class18

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Background

Pertussis (a.k.a whooping cough) is a common lung infection caused by the bacteria *B.Pertussis*.

The CDC tracks cases of Pertussis in the US: https://www.cdc.gov/pertussis/php/surveillance/pertussis-cases-by-year.html

Examining cases of Pertussis by year

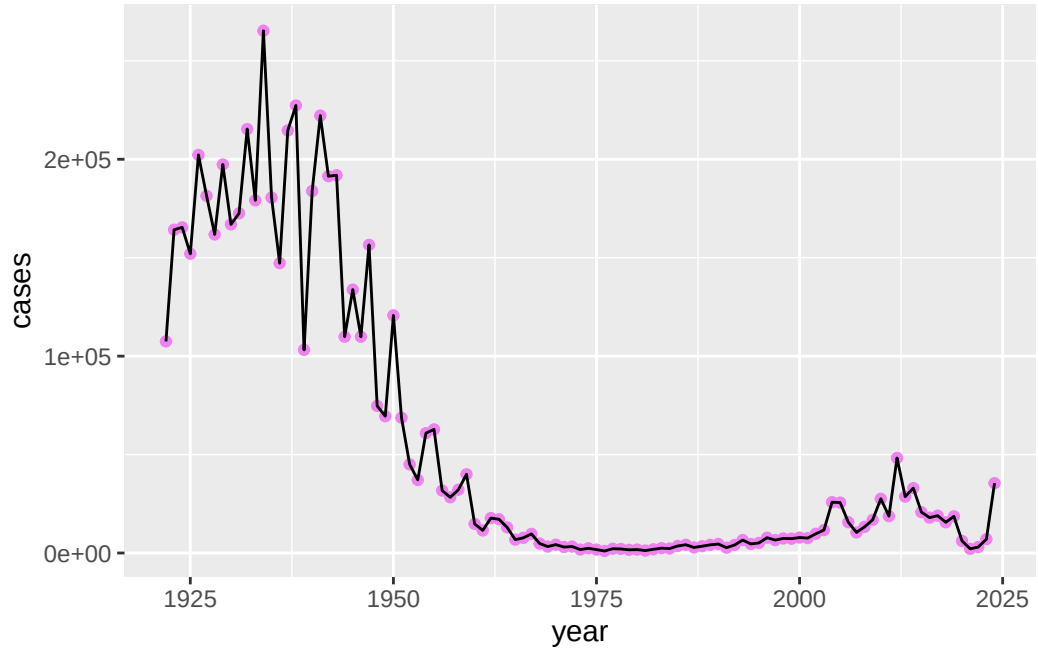
We can use

```
head(cdc)
```

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

Q1. Make a plot of pertussis cases peryear using ggplot

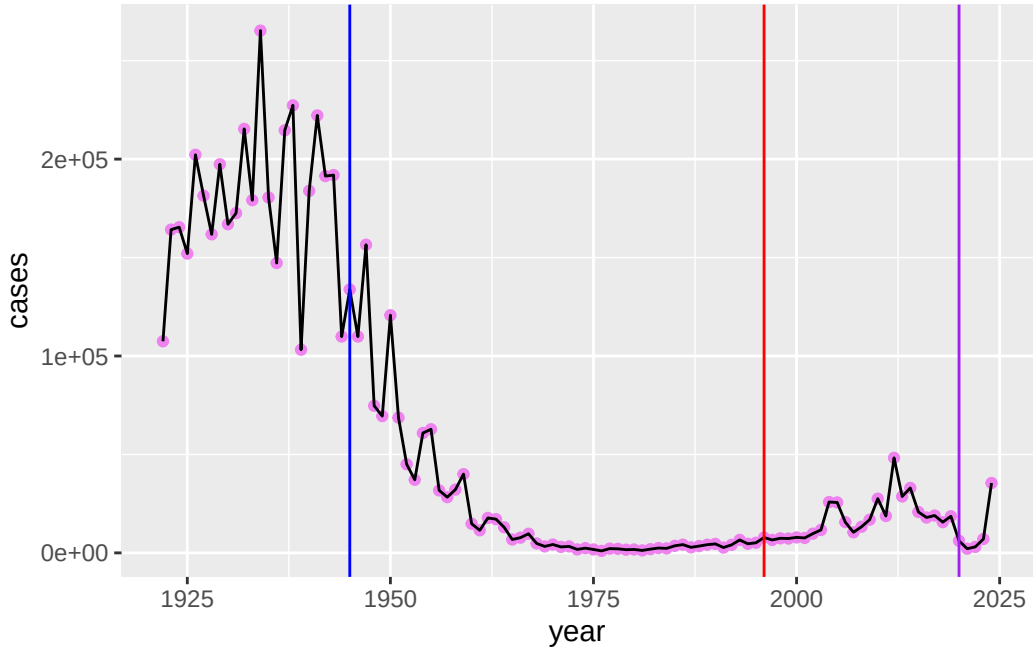
```
library(ggplot2)

cases <-  ggplot(cdc) +
          aes(year,cases) +
          geom_point(col = "violet") +
          geom_line()

cases
```



