Class18-Pertussis and the CMI-PB project

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

The CDC tracks Pertussis case numbers and we can find this data here: http://tinyurl.com/perssistuscdc

We can "scrape" this data using the **datapasta** package.

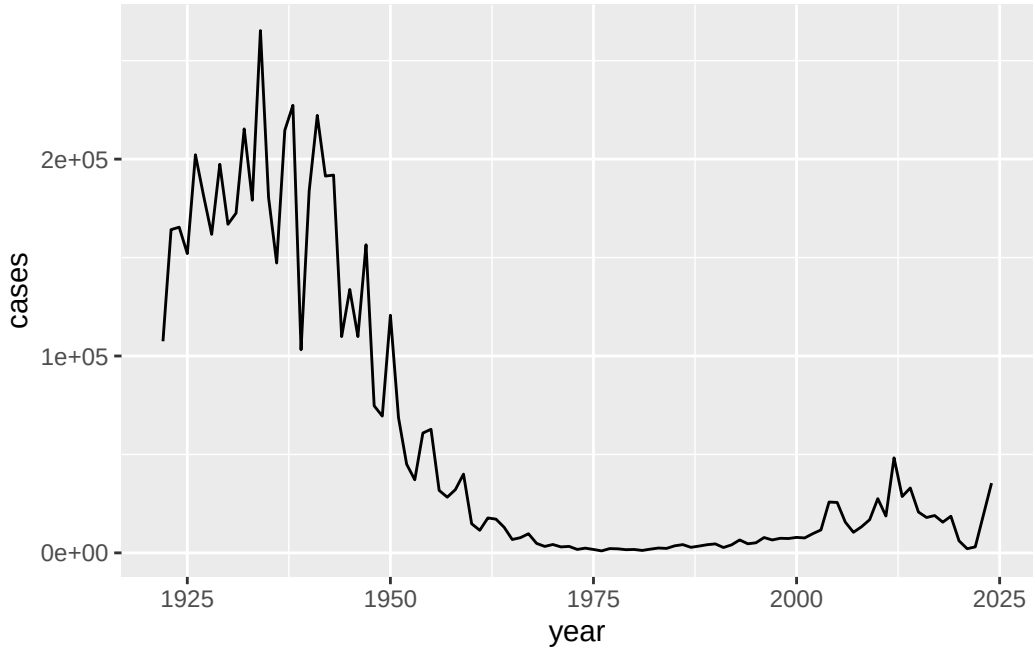
```
head(cdc)
```

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

Q1. Make plot of pertussis cases per year using ggplot

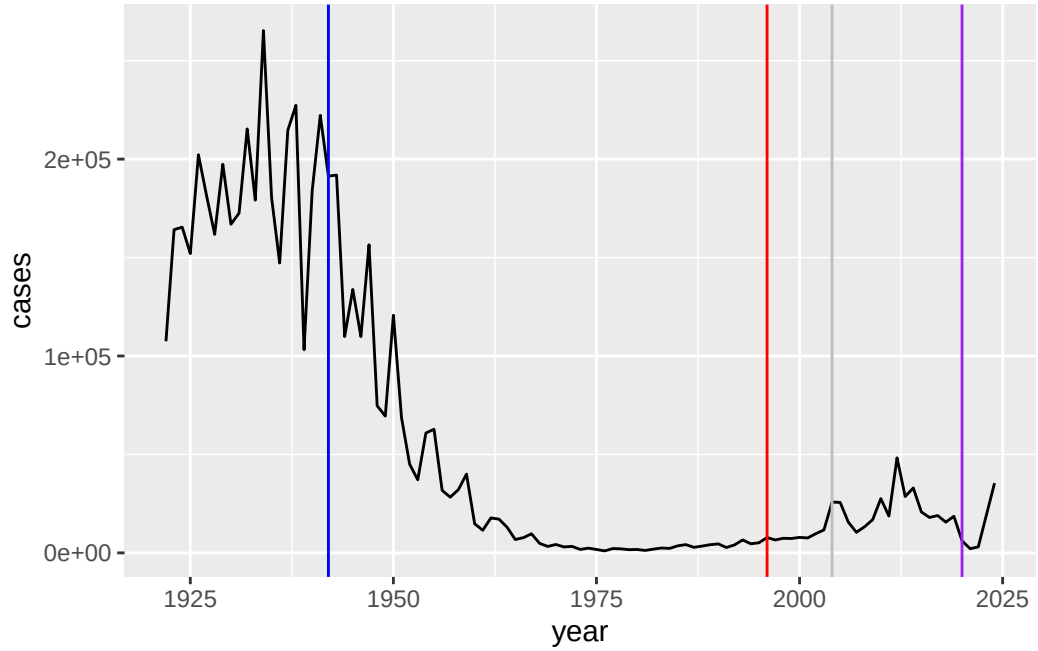
```
library(ggplot2)

ggplot(cdc) +
  aes(year, cases)+
  geom_line()
```



