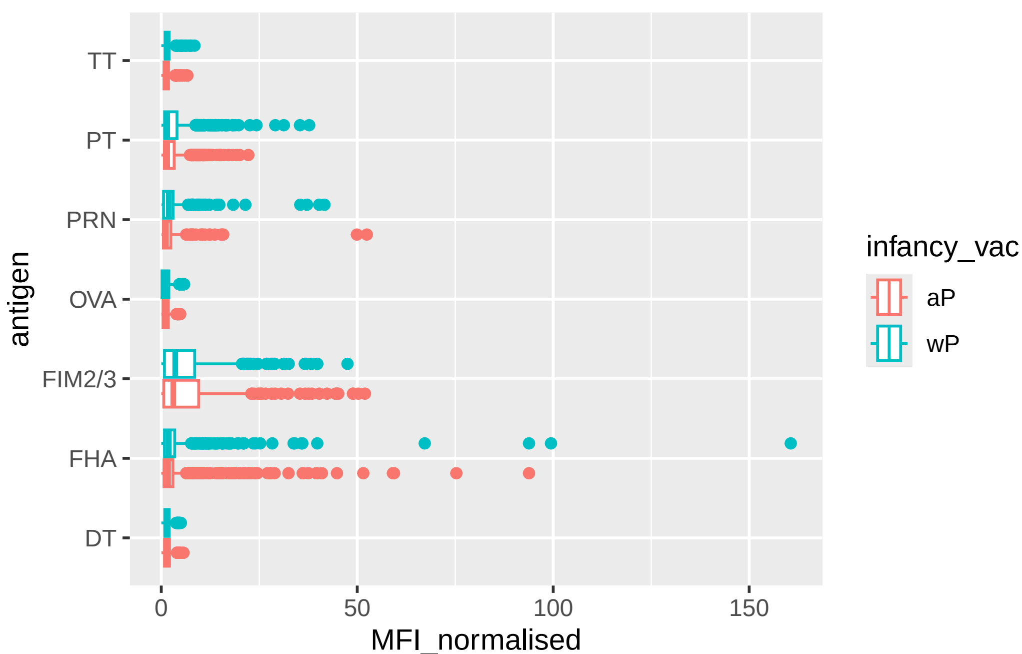
Isolate just isotype IgG.

```
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
```

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



This is still too muddy, across all time points before and after vaccination. Let's dig into a more specific point, time course of IgG isotype PT antigen levels across aP and wP individuals. First we filtered to include the 2021 dataset, then filtered to look at IgG and PT data only. We plotted this data and colored by infancy_vac, with a setup of wP vs aP.

```
abdata.21 <- abdata %>% 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)")
```