class17

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

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

```
cdc <- data.frame(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),
                                 No..Reported.Pertussis.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.

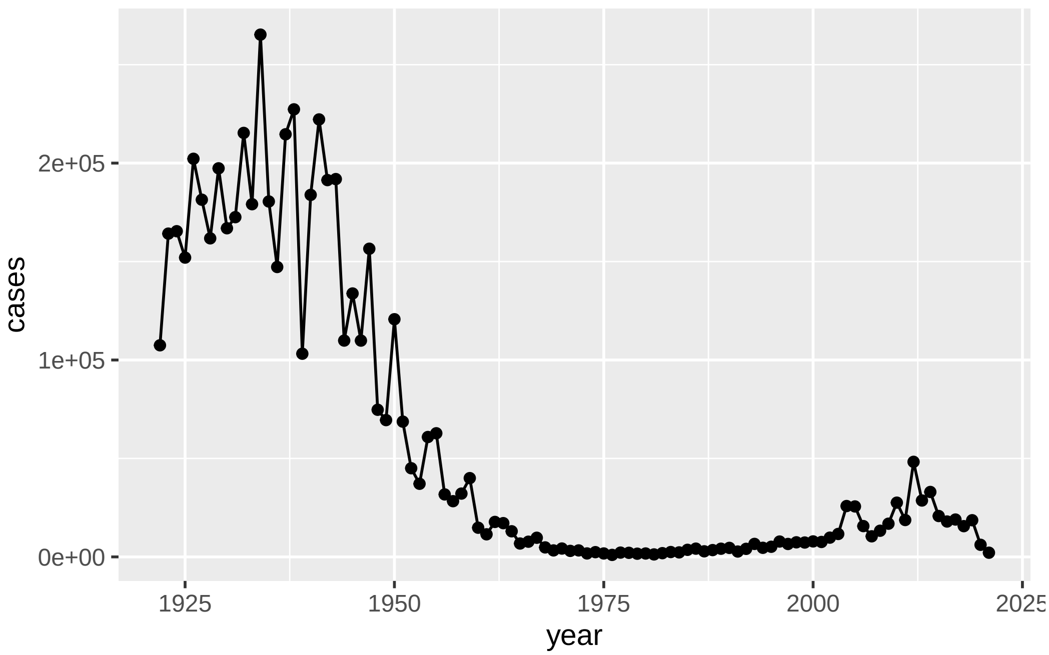
```
library(ggplot2)

ggplot(cdc) +
  aes(cdc$Year, cdc$No..Reported.Pertussis.Cases)+
  geom_point()+
  geom_line()+
  labs(x="year", y="cases")
```

```
Warning: Use of `cdc$Year` is discouraged.
i Use `Year` instead.
```

```
Warning: Use of `cdc$No..Reported.Pertussis.Cases` is discouraged.
i Use `No..Reported.Pertussis.Cases` instead.
```

