Class 19 Mini Project: Investigating Pertussis Resurgence

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Background

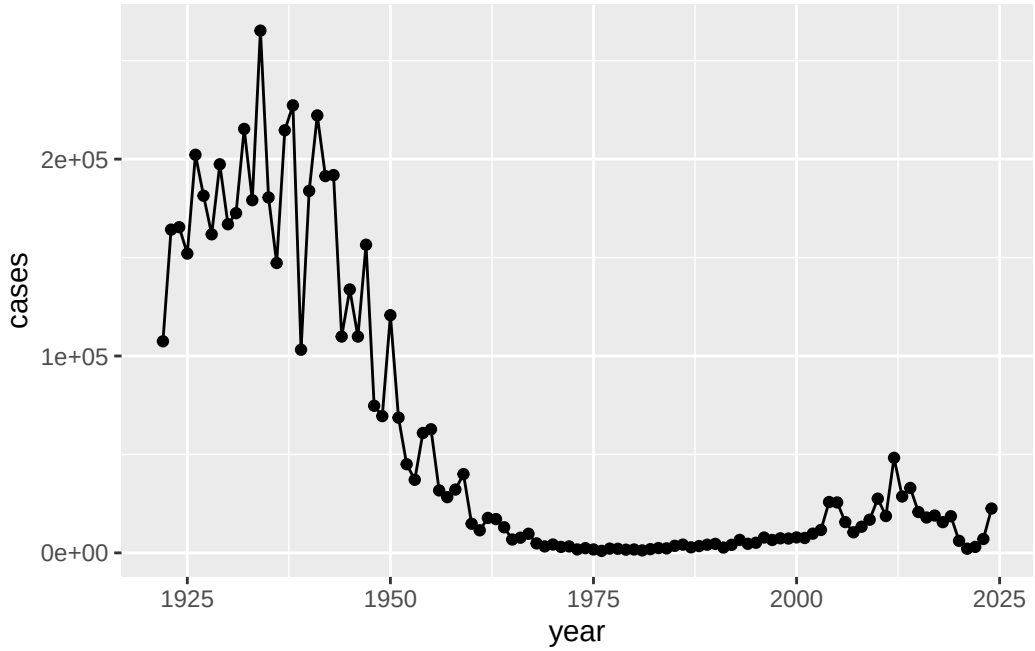
Pertussis is a bacterial lung infection also known as Whooping cough. Let's begin by examining CDC reported case numbers in the US

```
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,2023L, 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,
                                          6124,2116,3044,7063, 22538)
      )
```

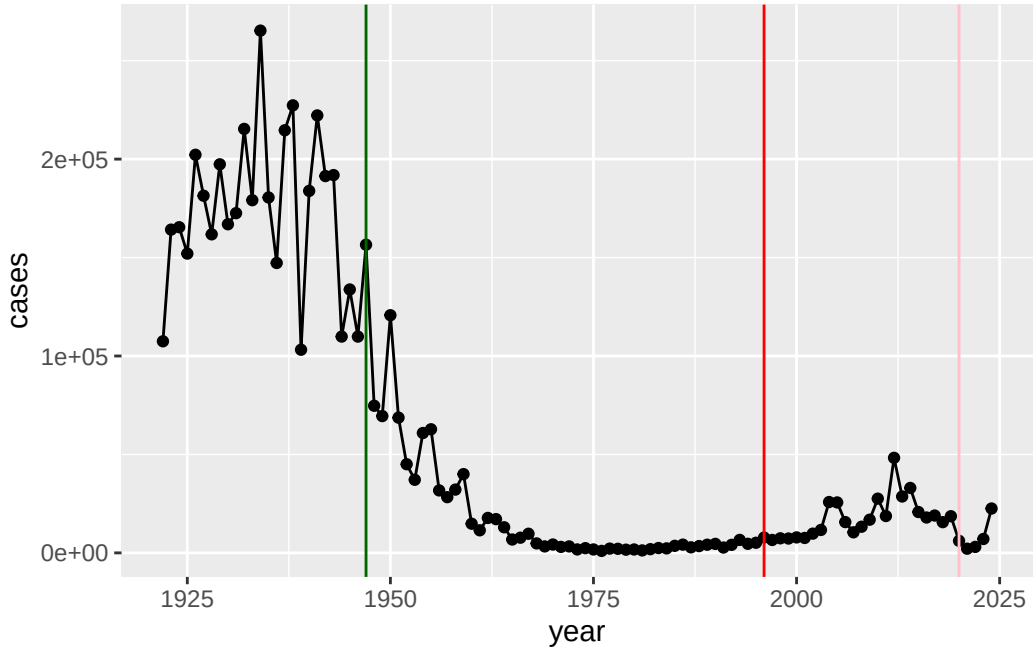
Plot of cases per year for Pertussis in the US

```
library(ggplot2)
ggplot(cdc) +
  aes(year, cases) +
  geom_point() +
  geom_line()
```



