Class 18: Pertussis Vaccination

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Investigating pertussis cases by year

Pertussis(whooping cough) is a highly contageous lung iinfection that is most deadly for the very young (under 1 year of age)

Let's begin by having a look at pertussis case numbers per year in the united states.

The CDC tracks pertussis case numbers and makes the data availible here: https://www.cdc.gov/pertussis/php/s cases-by-year.html?CDC_AAref_Val=https://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html

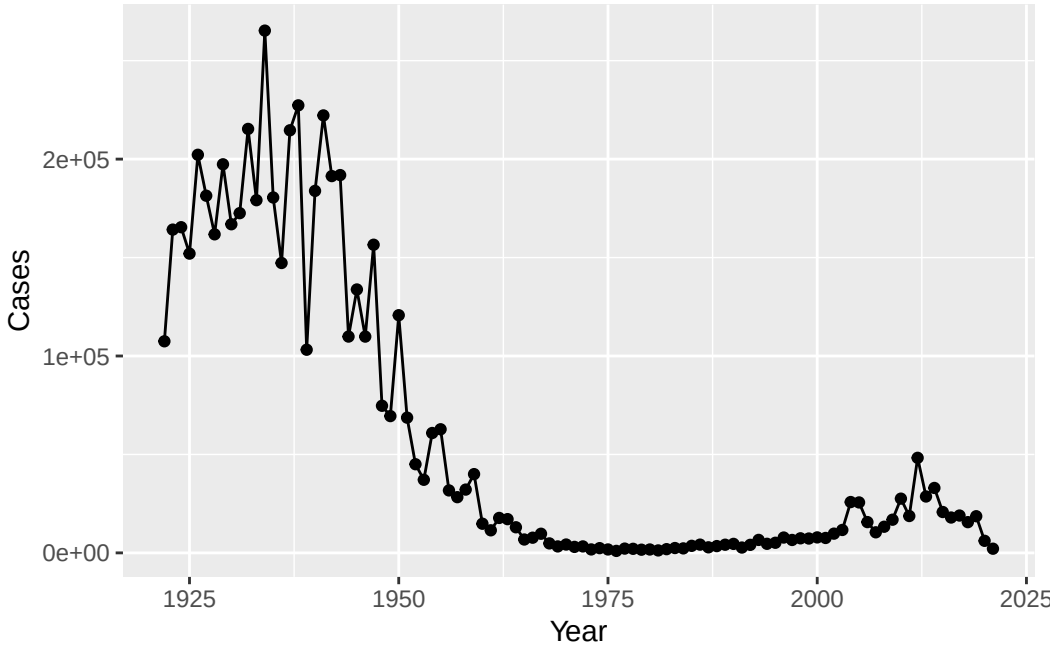
```
cdc <- data.frame(Year = c(1922L,1923L,1924L,1925L,
                           1926L,1927L,1928L,1929L,1930L,1931L,
                           1932L,1933L,1934L,1935L,1936L,
                           1937L,1938L,1939L,1940L,1941L,1942L,
                           1943L,1944L,1945L,1946L,1947L,
                           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)
        )
```

I want a plot of case numbers per year.