Q2. Let's add the key milestones of DTP (wP)vaccine roll out in 1942 and the switch to the new aP vaccine in 1996. We can use `geom_vline()` for this. Booster chots started in 2004

```
ggplot(cdc) +
  aes(year, cases)+
  geom_line()+
  geom_vline(xintercept = 1942, col = "blue") +
  geom_vline(xintercept = 1996, col = "red") +
  geom_vline(xintercept = 2020, col = "purple") +
  geom_vline(xintercept = 2004, col = "gray")
```



There were high case numbers pre 1946 (before the wP vaccine) then relatively rapid decrease in case numbers through the 1970s and on to 2004 when our first widespread outbreak occurd again.

Mounting evidence indicates that the aP vaccine induced immunity wanes faster than the older wP vaccine.

Enter the CMI-PB project

Computational Models of Immunity Pertussis Boost

One of the main goals of this project is to determine what is different in the immune response between wP and q primmed individuals.

Using the booster vaccine as a proxy for infection.

All data is available here: https://www.cmi-pb.org in JSON format. WE can use the **jsonlite** package to read this data into R.

```
library(jsonlite)
```

```
Warning: package 'jsonlite' was built under R version 4.3.3
```

```
subject <- read_json("http://cmi-pb.org/api/v5_1/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
```

Q. How many individuals "subjects" 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. Male/Female numbers

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

```
Female   Male
   112     60
```

Q. Breakdown of biological sex and race

```
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. Does this look to be representitive of the US population at large?

NO

Let's read some more CMI-PB data

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

ab_titer <- read_json("http://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_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
```

To use this data we need to "join" the various tables to find all the information I need to know about a particular measurement.

```
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 join `meta` with `ab_titer` data.

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

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

```
head(ab_data)
```

```
  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
```

Q. How many different antibody isotypes are we measuring?

```
table(ab_data$isotype)
```

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

Q. How many antigens?

