Mini Project: Investigating Pertussis Resurgence

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Pertussis, or whooping cough, is a highly contagous lung infection caused by a bacteria *B. pertussis*.

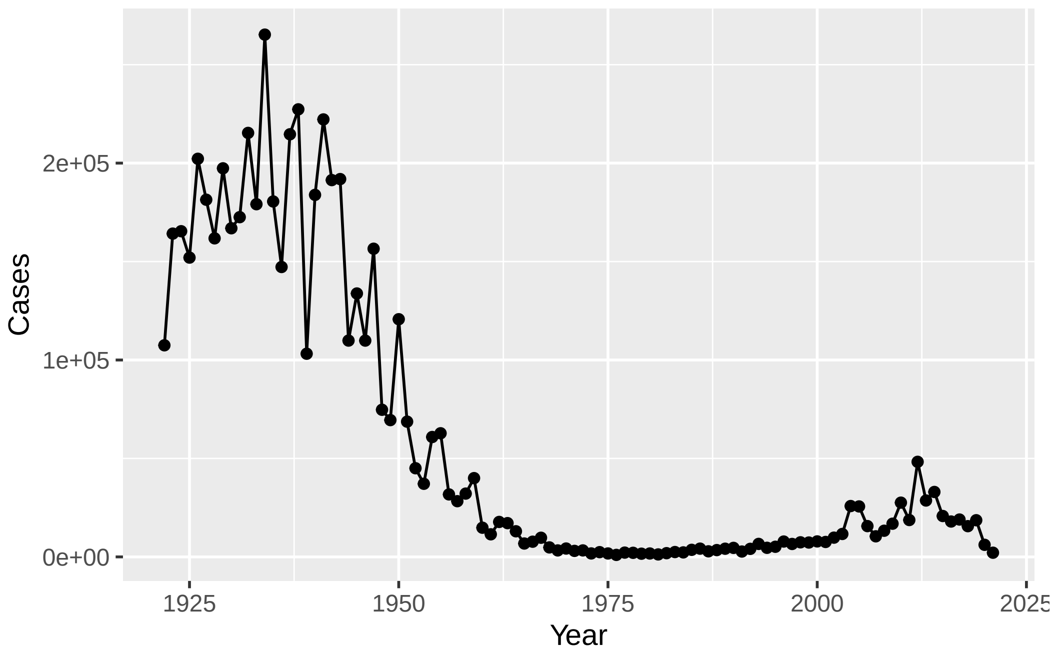
The CDC tracks reported cases in the U.S. since the 1920s

```
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),
                                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)
       )
```

We can now plot the number of reported pertussis cases per year in the U.S.

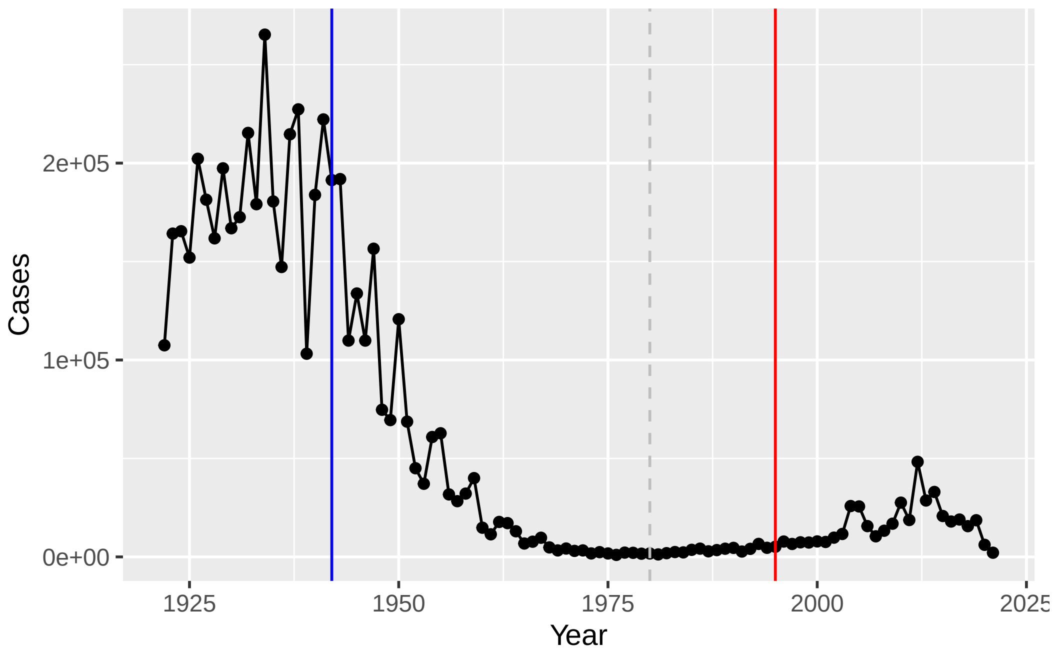
```
library(ggplot2)

ggplot(cdc) +
  aes(Year, Cases) +
  geom_point() +
  geom_line()
```