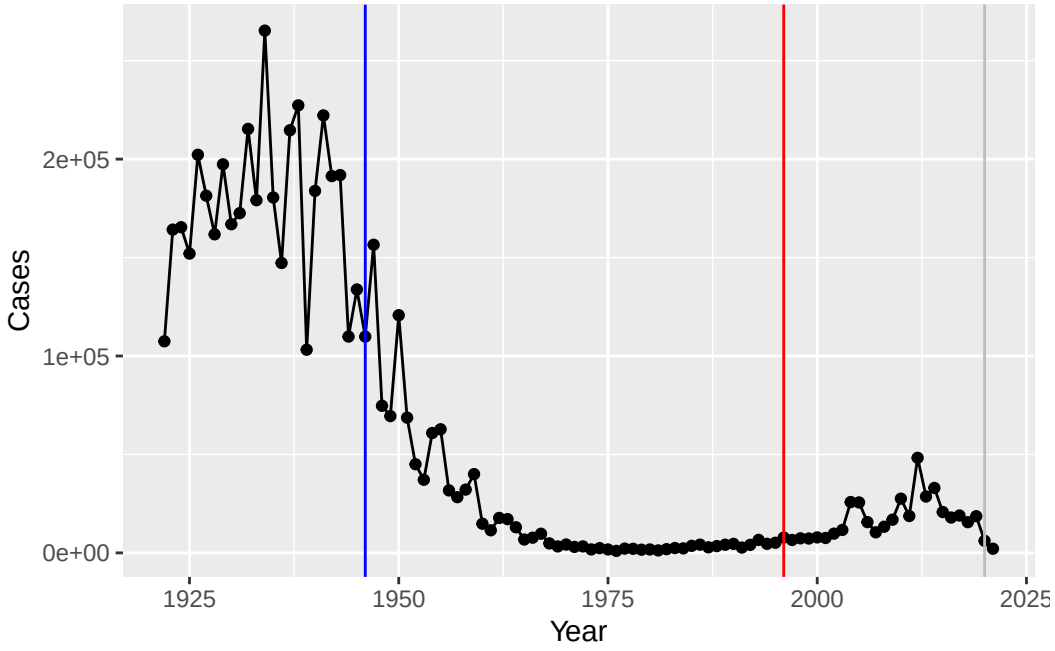
> Q1. With the help of the R "addin" package datapasta assign the CDC pertussis case number data to a data frame called cdc and use ggplot to make a plot of cases numbers over time.

```
library(ggplot2)

base <- ggplot(cdc) +
  aes(x = Year, y = Cases) +
  geom_point() +
  geom_line()

base
```



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(x = Year, y = Cases) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept=1946,col="blue") +
  geom_vline(xintercept=1996, col="red") +
  geom_vline(xintercept=2020, col="grey")
```



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

After the introduction of the aP vaccine (indicated by the red line), pertussis cases initially remained low but began to increase again. Possible explanations for this trend include more sensitive PCR-based testing, bacterial evolution allowing escape from vaccine immunity, waning immunity in adolescents who were vaccinated with the aP vaccine as infants, and increased vaccination hesitancy.

CMI-PB

A systems vaccinalogy project to figure out whatis going on with aP vs wP immune respnse.

The resouce has an API (application programming interface) that returns JSON format data.

Basically "key": "value" pair format.

We will use the jsonlite package to read this data into R.

```
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
```

How many individuals/subjects are in this dataset?

```
nrow(subject)
```

```
[1] 118
```

Q. How many wP and aP subjects are there?

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

```
aP wP
60 58
```

Q. How many male and female are there in the dataset?

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

```
Female   Male
    79     39
```

Q. What is the breakdown of race and gender in the dataset?

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

```
                                          Female Male
  American Indian/Alaska Native                0    1
  Asian                                       21   11
  Black or African American                    2    0
  More Than One Race                           9    2
  Native Hawaiian or Other Pacific Islander    1    1
  Unknown or Not Reported                     11    4
  White                                       35   20
```

Read other tables from the CMI-PB resource

```
specimen <- read_json("http://cmi-pb.org/api/specimen", simplifyVector = T)
ab_titer <- read_json("http://cmi-pb.org/api/v4/plasma_ab_titer",simplifyVector = T )
```

```
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
```

```
head(ab_titer)
```

```
  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 need to link or merge (join) these tables to get all the meta data I need about sibjects and specimens in one place. We will use the **dplyr** `join()` functions for this task.

```
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 we can take our new `meta`

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

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