Add some major milestone timepoints to out plot:

```
library(ggplot2)
ggplot(cdc) +
  aes(year, cases) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept = 1947, col = "darkgreen") +
  geom_vline(xintercept = 1996, col = "red") +
  geom_vline(xintercept = 2020, col = "pink")
```



The full introduction of the mandatory wP (whole-cell) Pertussis immunization in the mid 1940s lead to a dramatic reduction in case numbers (from over 200,000 to 100s).

The switch to the aP (newer acellular formalization) has steadly increased the amount of cases of pertussis. This vaccine is short lived compared to the wp. However, unlike the wP, the aP's side effects are a lot lower. There was an increase in this vaccine because of all of the wP side effects, lot's of people seemed to be concered about the long-term side effects

The 2020 lock-downs and social distancing measures most likely helped with the decline of the Pertussis bacteria. When people were practicing healthier habits like being 6 feet apart or wearing masks helped with the decline of spread for many other viruses and bacterias.

The CMI-BI project

The mission of CMI-PB is to provide the scientific community with a comprehensive, high-quality and freely accessible resource of Pertussis booster vaccination.

Website: https://www.cmi-pb.org/

They make their data available via JSON format API endpoints- basically the database tables in a key:value type format like "infancy_vac":"wP". To read this we can use the `read.json()` function for the **jsonlite** package. Install with `install.packages("jsonlite")`

```
library(jsonlite)

subject <- read_json(path = "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 "subjects"/individuals are in this dataset?

```
nrow(subject)
```

```
[1] 172
```

Q. How many wP and aP subjects are there?

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

```
aP wP
87 85
```

Q. What is the breakdown by "biological_sex' and"race"?

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

```
Female   Male
   112     60
```

```
table(subject$race)
```

```
                             American Indian/Alaska Native
                                                         1
                                                     Asian
                                                        44
                                 Black or African American
                                                         5
                                           More Than One Race
                                                        19
Native Hawaiian or Other Pacific Islander
                                                         2
                                    Unknown or Not Reported
                                                        21
                                                     White
                                                        80
```

```
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 breakdown is not particulary representative of the US population - thus is a series cavet for this study. However, it is still the largest sample of it's type every assembled.

```
specimen <- read_json("https://www.cmi-pb.org/api/v5_1/specimen", simplifyVector = TRUE)
ab_titer <- read_json("https://www.cmi-pb.org/api/v5_1/plasma_ab_titer", simplifyVector = TRU
```

```
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
```

We need to "join" or link these tables with the `subject` table so we can begin to anaylze this data and know who can give Ab sample was collected for and when.

```
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 let's join the `ab_titer` table to out `meta` table so we have all of the informations about a give Ab measurement

```
ab_data <- inner_join(meta, ab_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 Ab measurements do we have in total

```
nrow(ab_data)
```

```
[1] 61956
```