The first big “whole-cell” pertussis vaccine program started in 1942.

```
ggplot(cdc) +
  aes(Year, Cases) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept = 1942, color = "blue") +
  geom_vline(xintercept = 1980, color = "grey", linetype = 2) +
  geom_vline(xintercept = 1995, color = "red")
```



Somethinf big is happening with perussis cases and big outbreaks are once again a major public health concern!

One of the main hypothesis for the increasing case numbers is wanting vaccine efficiency with the newer aP vaccine.

Enter the CMI-PB project, which is studying this problem on large scale. Let's see what data they have.

Their data is available in JSON format ("key:value" pair style). We will use the "jsonlight" package to read their data.

```
library(jsonlite)

subject <- read_json("https://www.cmi-pb.org/api/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 may aP and wP infancy vaccinated subjects are in the dataset?

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

```
aP wP 
47 49 
```

> Q5. How many Male and Female subjects/patients are in the dataset?

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

```
Female   Male 
    66     30 
```

> Q6. What is the breakdown of race and biological sex (e.g. number of Asian females, White males etc…)?

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

```
            American Indian/Alaska Native 
                                        1 
                                    Asian 
                                       27 
                Black or African American 
                                        2 
                       More Than One Race 
                                       10 
Native Hawaiian or Other Pacific Islander 
```

```
                                       2 
                  Unknown or Not Reported 
                                      14 
                                   White 
                                      40 
```

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

```
                                            Female Male
  American Indian/Alaska Native                  0    1
  Asian                                         18    9
  Black or African American                      2    0
  More Than One Race                             8    2
  Native Hawaiian or Other Pacific Islander      1    1
  Unknown or Not Reported                       10    4
  White                                         27   13
```

Now let's read some more database tables from CMI-PB:

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

```
  specimen_id subject_id actual_day_relative_to_boost
1           1          1                           -3
2           2          1                          736
3           3          1                            1
4           4          1                            3
5           5          1                            7
6           6          1                           11
  planned_day_relative_to_boost specimen_type visit
1                             0         Blood     1
2                           736         Blood    10
3                             1         Blood     2
4                             3         Blood     3
5                             7         Blood     4
6                            14         Blood     5
```

I want to "join" (a.k.a "merge"/link/etc.) the `subject` and `specimen` tables together. I will use the **dplyr** package for this.

```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                          736                           736         Blood
3                            1                             1         Blood
4                            3                             3         Blood
```

```
5                            7                             7         Blood
6                           11                            14         Blood
  visit
1     1
2    10
3     2
4     3
5     4
6     5
```

```
ab <- read_json("http://cmi-pb.org/api/ab_titer", simplifyVector = TRUE)
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
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
```

Now I can join the `meta` that we made above and contains all info about the subjects and specimens with this `ab` data

```
abdata <- inner_join(meta, ab)
```

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

```
dim(abdata)
```

```
[1] 32675    20
```

Q11. How many specimens (i.e. entries in abdata) do we have for each isotype?

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

```

 IgE  IgG IgG1 IgG2 IgG3 IgG4 
6698 1413 6141 6141 6141 6141 
```

> . Q12. What do you notice about the number of visit 8 specimens compared to other visits?