```
table(ab_data$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
```

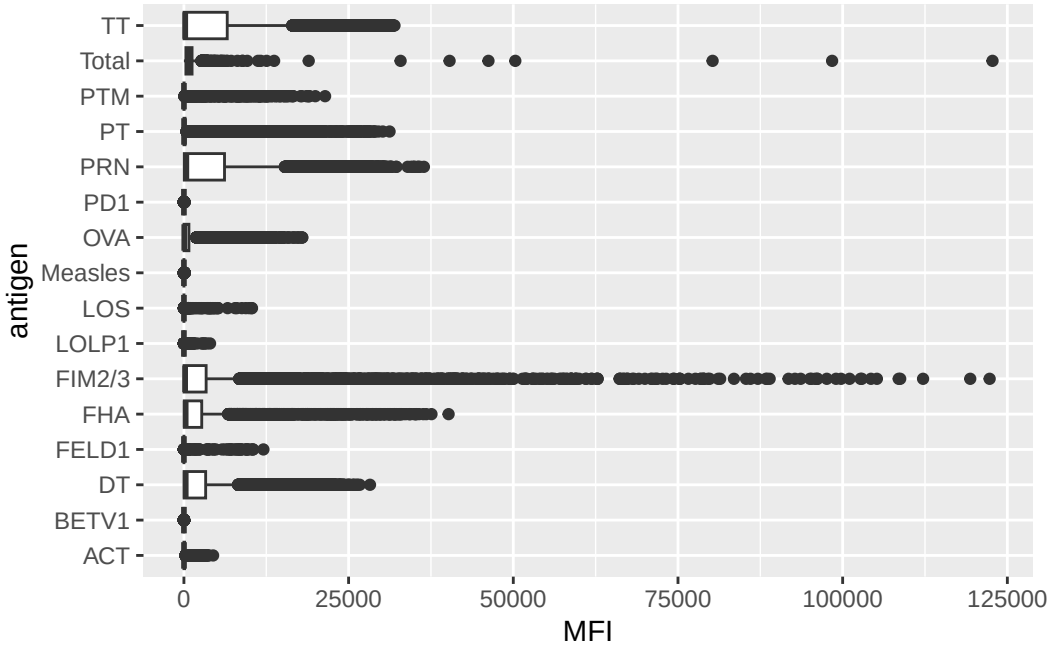
Q. Let's look at a boxplot of antigen levels over the whole dataset