```
Warning: Use of `cdc$Year` is discouraged.
i Use `Year` instead.
```

```
Warning: Use of `cdc$No..Reported.Pertussis.Cases` is discouraged.
i Use `No..Reported.Pertussis.Cases` instead.
```



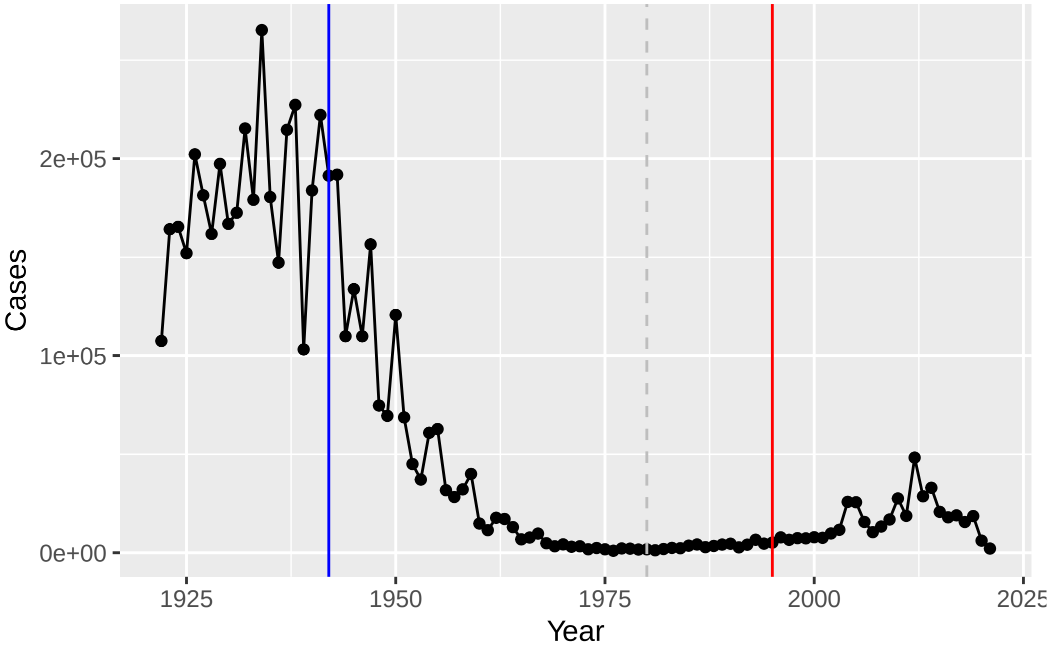
The first big “Whole-cell” pertussis vaccine was introduced in 1942

```
colnames(cdc) <- c('Year', 'Cases')

head(cdc)
```

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

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

```
Warning: Use of `cdc$Year` is discouraged.
i Use `Year` instead.

Warning: Use of `cdc$Cases` is discouraged.
i Use `Cases` instead.

Warning: Use of `cdc$Year` is discouraged.
i Use `Year` instead.

Warning: Use of `cdc$Cases` is discouraged.
i Use `Cases` instead.
```



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

One of the main hypothesis for the increasing case numbers is waning vaccine efficacy with the newer vaccine.

Enter the CMI-PB project, which is studing this problem on a 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 
```

```
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 data tabels from CMI-PB:

```
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.

```
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
```

```
colnames(subject)
```

```
[1] "subject_id"     "infancy_vac"    "biological_sex" "ethnicity"
[5] "race"           "year_of_birth"  "date_of_boost"  "dataset"
```

```
colnames(specimen)
```

```
[1] "specimen_id"                  "subject_id"
[3] "actual_day_relative_to_boost" "planned_day_relative_to_boost"
[5] "specimen_type"                "visit"
```

```
colnames(meta)
```

```
 [1] "subject_id"                     "infancy_vac"
 [3] "biological_sex"                 "ethnicity"
 [5] "race"                           "year_of_birth"
 [7] "date_of_boost"                  "dataset"
 [9] "specimen_id"                    "actual_day_relative_to_boost"
[11] "planned_day_relative_to_boost" "specimen_type"
[13] "visit"
```

```
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 `meta` that we made above and contained all info about the subject 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 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 isotope and visits 1 to 7 (i.e. exclude visit 8 as there are not as many specimen there yet).

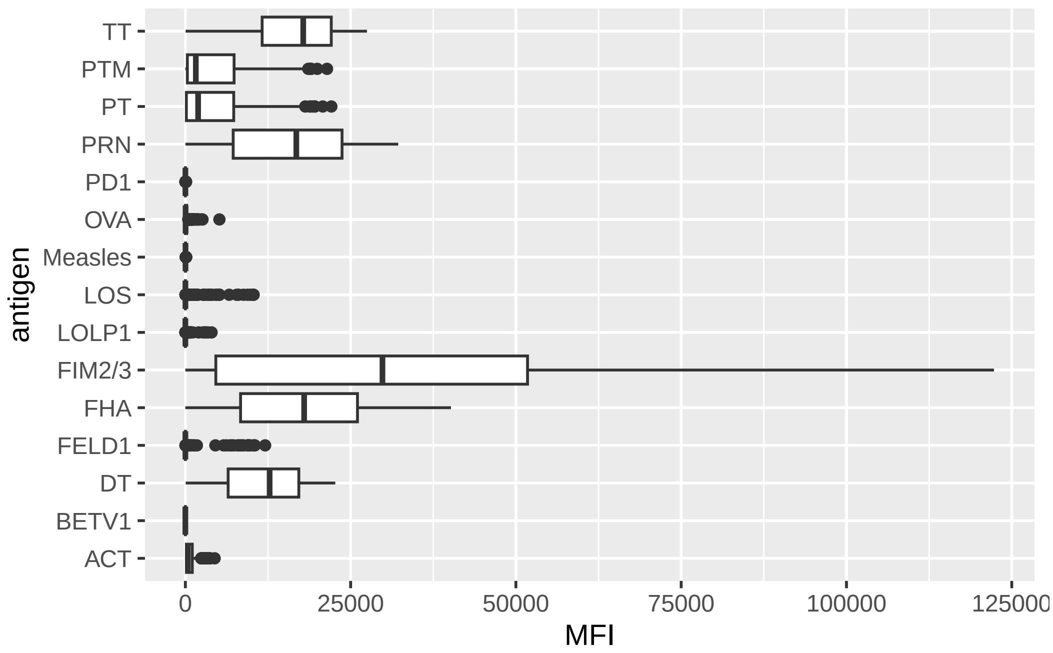
```
ig1 <- filter(abdata, isotype == "IgG1", visit!=8)
head(ig1)
```