```
table(abdata$visit)
```

```

   1    2    3    4    5    6    7    8 
5795 4640 4640 4640 4640 4320 3920   80 
```

There are way less visit 8 specimens because the project is still ongoing and we do not have the data for all individuals yet.

Examine IgG1 Ab titer levels

We will use the `filter` function from dplyr to focus on just IgG1 isotype and visit 1 to 7 (i.e. exclude visit 8 as there are not many specimens there yet).

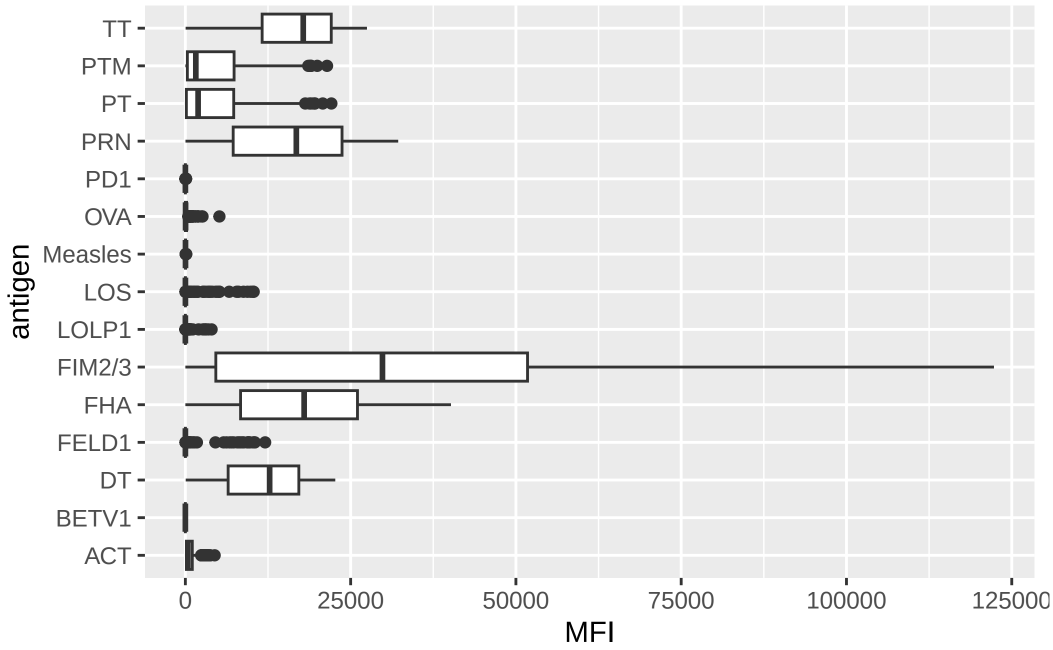
```
ig1 <- filter(abdata, isotype == "IgG1", visit!=8)
head(ig1)
```