Q2. Add some key time points in our history of interaction with Pertussis. These includewP roll-out (the first vaccine) in 1945 and the switch to aP in 1996

We can use `geom_vline()` for this

```
cases + geom_vline(xintercept =1945, col="blue") +
       geom_vline(xintercept =1996, col="red") +
       geom_vline(xintercept = 2020, col="purple")
```



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

Mounting ecidence suggests that the newer **aP** vaccine is less effective over the long term than the older **wP** vaccine that it replaced. In other, words, vaccine protection wanes more rappidly with aP than with wP.

Enter the CMI-PB project

CMI-PB (computational Models of Immunity - Pertussis boost) major goal is to incestigate how the immune responds differently to with aP vs wP vaccinated individuals and be able to predict this at an erarly stage.

CMI-PB makes all their collected data freely avavilable and they store it in a database composed different tables.

We can use the **jsonlite** package to read this 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
```

Q. How many subjects (i.e. enrolled people) are there in this dataset?

```
nrow(subject)
```

```
[1] 172
```

Q. How many "aP" and "wP" subjects are there?

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

```
aP wP
87 85
```

Q. How many Male/Female are in the dataset?

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

```
Female   Male
   112     60
```

Q. How about gender and race number

```
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
```

Q. Is this representative of the US population?

No, UCSD student population

Let's read another database table from CMI-PB

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

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

```
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_data)
```

```
  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
```

We want to "join" these tables to get all our information together. For this we will use the **dplyr** package and `inner_join()` function.

```
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
```

One more "join"to get ab_data

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

```
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] 61956    20
```

Q. How many Ab isotypes are there in the dataset?

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

```
  IgE   IgG  IgG1  IgG2  IgG3  IgG4
 6698  7265 11993 12000 12000 12000
```

Q. How many different antigens are measured in the dataset?

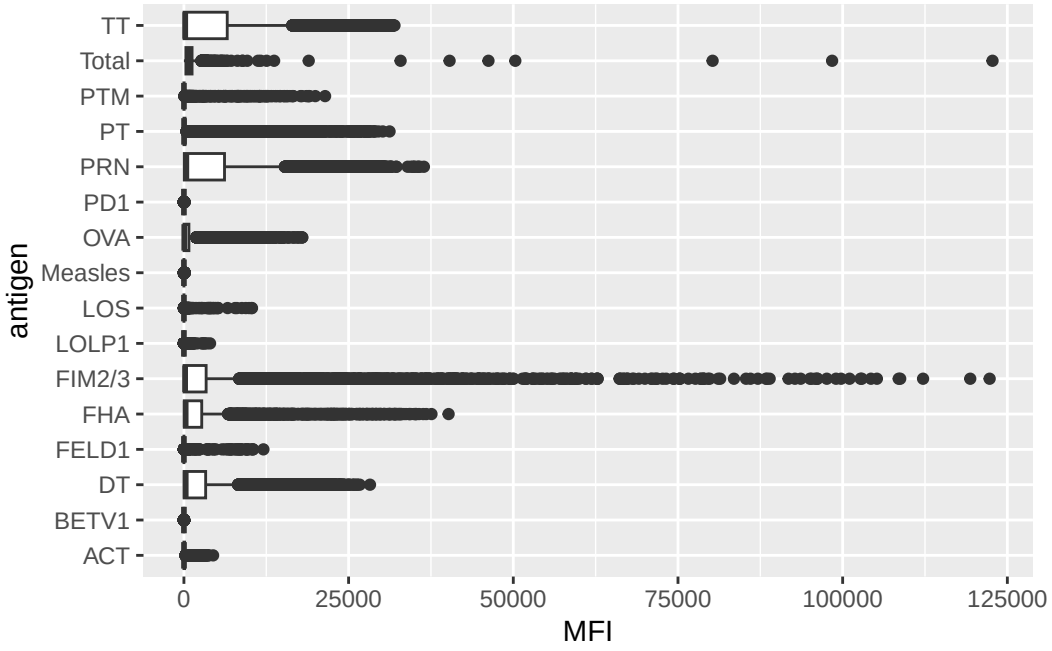
```
table(abdata$antigen)
```

