Pertussis Vaccination

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Pertussis (whooping cough) is a highly contagious lung infection 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 available here: https://www.cdc.gov/pertussis/php/cases-by-year.html?CDC_AAref_Val=https://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html

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.

```
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)
)
cdc
```

```
   Year  Cases
1  1922 107473
2  1923 164191
3  1924 165418
4  1925 152003
5  1926 202210
6  1927 181411
7  1928 161799
8  1929 197371
9  1930 166914
10 1931 172559
11 1932 215343
12 1933 179135
13 1934 265269
14 1935 180518
15 1936 147237
16 1937 214652
17 1938 227319
18 1939 103188
19 1940 183866
20 1941 222202
21 1942 191383
22 1943 191890
23 1944 109873
24 1945 133792
```

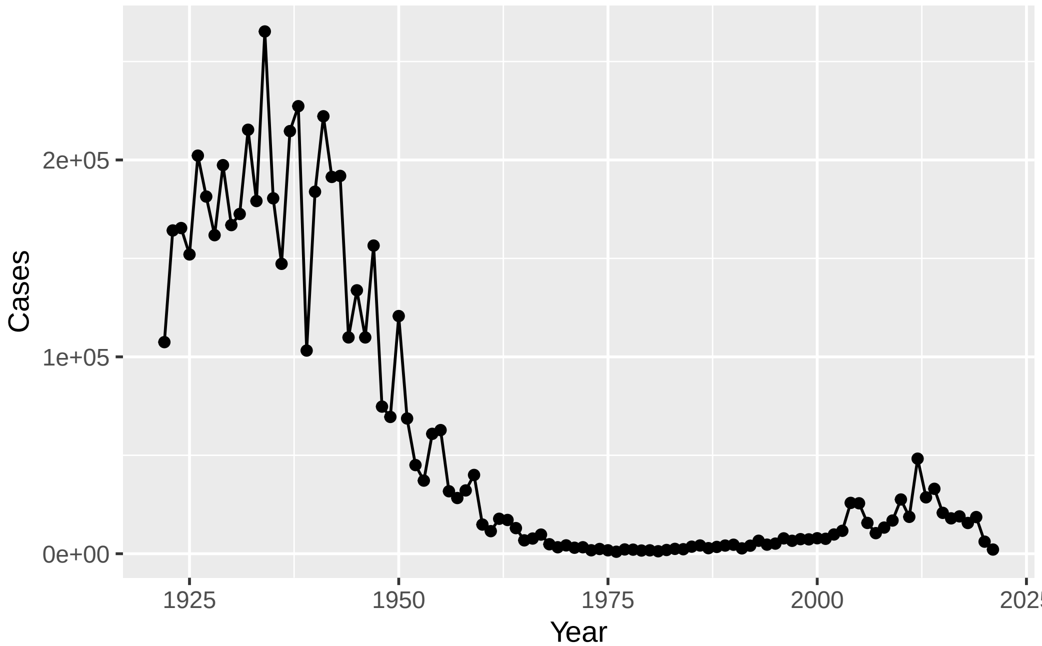
25	1946	109860
26	1947	156517
27	1948	74715
28	1949	69479
29	1950	120718
30	1951	68687
31	1952	45030
32	1953	37129
33	1954	60886
34	1955	62786
35	1956	31732
36	1957	28295
37	1958	32148
38	1959	40005
39	1960	14809
40	1961	11468
41	1962	17749
42	1963	17135
43	1964	13005
44	1965	6799
45	1966	7717
46	1967	9718
47	1968	4810
48	1969	3285
49	1970	4249
50	1971	3036
51	1972	3287
52	1973	1759
53	1974	2402
54	1975	1738
55	1976	1010
56	1977	2177
57	1978	2063
58	1979	1623
59	1980	1730
60	1981	1248
61	1982	1895
62	1983	2463
63	1984	2276
64	1985	3589
65	1986	4195
66	1987	2823
67	1988	3450

```
68  1989   4157
69  1990   4570
70  1991   2719
71  1992   4083
72  1993   6586
73  1994   4617
74  1995   5137
75  1996   7796
76  1997   6564
77  1998   7405
78  1999   7298
79  2000   7867
80  2001   7580
81  2002   9771
82  2003  11647
83  2004  25827
84  2005  25616
85  2006  15632
86  2007  10454
87  2008  13278
88  2009  16858
89  2010  27550
90  2011  18719
91  2012  48277
92  2013  28639
93  2014  32971
94  2015  20762
95  2016  17972
96  2017  18975
97  2018  15609
98  2019  18617
99  2020   6124
100 2021   2116
```

I want a plot of case number per year.

