Class17

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

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

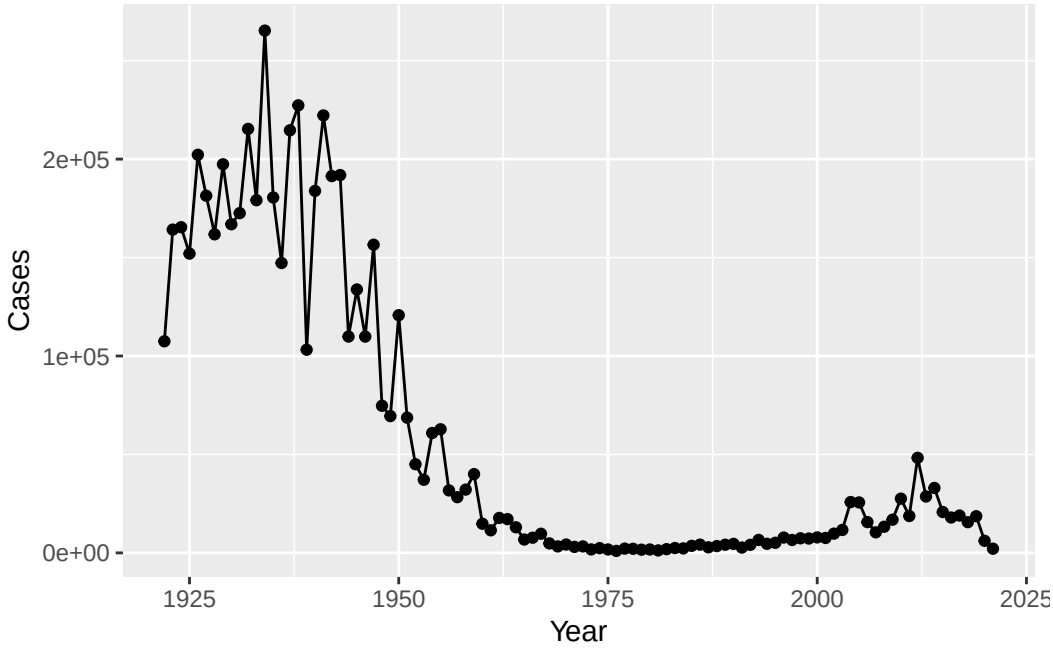
```
cdc <- data.frame(
                                Year = c(1922L,1923L,1924L,1925L,
                                         1926L,1927L,1928L,1929L,1930L,1931L,
                                         1932L,1933L,1934L,1935L,1936L,
                                         1937L,1938L,1939L,1940L,1941L,1942L,
                                         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)
      )
```

Q1.

```
library(ggplot2)

ggplot(cdc) +
  aes(Year, Cases) +
  geom_point() +
  geom_line() +
  labs(x="Year", y="Cases")
```

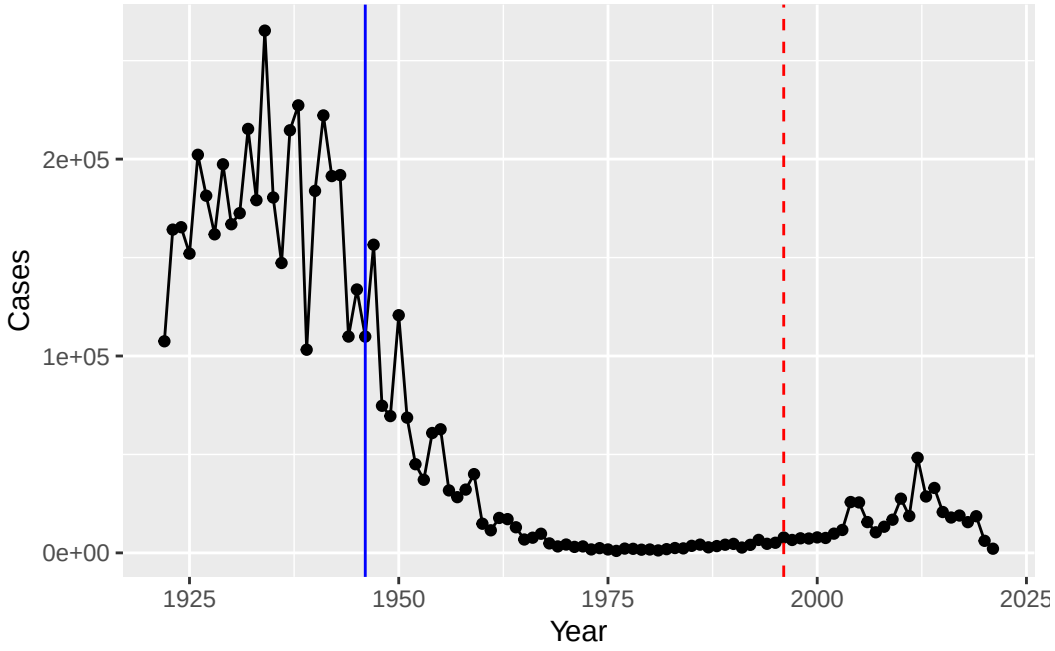


The first big "whole-cell" pertussi vaccine program started in 1942

Q2.

```
library(ggplot2)

ggplot(cdc) +
  aes(Year, Cases) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept=1946, col="blue") +
  geom_vline(xintercept=1996, col="red", linetype=2)
```