```
dim(abdata)
```

```
[1] 41775    20
```

```
head(abdata)
```

```
  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 subject_id infancy_vac biological_sex
1 UG/ML                 2.096133          1          wP         Female
2 IU/ML                29.170000          1          wP         Female
3 IU/ML                 0.530000          1          wP         Female
4 IU/ML                 6.205949          1          wP         Female
5 IU/ML                 4.679535          1          wP         Female
6 IU/ML                 2.816431          1          wP         Female
                ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
5 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
6 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
  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
1     1
2     1
3     1
4     1
5     1
6     1
```

What Ab are measured/recoreded in the `ab_data` table:

```
table(ab_titer$isotype)
```

```
 IgE  IgG IgG1 IgG2 IgG3 IgG4
6698 3233 7961 7961 7961 7961
```

```
table(ab_titer$antigen)
```

```
   ACT   BETV1      DT   FELD1     FHA  FIM2/3   LOLP1     LOS Measles     OVA
  1970    1970    3435    1970    3829    3435    1970    1970    1970    3435
   PD1     PRN      PT     PTM   Total      TT
  1970    3829    3829    1970     788    3435
```

We have our merged dataset with all the needed metadata and antibody mesaurments called `abdata`

```
head(abdata, 2)
```

```
  specimen_id isotype is_antigen_specific antigen      MFI MFI_normalised  unit
1           1     IgE               FALSE   Total 1110.212       2.493425 UG/ML
2           1     IgE               FALSE   Total 2708.916       2.493425 IU/ML
  lower_limit_of_detection subject_id infancy_vac biological_sex
1                 2.096133          1          wP         Female
2                29.170000          1          wP         Female
              ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -3                             0         Blood
2                           -3                             0         Blood
  visit
1     1
2     1
```

Examine IgG Ab Titer Levels

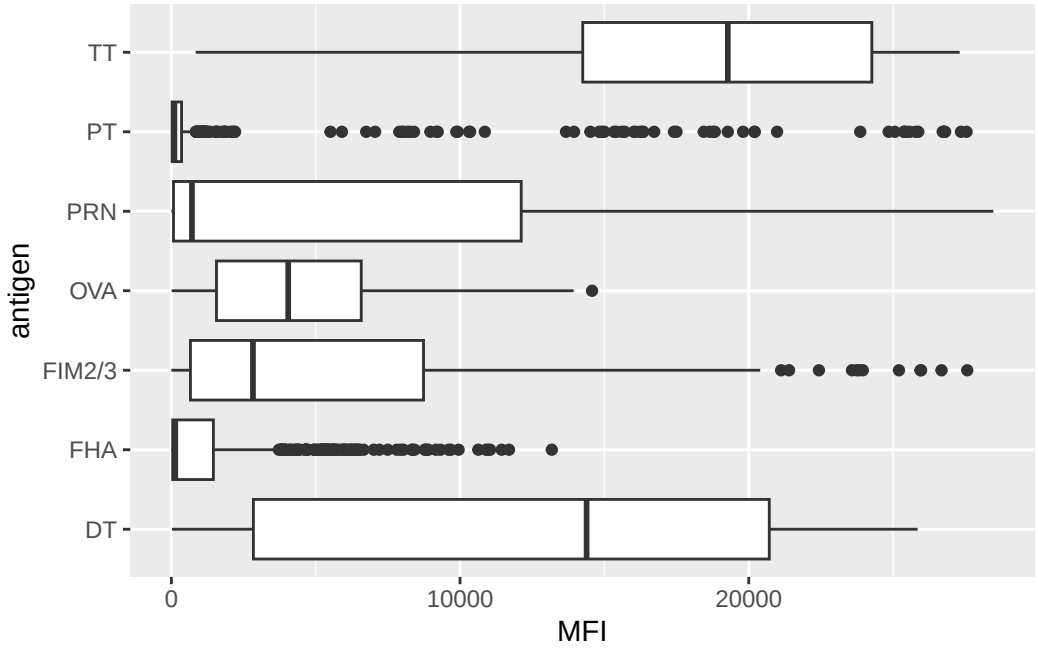
Now using our joined/merged/linked absata dataset filter() for IgG isotype.