Q. How many different isotopes (types of Ab) are in the dataset

```
unique(ab_data$isotype)
```

```
[1] "IgE"  "IgG"  "IgG1" "IgG2" "IgG3" "IgG4"
```

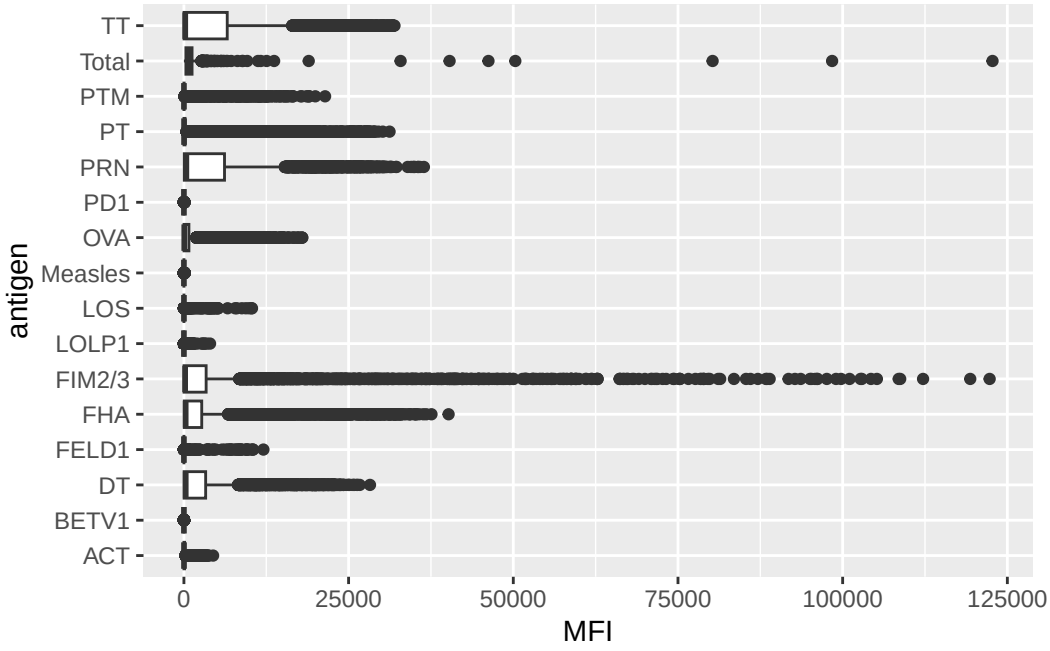
Q. How many different antigens?

```
unique(ab_data$antigen)
```

```
 [1] "Total"   "PT"      "PRN"     "FHA"     "ACT"     "LOS"     "FELD1"
 [8] "BETV1"   "LOLP1"   "Measles" "PTM"     "FIM2/3"  "TT"      "DT"
[15] "OVA"     "PD1"
```