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

We could possibly have a better system of detection of the disease, parents may not vaccinate children because they think that vaccinations for TDaP and other vaccines bring neurological diseases, or the bacterium became stronger and the vaccine is no longer effective to destroy it.

Something bi is happening witgh pertussis cases and big outbreaks are once againa a major public health concern! BUGGER

One of the main hypothesis for the increasing case numbers is waning vaccine efficacy 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, 3)
```

```
  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
  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
```

Q4. How many 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?

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

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

```
Female   Male
    66     30
```

```
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
```

```
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
```

Let's read more database tables from CMI-PB:

```
specimen <- read_json("https://www.cmi-pb.org/api/specimen",
                      simplifyVector = TRUE)
head(specimen, 3)
```

```
  specimen_id subject_id actual_day_relative_to_boost
1           1          1                           -3
2           2          1                          736
3           3          1                            1
  planned_day_relative_to_boost specimen_type visit
1                             0         Blood     1
2                           736         Blood    10
3                             1         Blood     2
```

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

```
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                          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("https://www.cmi-pb.org/api/ab_titer",
                        simplifyVector = TRUE)
```

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)`
```

```
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
```

```
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 vsiit 8 specimens because the project is still ongoing and we have not got that data for all individuals yet.

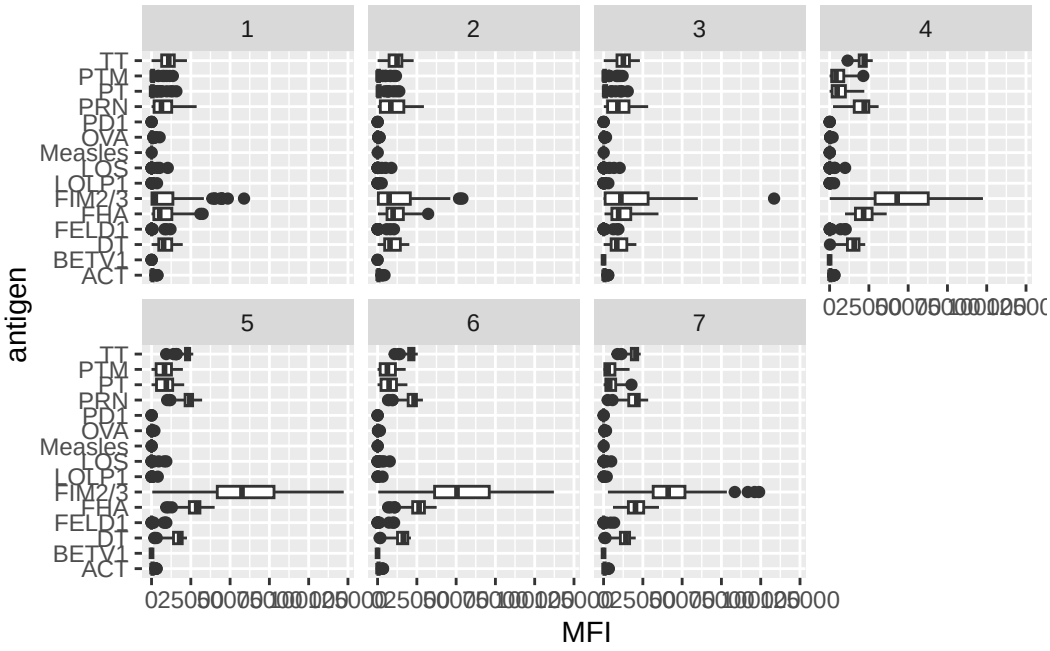
##Examine IgG1 Ab titer levels

We will use the filter() function from dplyr to focus on just IgG1 isotype and visits 1 to 7 (i.e. examine our)