```
dim(ab_data)
```

```
[1] 61956    20
```

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

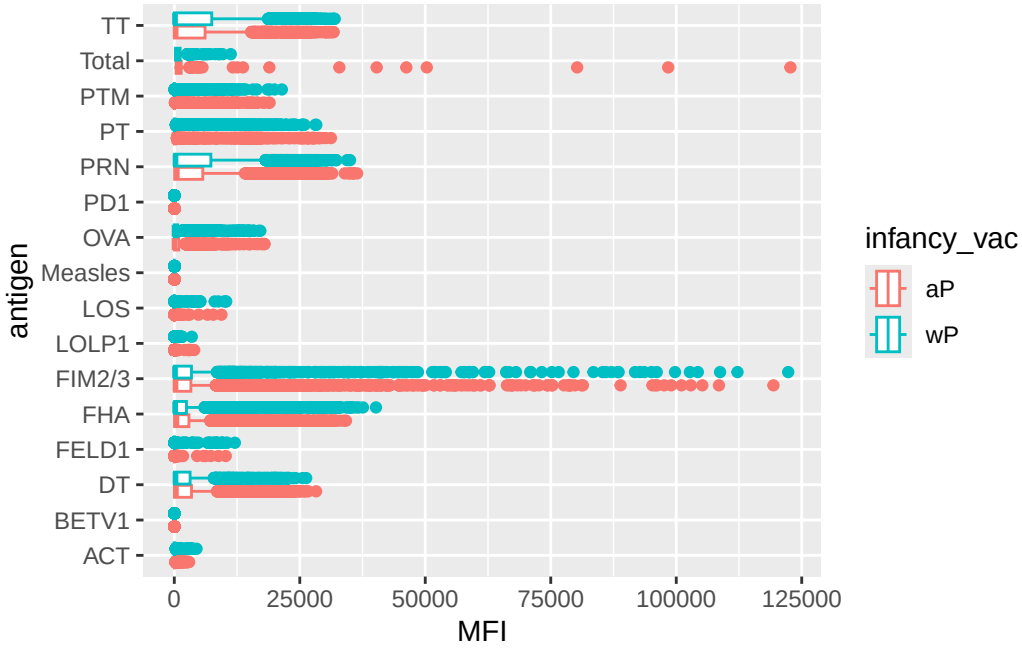
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



Q. Break this plot down by aP or wP

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

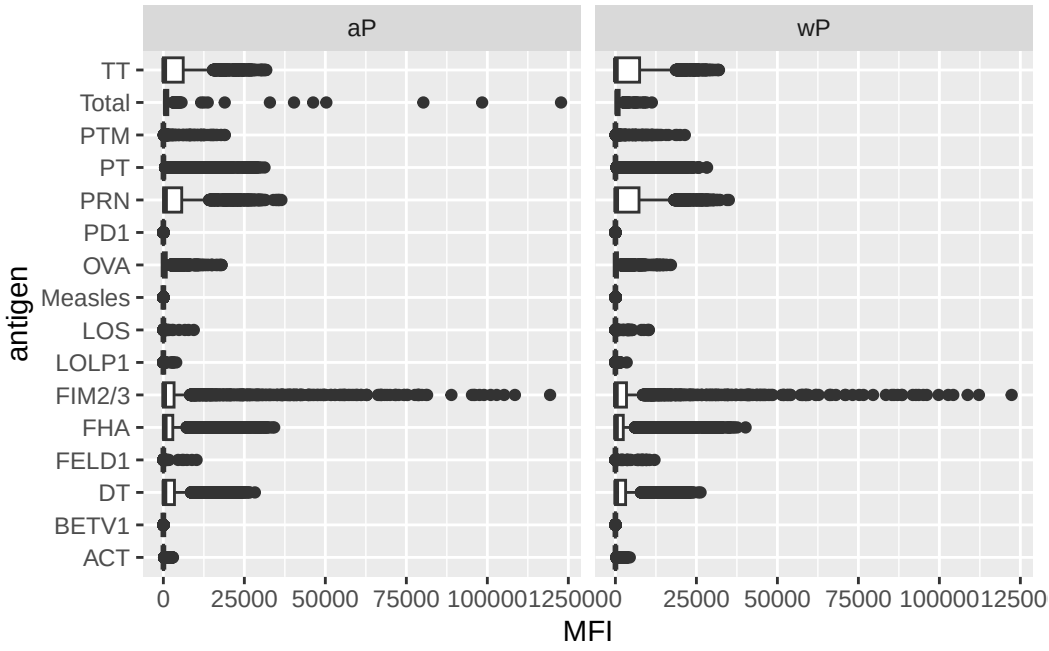
```
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).
```



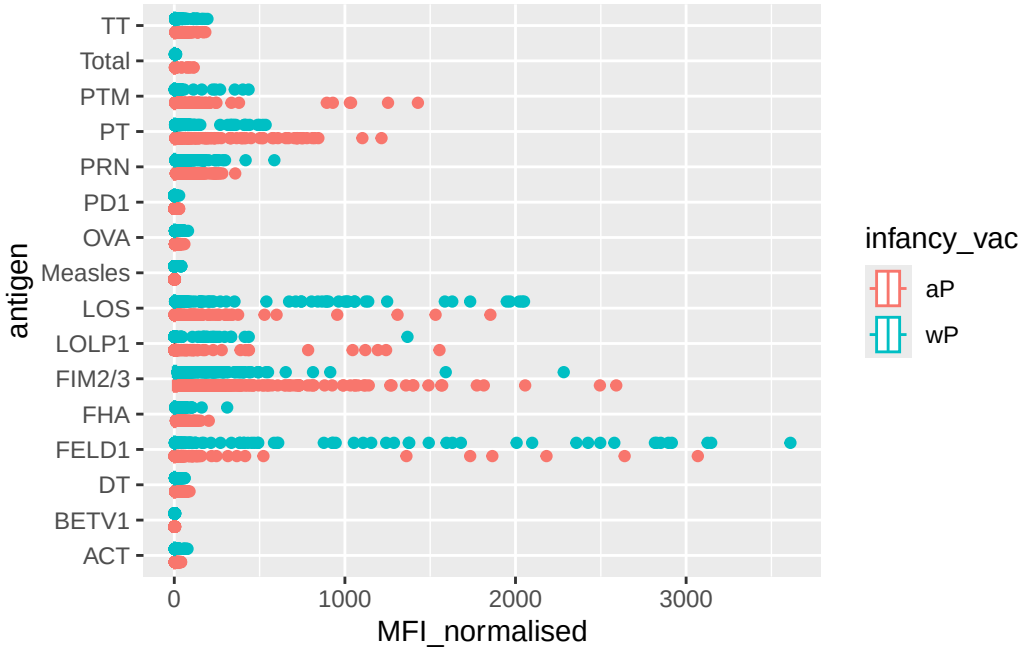
We can facet the plot by `infancy_vac`