```
igg <- abdata %>% filter (isotype == "IgG")
head(igg)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1     IgG               TRUE      PT   68.56614       3.736992
2           1     IgG               TRUE     PRN  332.12718       2.602350
```

```
3           1     IgG               TRUE     FHA 1887.12263      34.050956
4          19     IgG               TRUE      PT   20.11607       1.096366
5          19     IgG               TRUE     PRN  976.67419       7.652635
6          19     IgG               TRUE     FHA   60.76626       1.096457
   unit lower_limit_of_detection subject_id infancy_vac biological_sex
1 IU/ML                 0.530000          1          wP         Female
2 IU/ML                 6.205949          1          wP         Female
3 IU/ML                 4.679535          1          wP         Female
4 IU/ML                 0.530000          3          wP         Female
5 IU/ML                 6.205949          3          wP         Female
6 IU/ML                 4.679535          3          wP         Female
               ethnicity  race year_of_birth date_of_boost      dataset
1 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
2 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
3 Not Hispanic or Latino White    1986-01-01    2016-09-12 2020_dataset
4                Unknown White    1983-01-01    2016-10-10 2020_dataset
5                Unknown White    1983-01-01    2016-10-10 2020_dataset
6                Unknown White    1983-01-01    2016-10-10 2020_dataset
  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
1     1
2     1
3     1
4     1
5     1
6     1
```

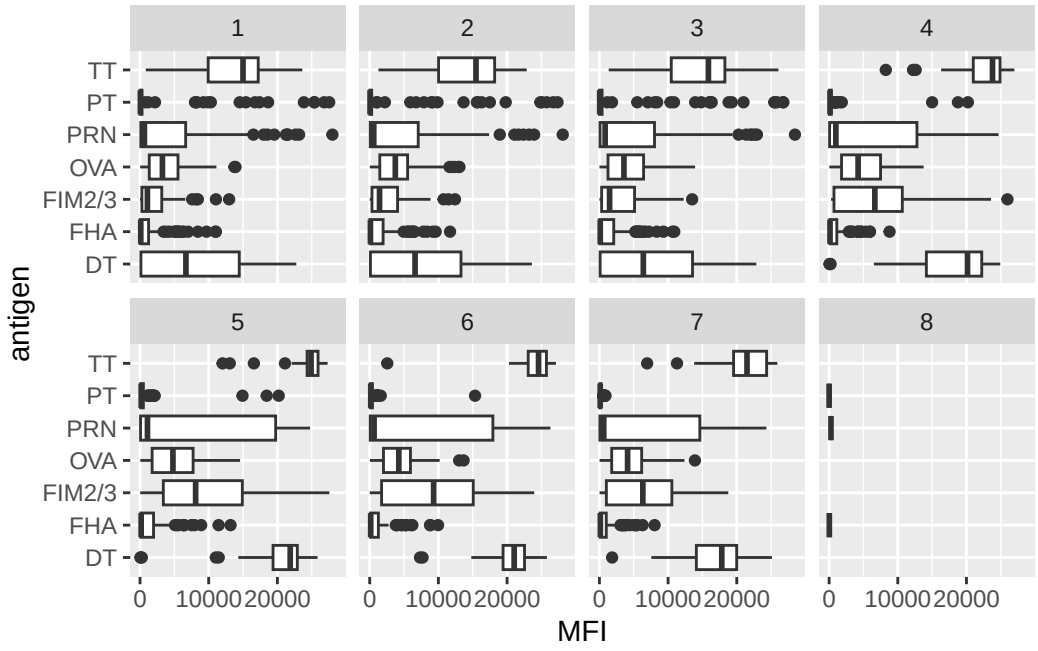
```
base <- ggplot(igg) +
  aes(MFI, antigen) +
geom_boxplot()