```
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
```

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

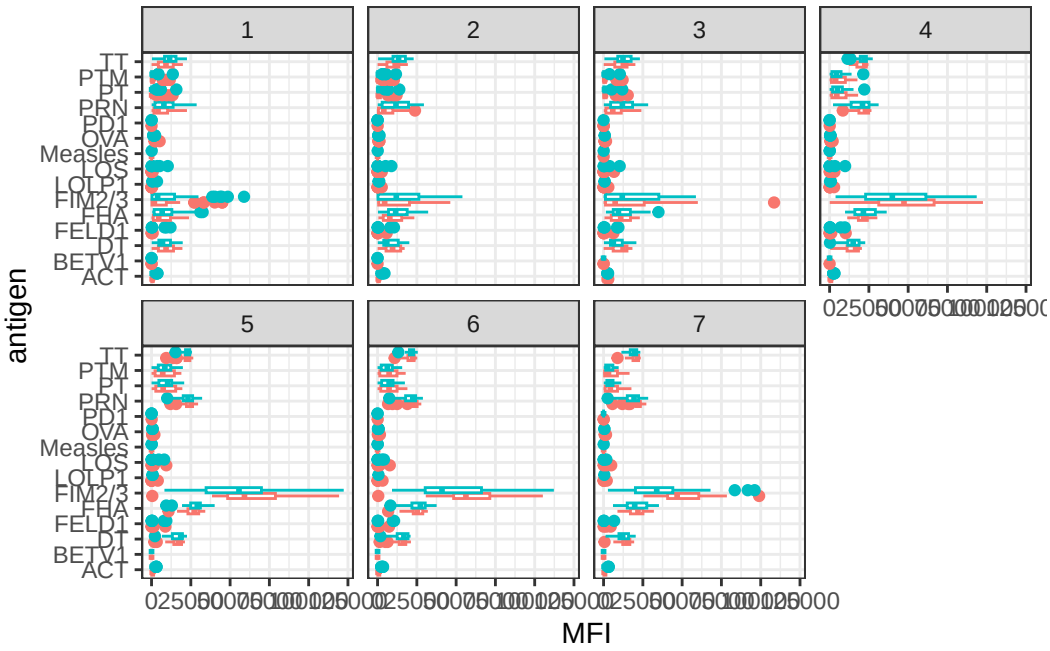


Q14. What antigens show differences in the level of IgG1 antibody titers recognizing them over time? Why these and not others?

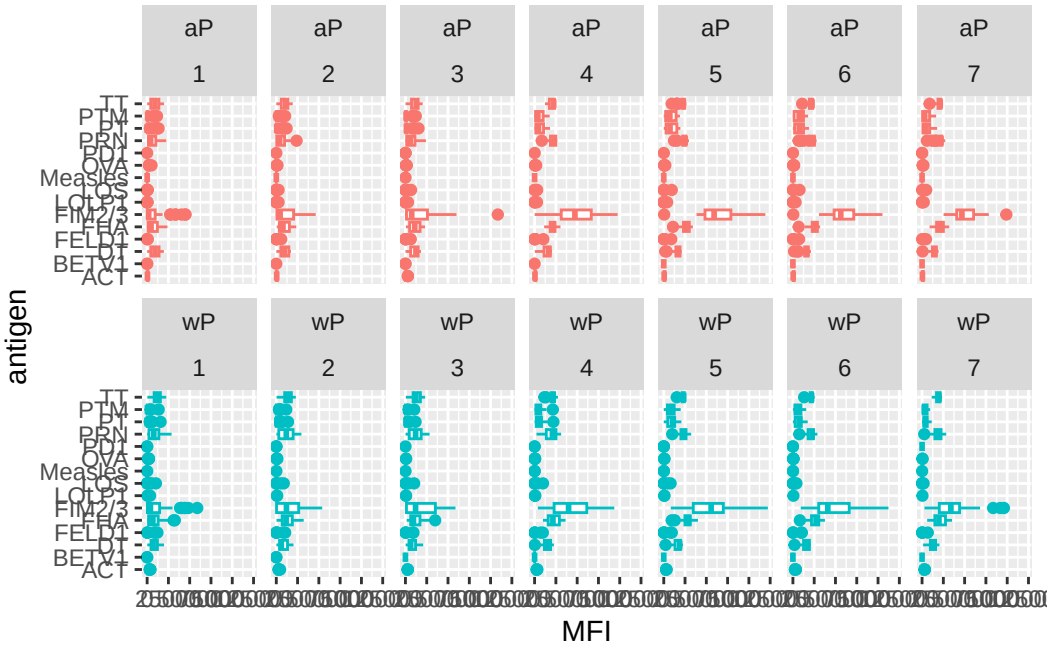
FIM2/3 show differences in MFI. This is "Fimbrial protein" that makes the backteria pilus and is involved in cell adhesion.

PT Pertosuss Toxin FHA Filementous Hemagluttinin

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

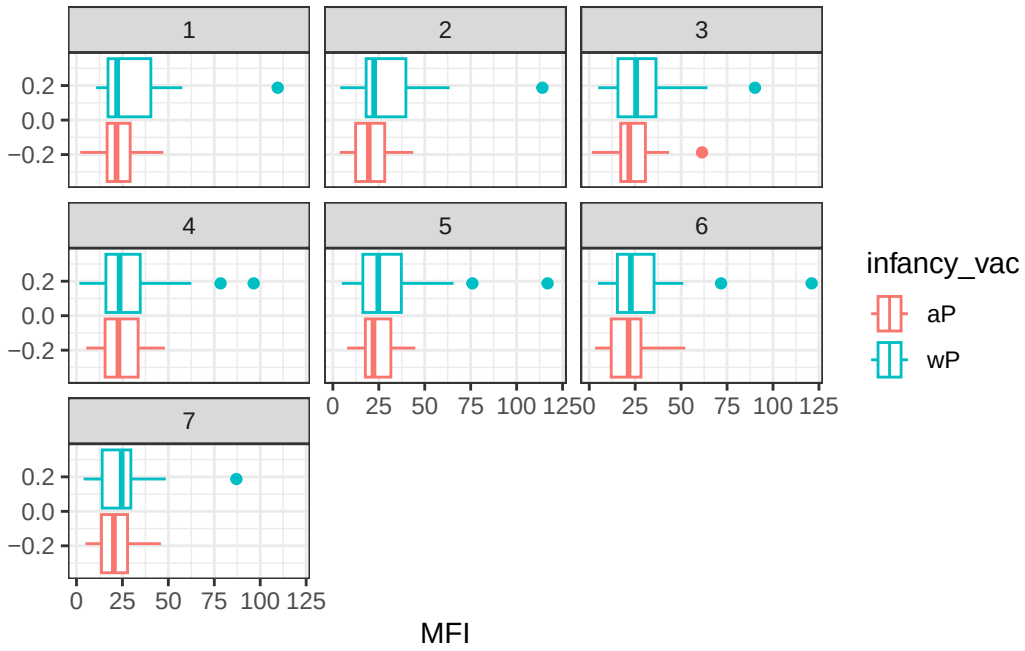