```
   ACT   BETV1      DT   FELD1     FHA  FIM2/3   LOLP1     LOS Measles     OVA
  1970    1970    6318    1970    6712    6318    1970    1970    1970    6318
   PD1     PRN      PT     PTM   Total      TT
  1970    6712    6712    1970     788    6318
```

Q. Make a boxplot of antigen levels accross the whole dataset

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

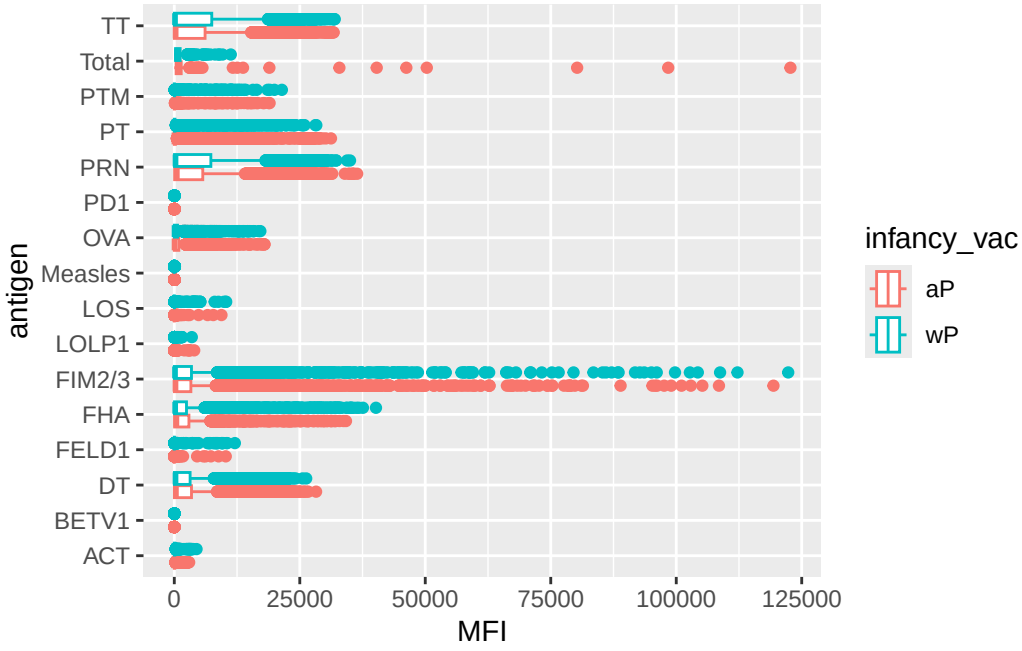
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Q. Are there obvious differenes between aP and wP values