```
  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
```

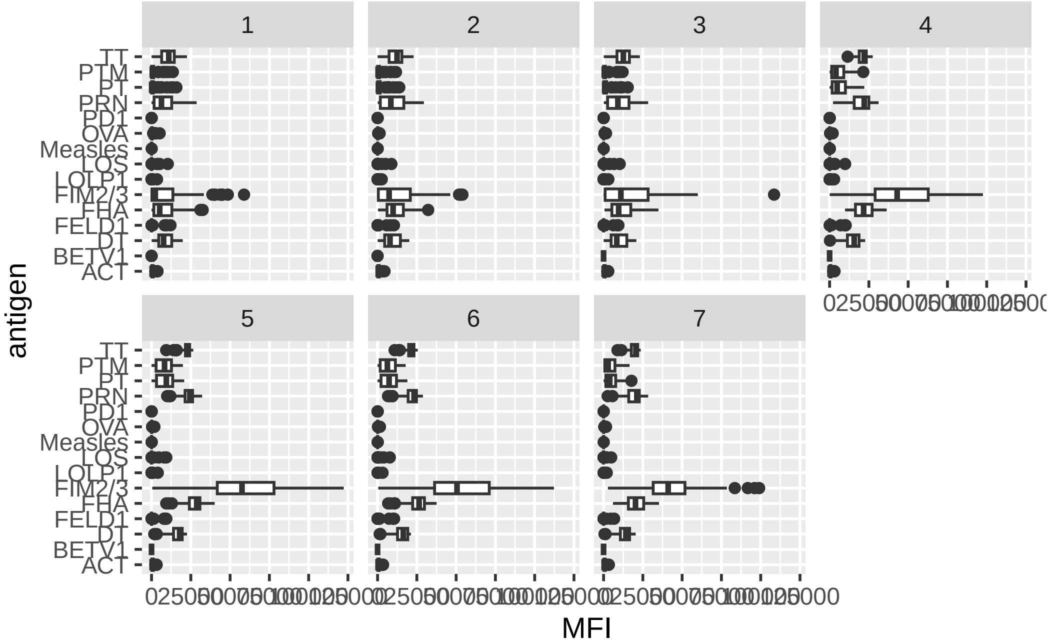
Q13. Complete the following code to make a summary boxplot of Ab titer levels for all antigens:

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



and facet by visit

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

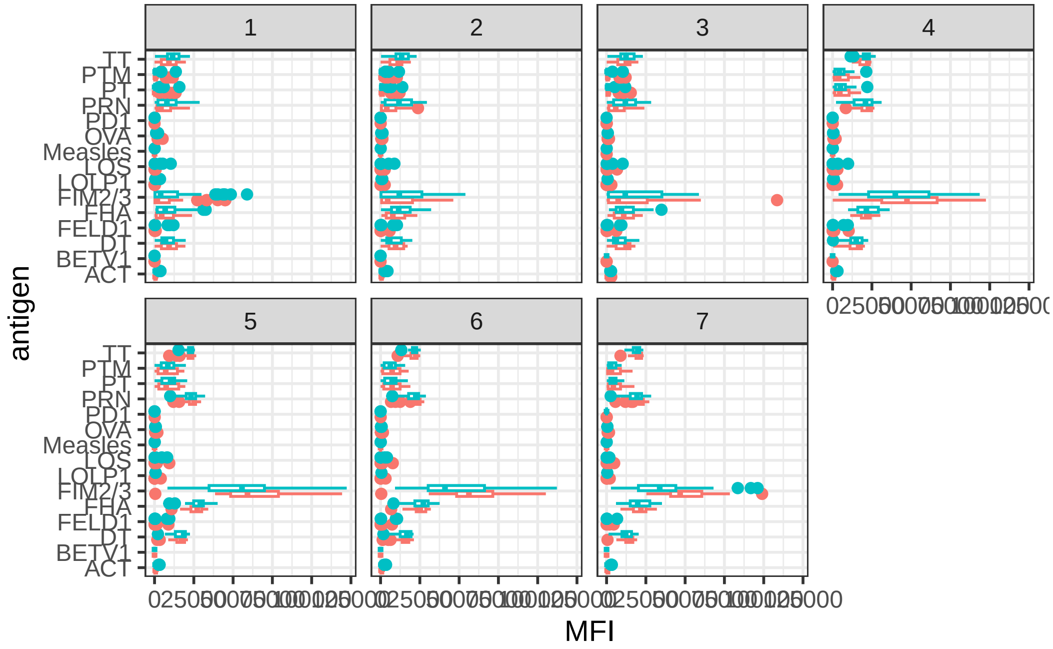