base
```




```
table(igg$visit)
```

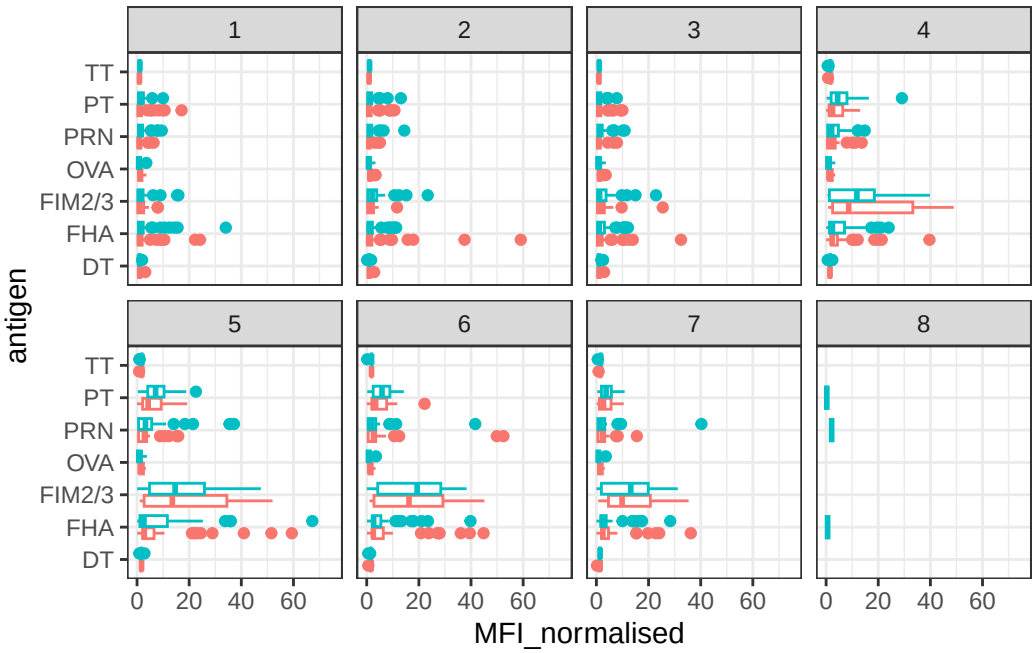
```
  1   2   3   4   5   6   7   8
524 531 552 426 426 393 378   3
```

```
base +
  facet_wrap(vars(visit), nrow=2)
```




```
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()
```

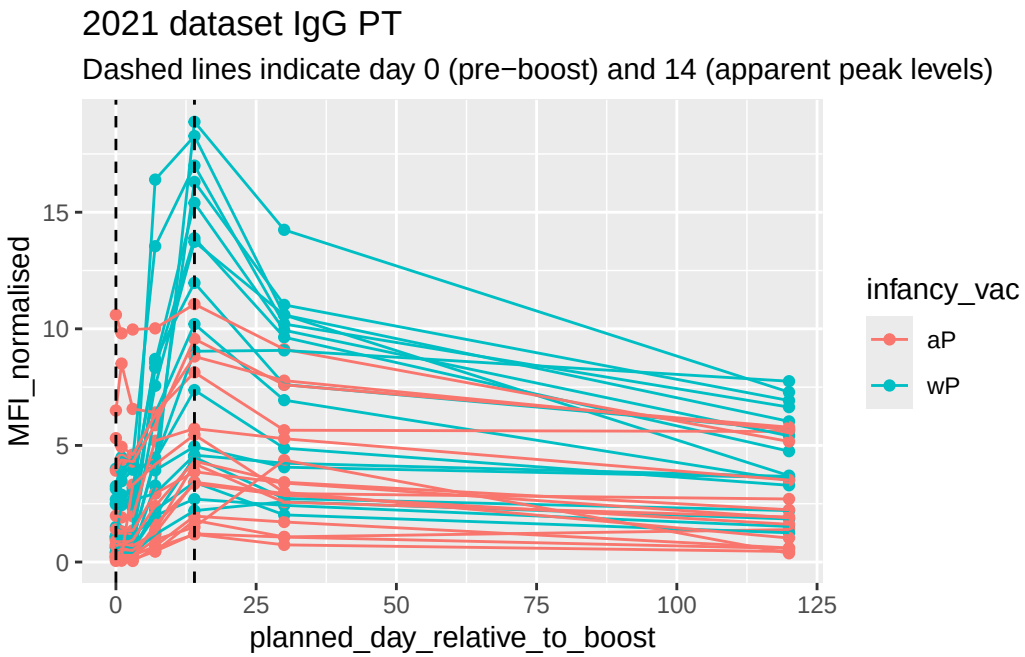
```
Warning: Removed 5 rows containing non-finite outside the scale range
(`stat_boxplot()`).
```