```
ggplot(abdata) +
  aes(MFI, antigen, col=infancy_vac) +
  geom_boxplot()
```

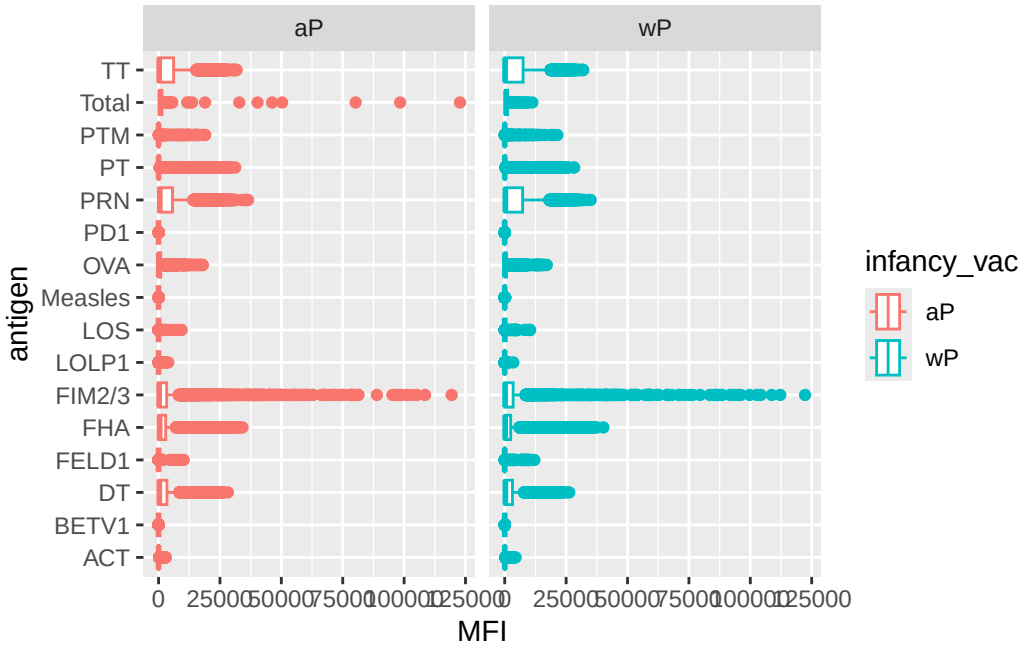
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Or we can `infancy_vac` to get two individual plots one for each value of `infancy_vac`

```
ggplot(abdata) +
  aes(MFI, antigen, col=infancy_vac) +
  geom_boxplot() +
  facet_wrap(~infancy_vac)
```

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



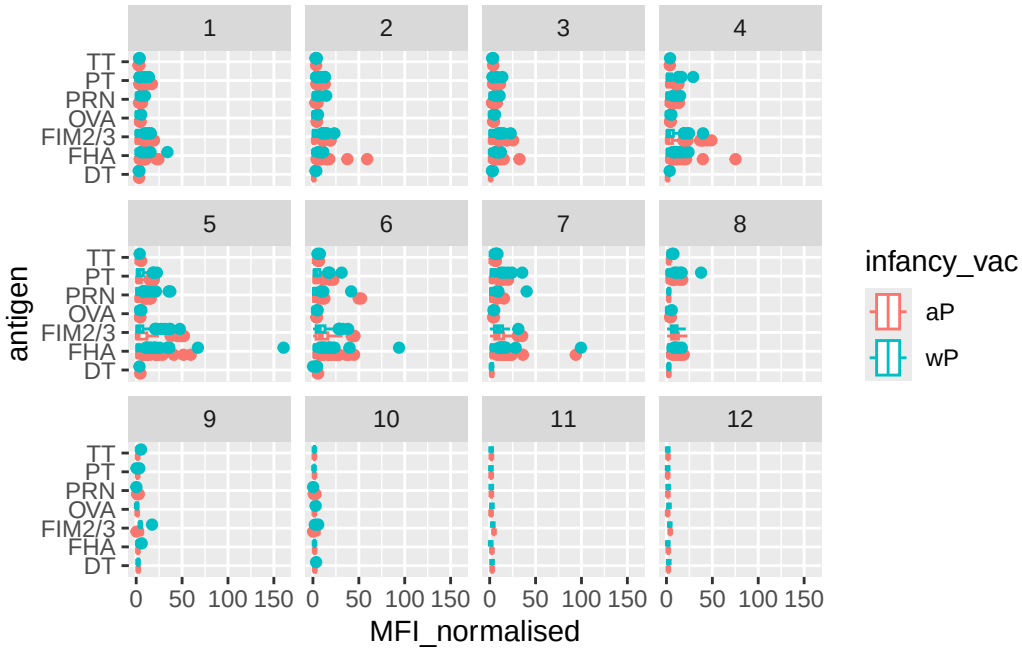
viral infections.

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

head(igg)
```

```
  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           2
5    1986-01-01    2016-09-12 2020_dataset           2
6    1986-01-01    2016-09-12 2020_dataset           2
  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                           1                           1         Blood
5                           1                           1         Blood
6                           1                           1         Blood
  visit isotype is_antigen_specific antigen        MFI MFI_normalised  unit
1     1     IgG                TRUE      PT   68.56614       3.736992 IU/ML
2     1     IgG                TRUE     PRN  332.12718       2.602350 IU/ML
3     1     IgG                TRUE     FHA 1887.12263      34.050956 IU/ML
4     2     IgG                TRUE      PT   41.38442       2.255534 IU/ML
5     2     IgG                TRUE     PRN  174.89761       1.370393 IU/ML
6     2     IgG                TRUE     FHA  246.00957       4.438960 IU/ML
  lower_limit_of_detection
1                 0.530000
2                 6.205949
3                 4.679535
4                 0.530000
5                 6.205949
6                 4.679535
```