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

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

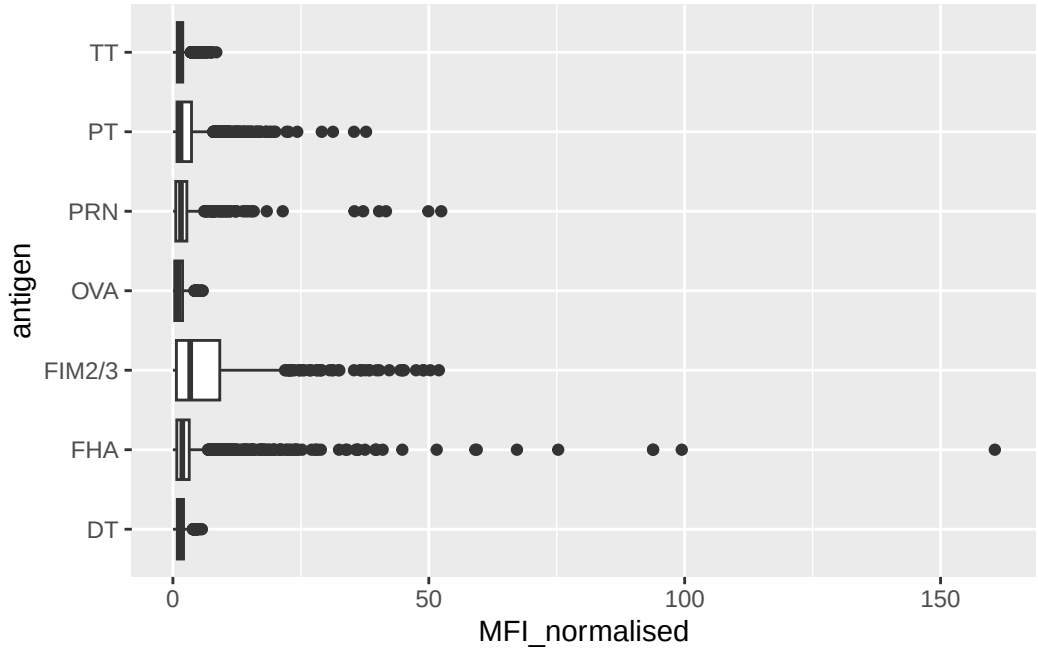


Examine IgG Ab titer levels

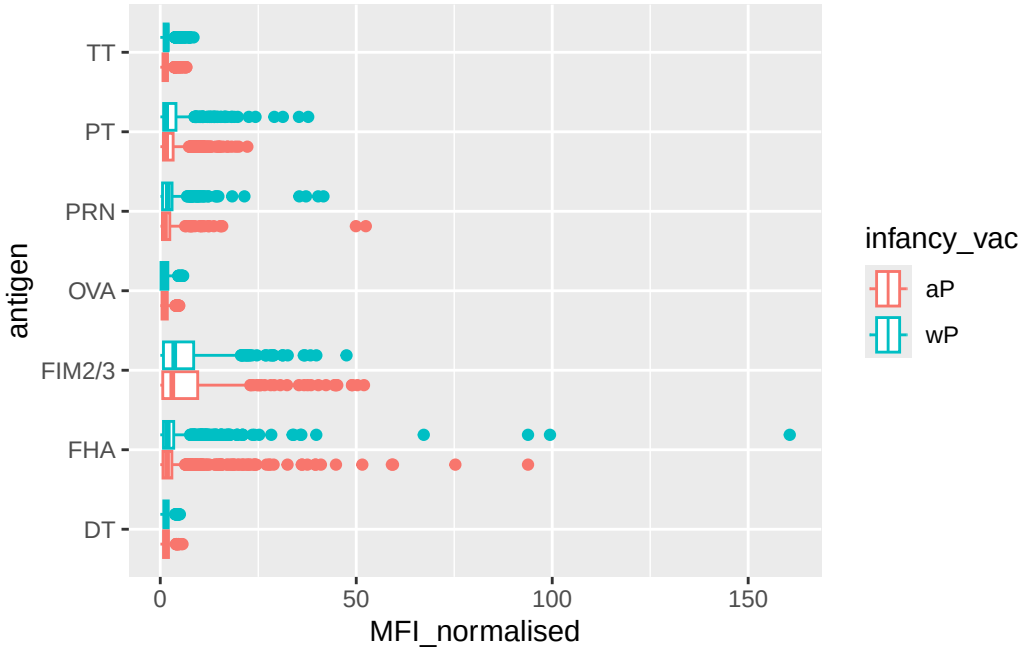
IgG is crucial for long-term immunity and responding to bacterial and viral infections