Clearly FIM2/3 changes. This is “Fimbrial protein” that makes the bacteria pilus and is involved in cell adhesion.

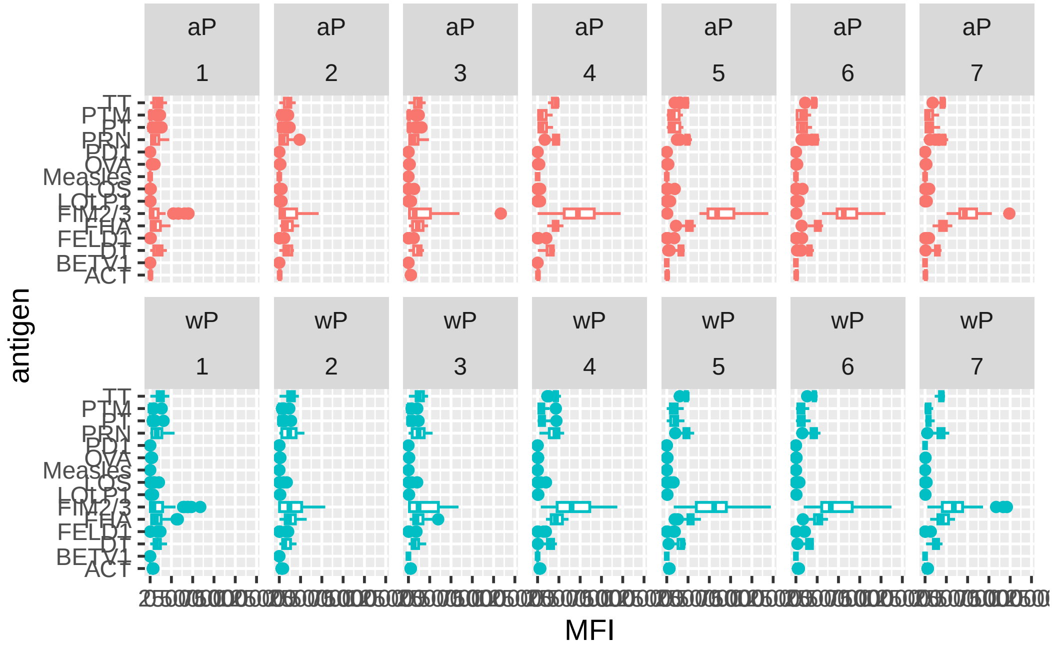
PT Pertussis toxin

FHA is Filamentous hemagglutain

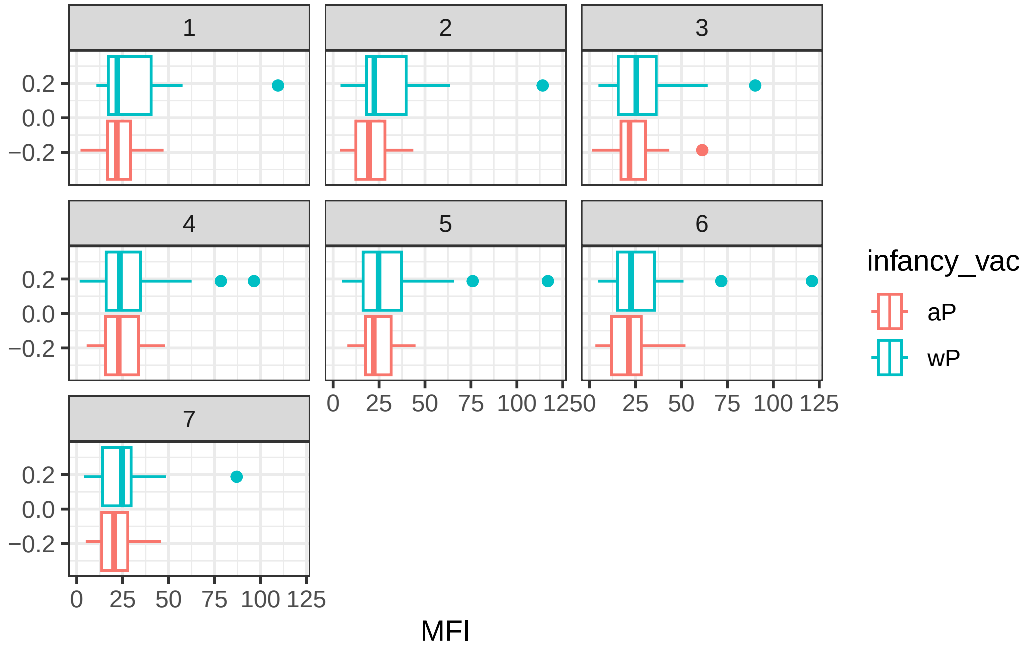
```
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(visit), nrow=2) +
  theme_bw()
```



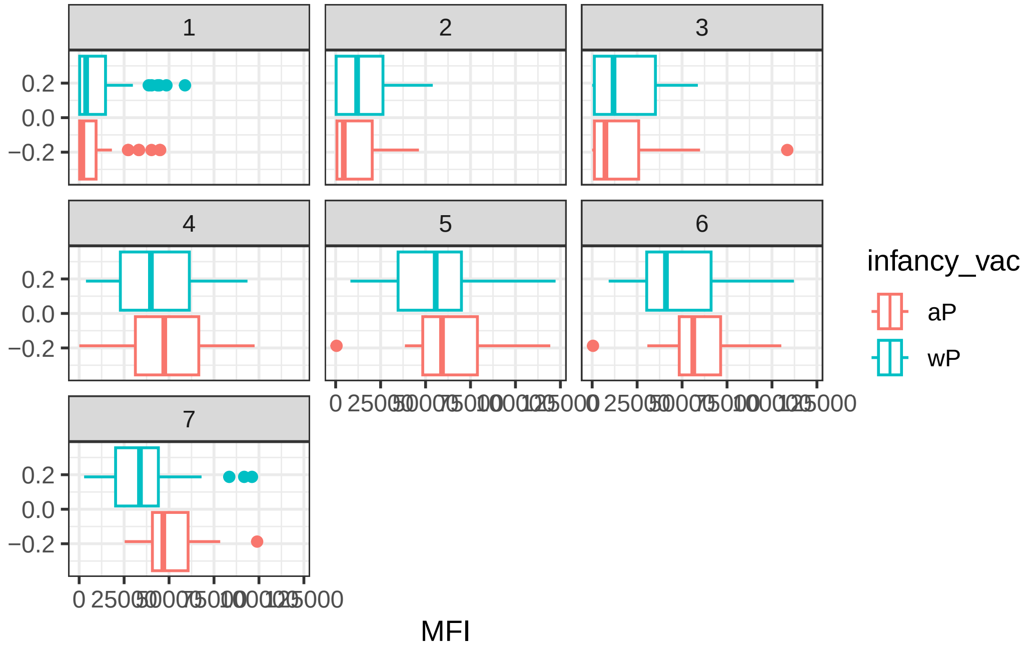