```
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(infancy_vac, visit), nrow=2)
```

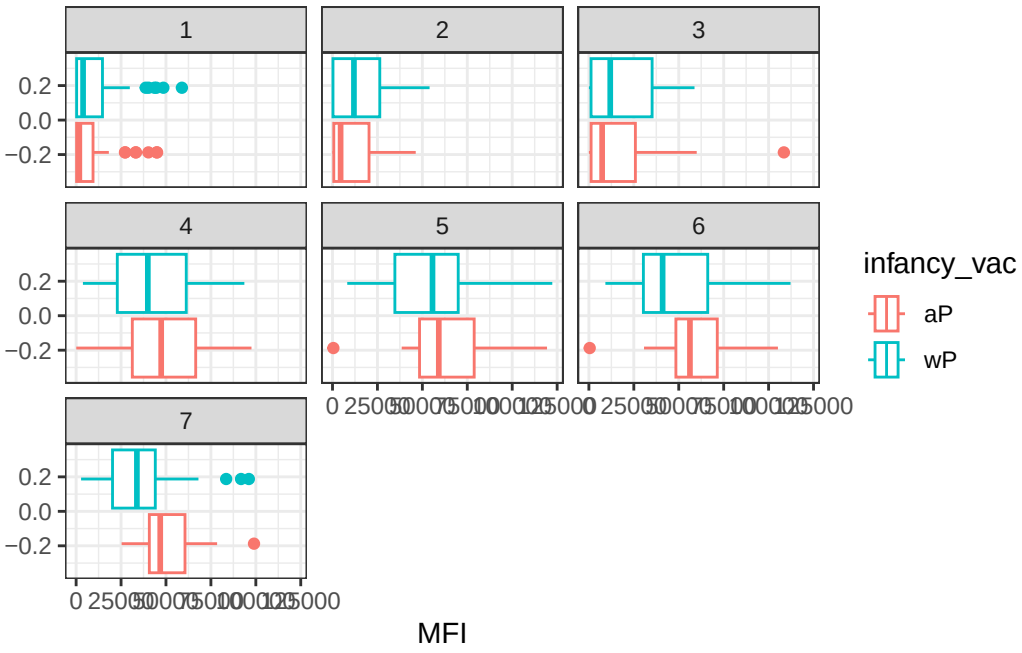


Q15. Filter to pull out only two specific antigens for analysis and create a boxplot for each. You can chose any you like. Below I picked a "control" antigen ("Measles", that is not in our vaccines) and a clear antigen of interest ("FIM2/3", extra-cellular fimbriae proteins from B. pertussis that participate in substrate attachment).

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




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



FIM2/3 MFI levels rise more in comparison to Measles antigen in both aP and wP subjects.