```
ggplot(ab_data) +
  aes(MFI, antigen) +
  geom_boxplot() +
  facet_wrap(~infancy_vac)
```

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



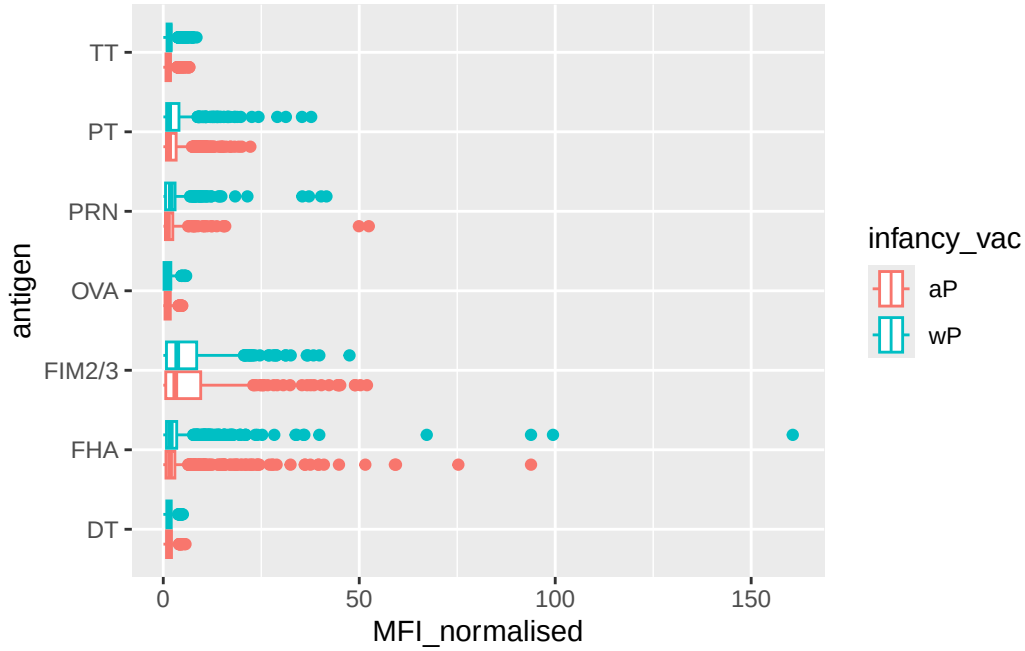