```r
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(infancy_vac, visit), nrow=2)
```



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



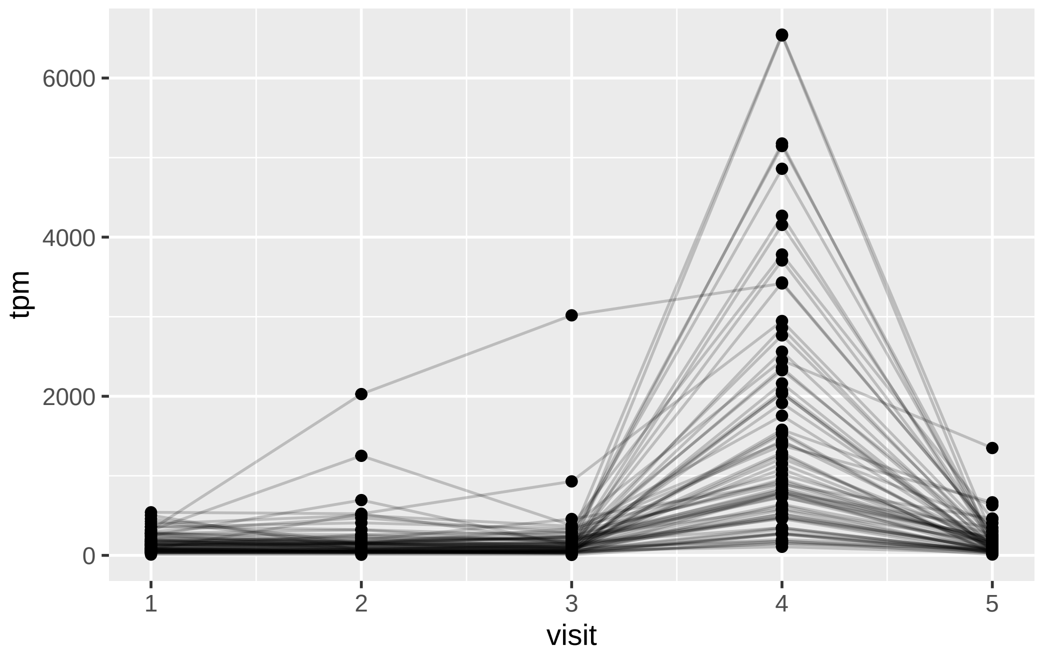
```
filter(ig1, antigen=="FIM2/3") %>%
  ggplot() +
  aes(MFI, col=infancy_vac) +
  geom_boxplot(show.legend = TRUE) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