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



Focus in furthwer in jsut one of these anitgens - let's pick **PT** (Pertussis Toxin, one of the main toxins of the bacteria)

```
table(igg$dataset)
```

```
2020_dataset 2021_dataset 2022_dataset 2023_dataset
        1182         1617         1456         3010
```

```
pt_igg <- abdata |>
          filter(isotype == "IgG",
                 antigen == "PT",
                 dataset == "2021_dataset")

head(pt_igg)
```

```
  subject_id infancy_vac biological_sex              ethnicity
1         61          wP         Female Not Hispanic or Latino
2         61          wP         Female Not Hispanic or Latino
3         61          wP         Female Not Hispanic or Latino
4         61          wP         Female Not Hispanic or Latino
5         61          wP         Female Not Hispanic or Latino
```

```
6         61          wP         Female Not Hispanic or Latino
                     race year_of_birth date_of_boost      dataset specimen_id
1 Unknown or Not Reported    1987-01-01    2019-04-08 2021_dataset         468
2 Unknown or Not Reported    1987-01-01    2019-04-08 2021_dataset         469
3 Unknown or Not Reported    1987-01-01    2019-04-08 2021_dataset         470
4 Unknown or Not Reported    1987-01-01    2019-04-08 2021_dataset         471
5 Unknown or Not Reported    1987-01-01    2019-04-08 2021_dataset         472
6 Unknown or Not Reported    1987-01-01    2019-04-08 2021_dataset         473
  actual_day_relative_to_boost planned_day_relative_to_boost specimen_type
1                           -4                             0         Blood
2                            1                             1         Blood
3                            3                             3         Blood
4                            7                             7         Blood
5                           14                            14         Blood
6                           30                            30         Blood
  visit isotype is_antigen_specific antigen    MFI MFI_normalised unit
1     1     IgG               FALSE      PT 112.75      1.0000000  MFI
2     2     IgG               FALSE      PT 111.25      0.9866962  MFI
3     3     IgG               FALSE      PT 125.50      1.1130820  MFI
4     4     IgG               FALSE      PT 224.25      1.9889135  MFI
5     5     IgG               FALSE      PT 304.00      2.6962306  MFI
6     6     IgG               FALSE      PT 274.00      2.4301552  MFI
  lower_limit_of_detection
1                 5.197441
2                 5.197441
3                 5.197441
4                 5.197441
5                 5.197441
6                 5.197441
```

```r
dim(pt_igg)
```

```
[1] 231  20
```

```r
ggplot(pt_igg) +
  aes(actual_day_relative_to_boost, MFI_normalised,
      col = infancy_vac,
      # connect lines with the same subject_id
      group=subject_id) +
  geom_point() +
  geom_line() +
```

```
  theme_bw() +
  geom_vline(xintercept = 0) +
  geom_vline(xintercept = 14)
```