```
ggplot(ab_data) +
  aes(MFI_normalised, antigen, col = infancy_vac) +
  geom_boxplot()
```



Let's focus on just IgG

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

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

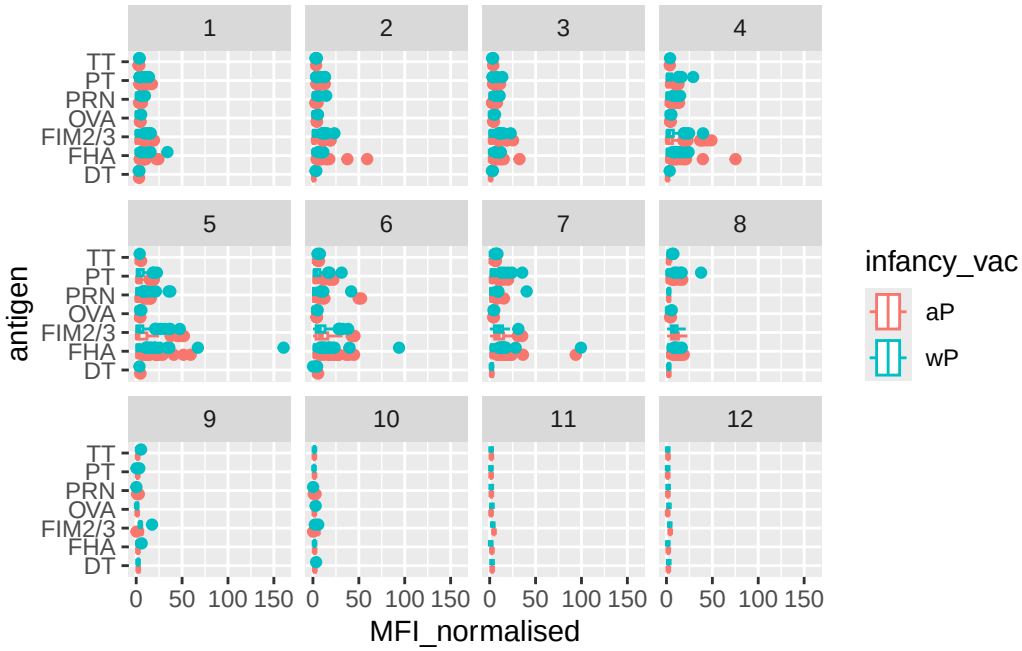



```
head(igg)
```

```
  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
```

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



Let's focus on PT(Pertussis Toxin) and igg levels over time.