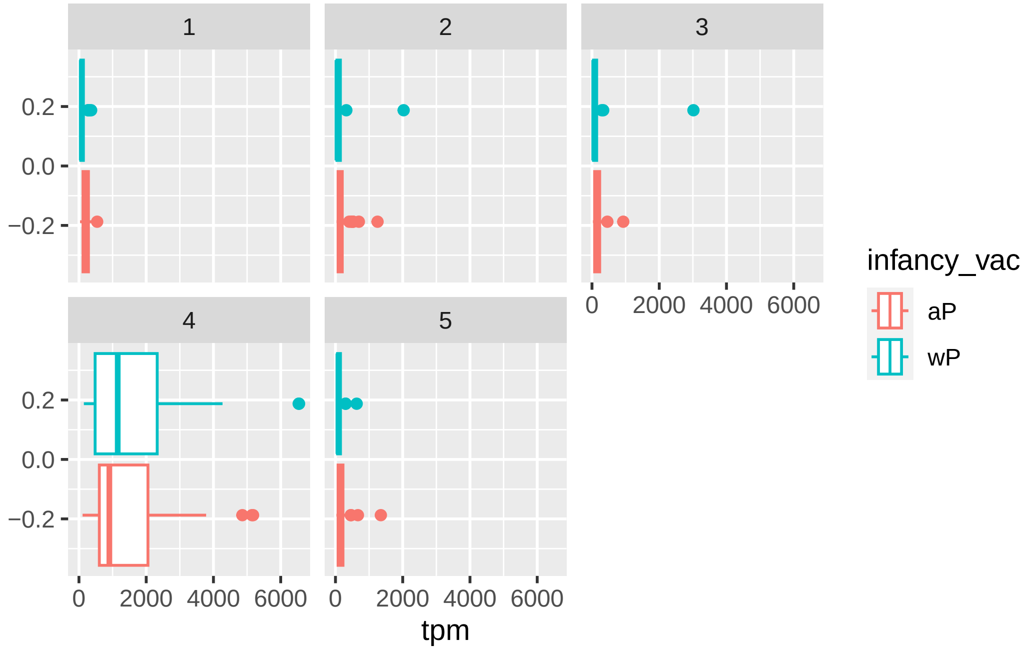
```
url <- "https://www.cmi-pb.org/api/v2/rnaseq?versioned_ensembl_gene_id=eq.ENSG00000211896.
rna <- read_json(url, simplifyVector = TRUE)
#meta <- inner_join(specimen, subject)
ssrna <- inner_join(rna, meta)
```