```
table(abdata$dataset)
```

```
2020_dataset 2021_dataset 2022_dataset
       31520         8085         2170
```

```
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)")
```



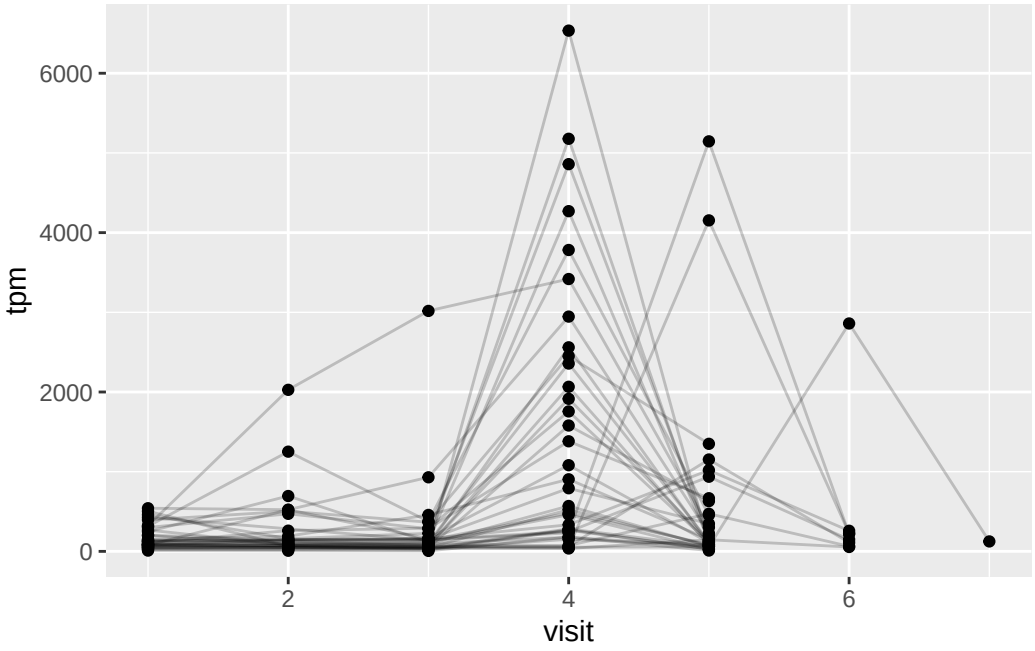

```
url <- "https://www.cmi-pb.org/api/v2/rnaseq?versioned_ensembl_gene_id=eq.ENSG00000211896.
```

```
rna <- read_json(url, simplifyVector = TRUE)
```

```
#meta <- inner_join(specimen, subject)
ssrna <- inner_join(rna, meta)
```

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

```
library(ggplot2)
ggplot(ssrna) +
  aes(x = visit, y = tpm, group = subject_id) +
  geom_point() +
  geom_line(alpha = 0.2)
```



What do you notice about the expression of this gene (i.e. when is it at it's maximum level)?

The expression of the IGHG1 gene reaches its maximum level at visit 4, as indicated by the peak in the tpm values at this time point. This suggests that the highest expression of this gene occurs during this visit, with a significant increase compared to other visits.Additionally, there is considerable variability among subjects, with some showing high expression while others remain low, and a secondary peak at visit 5. By visit 6, the expression levels return to the lower baseline observed at the earlier visits.