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

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

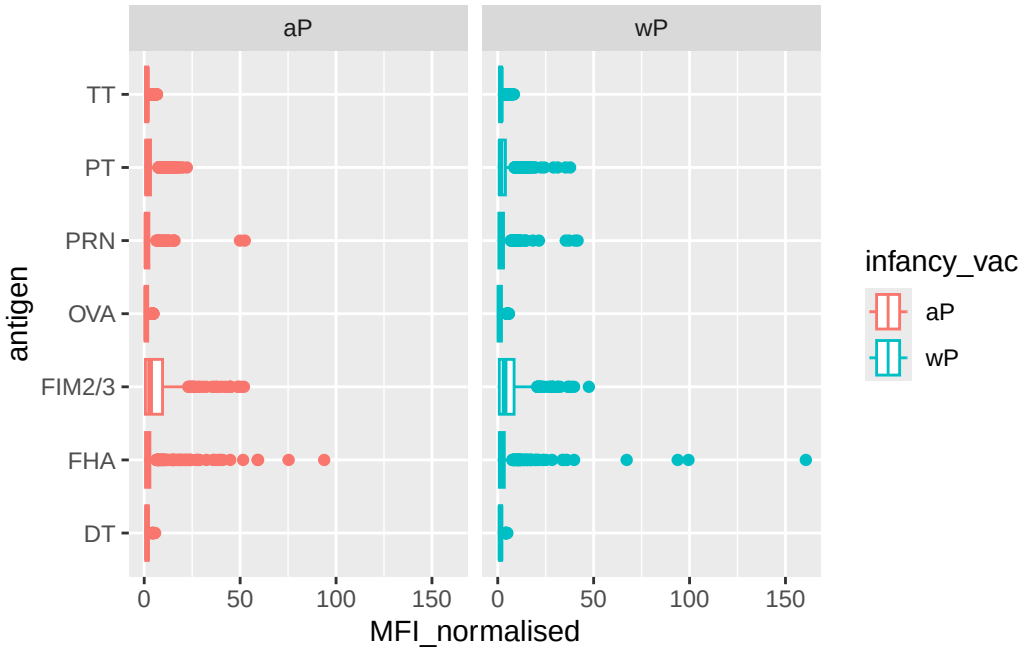



```
ggplot(igg) +
  aes(MFI_normalised, antigen, col= infancy_vac) +
  geom_boxplot()
```