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

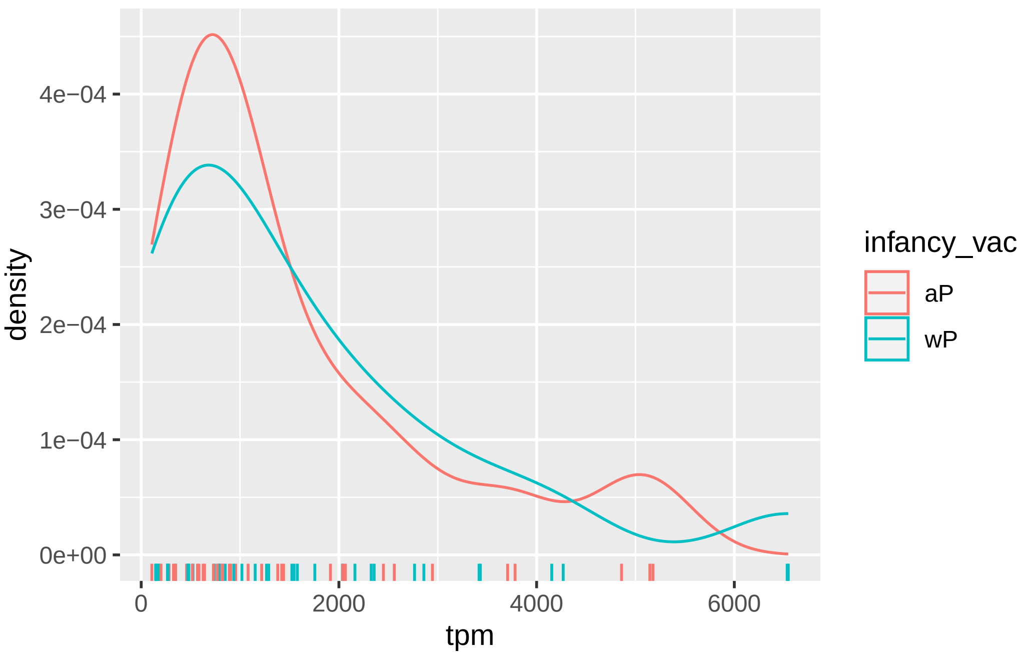
```
rna <- read_json(url, simplifyVector = TRUE)
ggplot(ssrna) +
  aes(visit, tpm, group=subject_id) +
  geom_point() +
  geom_line(alpha=0.2)
```



```
ggplot(ssrna) +
  aes(tpm, col=infancy_vac) +
  geom_boxplot() +
  facet_wrap(vars(visit))
```



```
ssrna %>%
  filter(visit==4) %>%
  ggplot() +
    aes(tpm, col=infancy_vac) + geom_density() +
    geom_rug()
```



4e−04
3e−04
2e−04
1e−04
0e+00
density
0
2000
4000
6000
tpm
infancy_vac
aP
wP