```
  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    IgG1                TRUE     ACT 274.355068      0.6928058 IU/ML
2     1    IgG1                TRUE     LOS  10.974026      2.1645083 IU/ML
3     1    IgG1                TRUE   FELD1   1.448796      0.8080941 IU/ML
4     1    IgG1                TRUE   BETV1   0.100000      1.0000000 IU/ML
5     1    IgG1                TRUE   LOLP1   0.100000      1.0000000 IU/ML
6     1    IgG1                TRUE Measles  36.277417      1.6638332 IU/ML
  lower_limit_of_detection
1                 3.848750
2                 4.357917
3                 2.699944
4                 1.734784
5                 2.550606
6                 4.438966
```

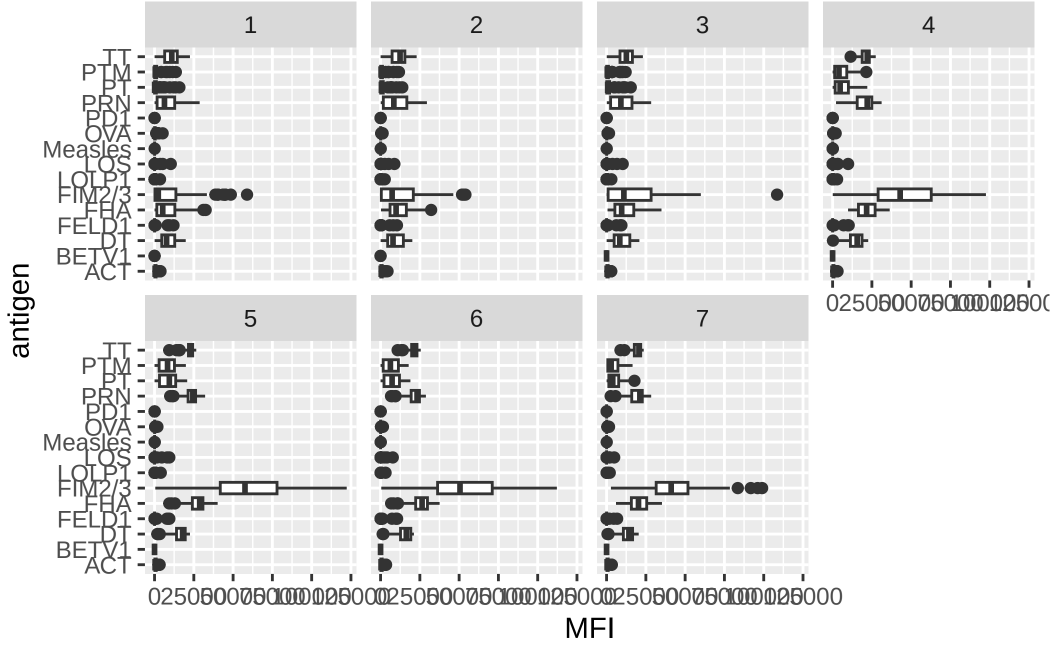
Box plot of antigen leves over time.

```
ggplot(ig1) +
  aes(MFI, antigen) +
  geom_boxplot()
```



and facet by visit:

```
ggplot(ig1) +
  aes(MFI, antigen) +
  geom_boxplot() +
  facet_wrap(vars(visit), nrow=2)
```

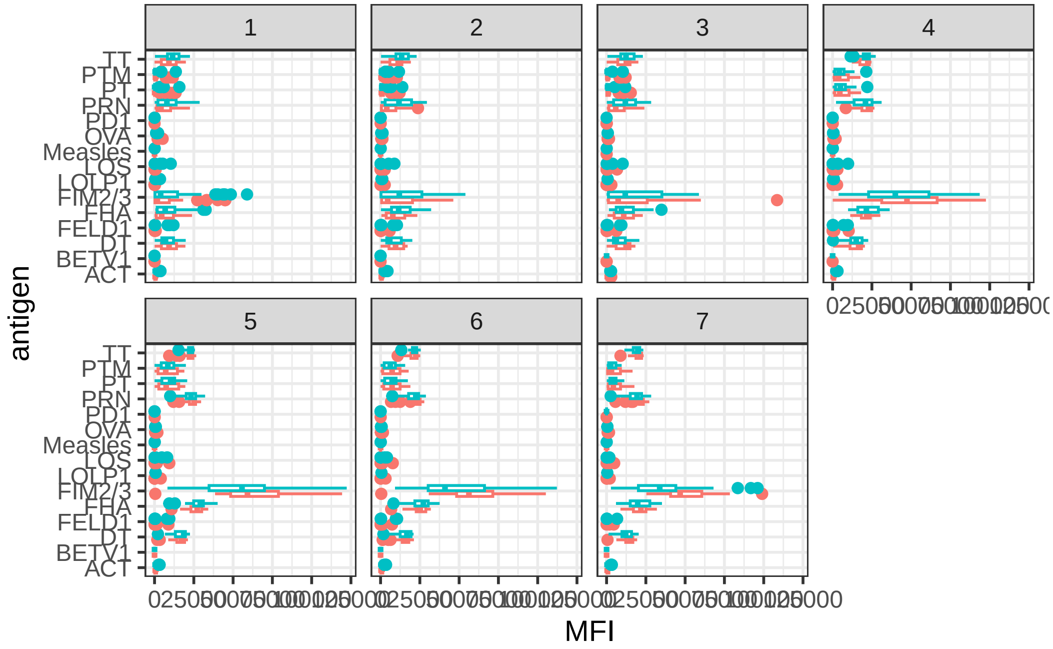


Clearly FIM2/3 changes. This is “Fimbrial protein” that makes the bacteria pilus and is involved in cell adhesion.

PT Pertussis Toxin

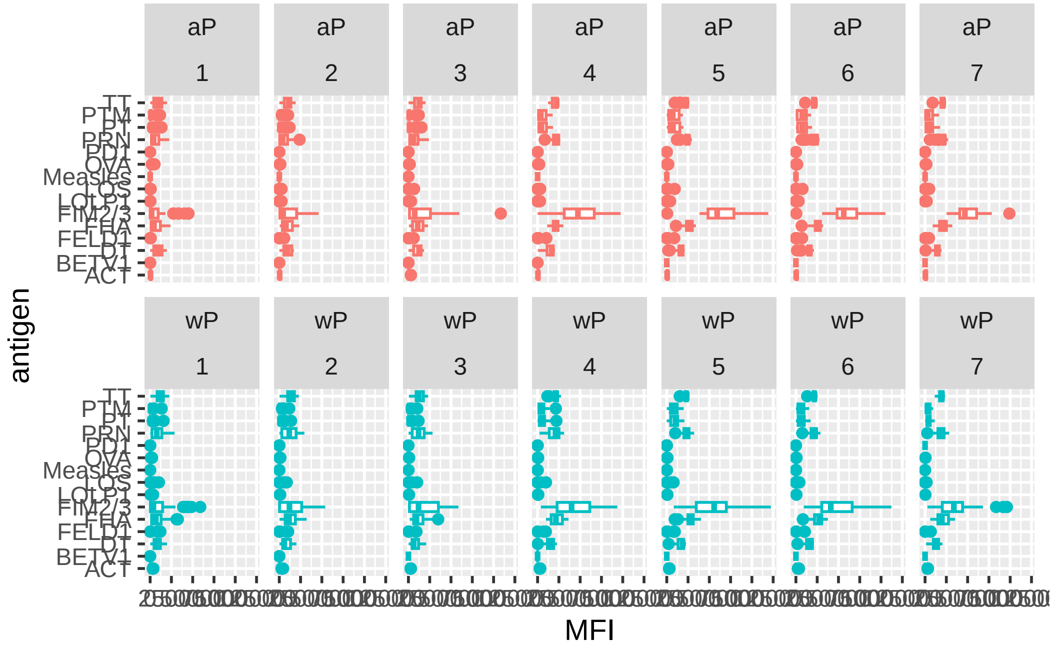
FHA is Filamentous hemagglutinin surface associated adherence protein of bacteria pertussis, which is a component of some new acellular pertussis vaccines.

```r
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(visit), nrow=2) +
  theme_bw()
```



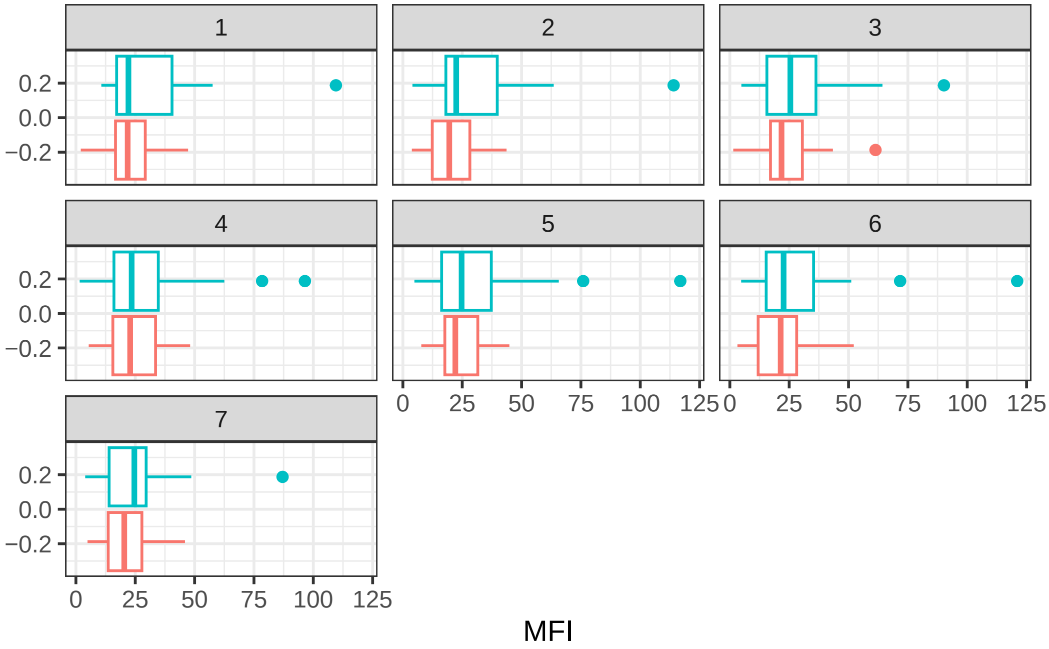
Another version of this plot adding `infanvy_vac` to the faceting:

```
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(infancy_vac, visit), nrow=2)
```



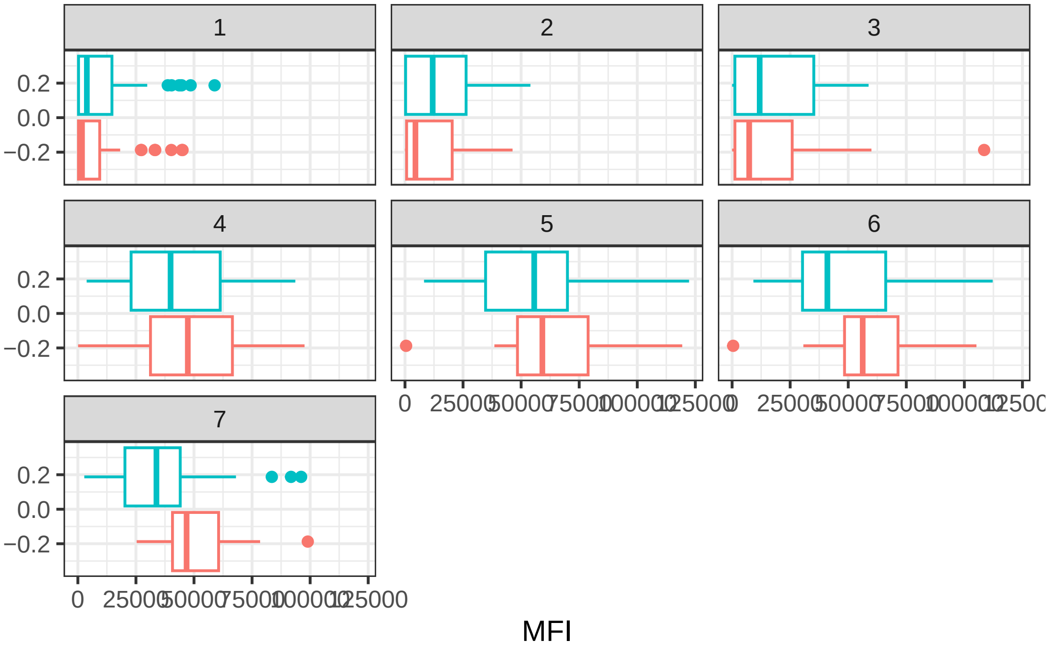
Measles antigen levels per visit (aP red, wP teal):

```
filter(ig1, antigen=="Measles") %>%
  ggplot() +
  aes(MFI, col=infancy_vac) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



FIM2/3 antigen levels per visit (aP red, wP teal):

```
filter(ig1, antigen== "FIM2/3") %>%
  ggplot() +
  aes(MFI, col=infancy_vac) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(visit)) +
  theme_bw()
```


1
2
3
4
5
6
7
0.2
0.0
−0.2
0
25000
50000
75000
100000
125000
MFI