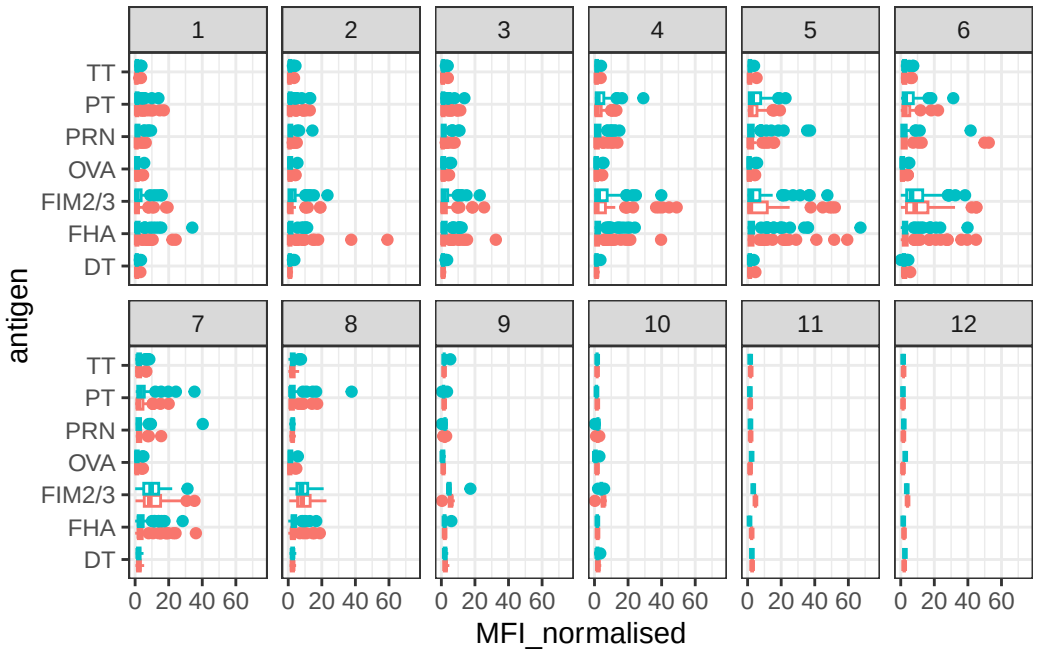
We can "facet" out plot by wP vs aP

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



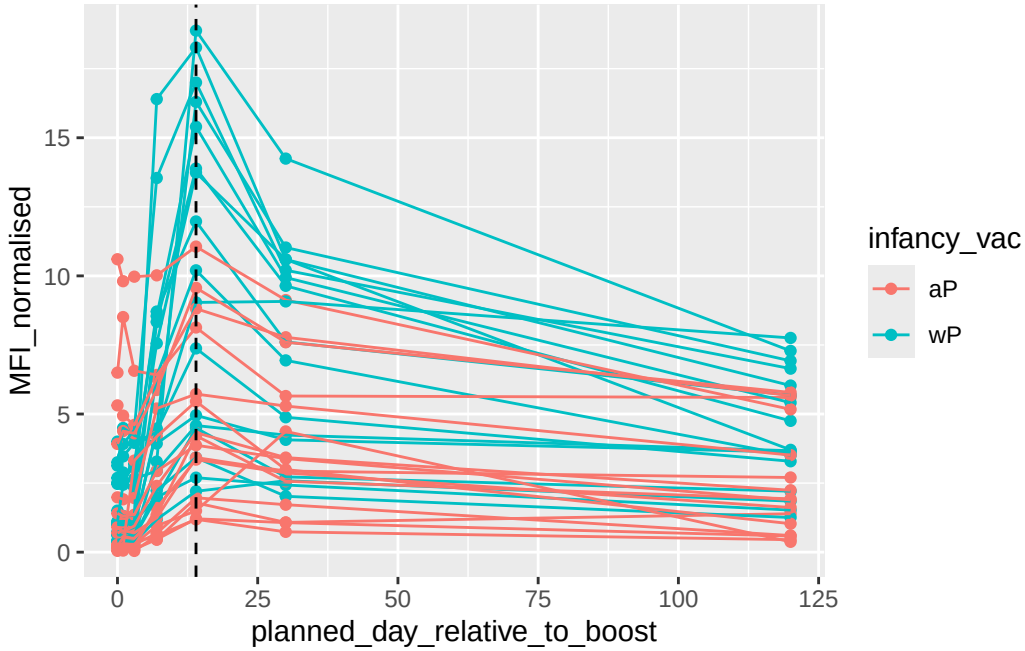

```
ggplot(igg) +
  aes(MFI_normalised, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(visit), nrow=2) +
  xlim(0,75) +
  theme_bw()
```

```
Warning: Removed 5 rows containing non-finite outside the scale range
(`stat_boxplot()`).
```



More advanced anaylsis digging into individual antigen responses over time:

```
filter(igg, antigen=="PT", dataset == "2021_dataset") |>
  ggplot() +
  aes(x=planned_day_relative_to_boost,
        y=MFI_normalised,
        col=infancy_vac,
        group=subject_id) +
    geom_point() +
    geom_line() +
  geom_vline(xintercept= 14, linetype="dashed")
```



This plot shows the time course of Pertussis toxin (PT) antibody responses for a large set of wP (teal color) and aP (red color) individuals. Levels peak at day 14 and are larger in magnitude for wP than aP individuals.

There are lots of cool things to explore in this data-set and we need coding and biology knowlegde to do it effectively - i.e. us!!!