```
table(ab_data$dataset)
```

```
2020_dataset 2021_dataset 2022_dataset 2023_dataset
       31520         8085         7301        15050
```

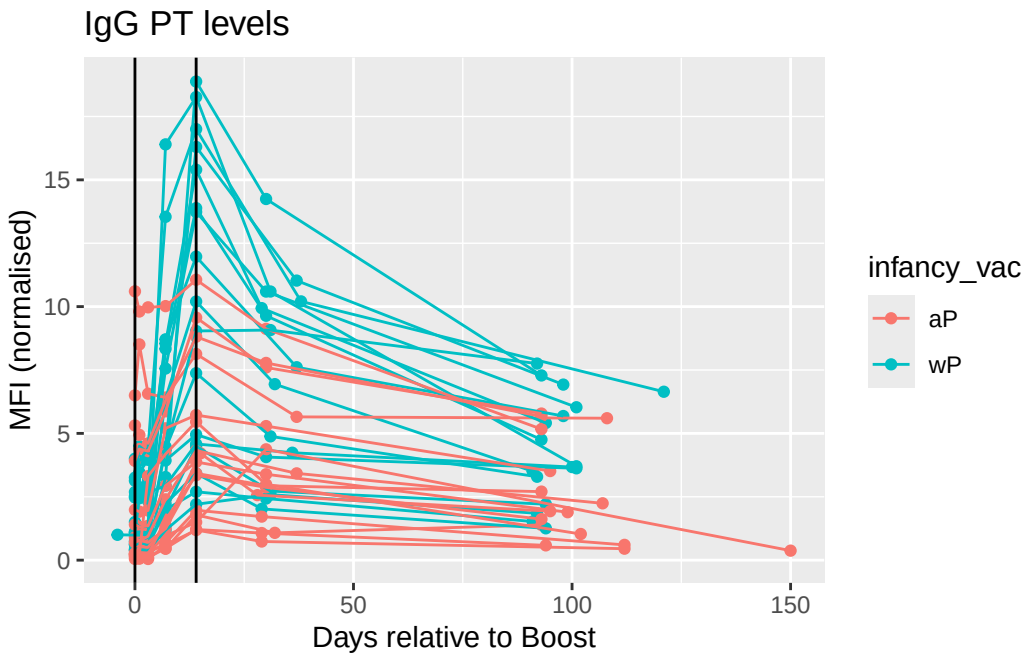
Filter to focus on one antigen "PT" and IgG levels

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

A plot of `actual_day_relative_to_boost` vs `MFI_normalised`

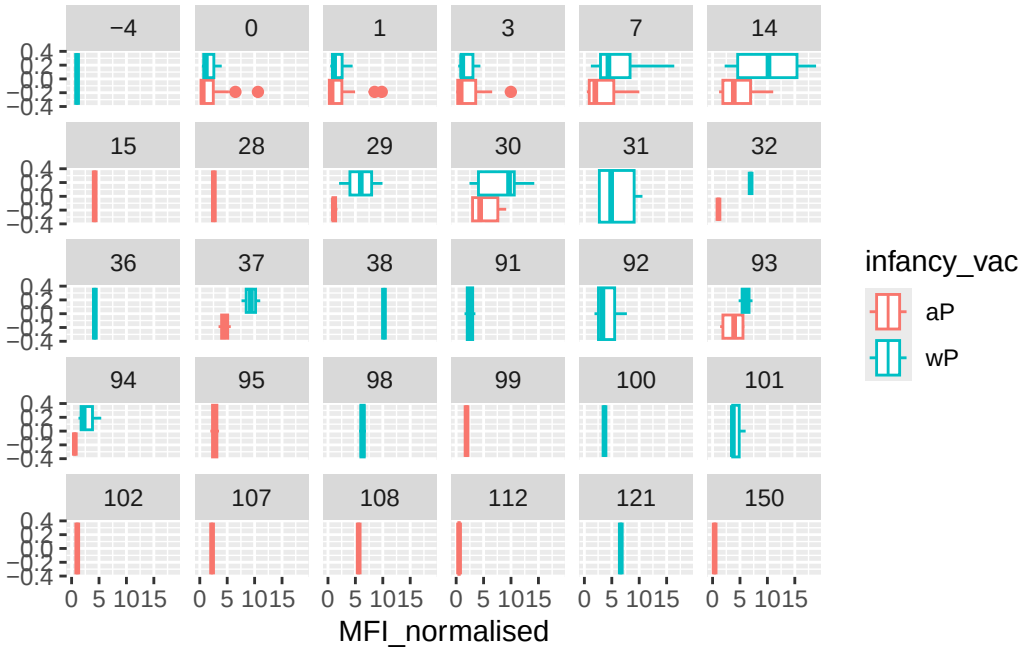
```
ggplot(pt_igg) +
  aes(actual_day_relative_to_boost, MFI_normalised,
      col=infancy_vac, group = subject_id) +
  geom_point() +
  geom_line() +
  geom_vline(xintercept = 14) +
  geom_vline(xintercept = 0) +
```

```
  labs(title="IgG PT levels") +
  xlab("Days relative to Boost")+
  ylab("MFI (normalised)")
```




```
  #geom_smooth()
```

```
ggplot(pt_igg) +
  aes(MFI_normalised, col=infancy_vac) +
  geom_boxplot() +
  facet_wrap(~actual_day_relative_to_boost)
```



Side-Note: Working with dates

Two of the columns of subject contain dates in the Year-Month-Day format. Recall from our last mini-project that dates and times can be annoying to work with at the best of times. However, in R we have the excellent lubridate package, which can make life allot easier. Here is a quick example to get you started:

```
subject$year_of_birth
```

```
  [1] "1986-01-01" "1968-01-01" "1983-01-01" "1988-01-01" "1991-01-01"
  [6] "1988-01-01" "1981-01-01" "1985-01-01" "1996-01-01" "1982-01-01"
 [11] "1986-01-01" "1982-01-01" "1997-01-01" "1993-01-01" "1989-01-01"
 [16] "1987-01-01" "1980-01-01" "1997-01-01" "1994-01-01" "1981-01-01"
 [21] "1983-01-01" "1985-01-01" "1991-01-01" "1992-01-01" "1988-01-01"
 [26] "1983-01-01" "1997-01-01" "1982-01-01" "1997-01-01" "1988-01-01"
 [31] "1989-01-01" "1997-01-01" "1990-01-01" "1983-01-01" "1991-01-01"
 [36] "1997-01-01" "1998-01-01" "1997-01-01" "1985-01-01" "1994-01-01"
 [41] "1985-01-01" "1997-01-01" "1998-01-01" "1998-01-01" "1997-01-01"
 [46] "1998-01-01" "1996-01-01" "1998-01-01" "1997-01-01" "1997-01-01"
 [51] "1997-01-01" "1998-01-01" "1998-01-01" "1997-01-01" "1997-01-01"
 [56] "1997-01-01" "1996-01-01" "1997-01-01" "1997-01-01" "1997-01-01"
 [61] "1987-01-01" "1993-01-01" "1995-01-01" "1993-01-01" "1990-01-01"
```

```
 [66] "1976-01-01" "1972-01-01" "1972-01-01" "1990-01-01" "1998-01-01"
 [71] "1998-01-01" "1991-01-01" "1995-01-01" "1995-01-01" "1998-01-01"
 [76] "1998-01-01" "1988-01-01" "1993-01-01" "1987-01-01" "1992-01-01"
 [81] "1993-01-01" "1998-01-01" "1999-01-01" "1997-01-01" "2000-01-01"
 [86] "1998-01-01" "2000-01-01" "2000-01-01" "1997-01-01" "1999-01-01"
 [91] "1998-01-01" "2000-01-01" "1996-01-01" "1999-01-01" "1998-01-01"
 [96] "2000-01-01" "1986-01-01" "1993-01-01" "1999-01-01" "2001-01-01"
[101] "2003-01-01" "2003-01-01" "1994-01-01" "1989-01-01" "1994-01-01"
[106] "1996-01-01" "1998-01-01" "1995-01-01" "1989-01-01" "1997-01-01"
[111] "1996-01-01" "1996-01-01" "1996-01-01" "1990-01-01" "2002-01-01"
[116] "2000-01-01" "1994-01-01" "1998-01-01" "1998-01-01" "1995-01-01"
[121] "2000-01-01" "1999-01-01" "1996-01-01" "2000-01-01" "1993-01-01"
[126] "1993-01-01" "1996-01-01" "1994-01-01" "1991-01-01" "1996-01-01"
[131] "1998-01-01" "1995-01-01" "1997-01-01" "1990-01-01" "1995-01-01"
[136] "1995-01-01" "1998-01-01" "2000-01-01" "1993-01-01" "2001-01-01"
[141] "1996-01-01" "1991-01-01" "2003-01-01" "1999-01-01" "2002-01-01"
[146] "1992-01-01" "2000-01-01" "1988-01-01" "1991-01-01" "1991-01-01"
[151] "1992-01-01" "1995-01-01" "1998-01-01" "1997-01-01" "1997-01-01"
[156] "2001-01-01" "1997-01-01" "2000-01-01" "1994-01-01" "1996-01-01"
[161] "1993-01-01" "1999-01-01" "1993-01-01" "1991-01-01" "1993-01-01"
[166] "2001-01-01" "1997-01-01" "1991-01-01" "2003-01-01" "1992-01-01"
[171] "2003-01-01" "1986-01-01"
```

```r
library(lubridate)
```

```
Warning: package 'lubridate' was built under R version 4.3.3
```

```
Attaching package: 'lubridate'
```

```
The following objects are masked from 'package:base':

    date, intersect, setdiff, union
```

```r
today() - ymd("1991-04-27")
```

```
Time difference of 12368 days
```

```
time_length( today() - ymd("1991-04-27"), "years")
```

```
[1] 33.86174
```

```
subject$age <- time_length( today() - ymd(subject$year_of_birth), "years")
```

```
ggplot(subject) +
  aes(age, fill=infancy_vac) +
  geom_histogram() +
  facet_wrap(~infancy_vac, ncol=1)
```

```
`stat_bin()` using `bins = 30`. Pick better value with `binwidth`.
```