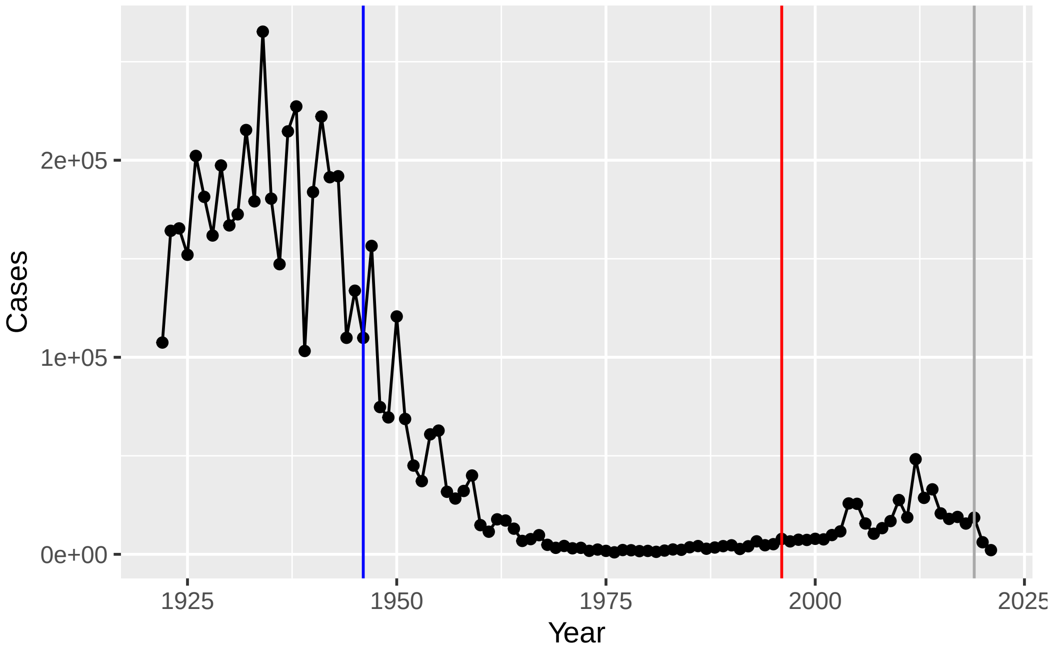
```
library(ggplot2)

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

```r
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?

```r
base +
  geom_vline(xintercept=1946, col="blue") +
  geom_vline(xintercept=1996, col="red") +
  geom_vline(xintercept=2019, col="darkgray")
```



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

It is possible that the trend of less vaccination of infants led to an increase of childhood illness such as Pertussis. Also, the aP vaccine could be less effective than the wP vaccine.

CMI-PB

A systems vaccinology project to figure out what is going on with aP vs. wP immune responses.

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

Basically "key":"value" pair format.

We will use the jsonlite pakage 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
```

Q. How many individuals/subjects are in this dataset?

```r
nrow(subject)
```

```
[1] 118
```

Q4. How many aP and wP infancy vaccinated subjects are in the dataset?

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

```

aP wP 
60 58 
```

Q5. How many Male and Female subjects/patients are in the dataset?

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

```

Female   Male 
    79     39 
```

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

```r
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.

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

```r
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 subjects and specimens in one place

```r
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
```

```r
meta <- inner_join(subject, specimen)
```

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

```r
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 take our new `meta` table and join it with our Ab table `ab_titer`:

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

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

```r
dim(abdata)
```

```
[1] 41775    20
```

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

```r
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 measurements 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
```

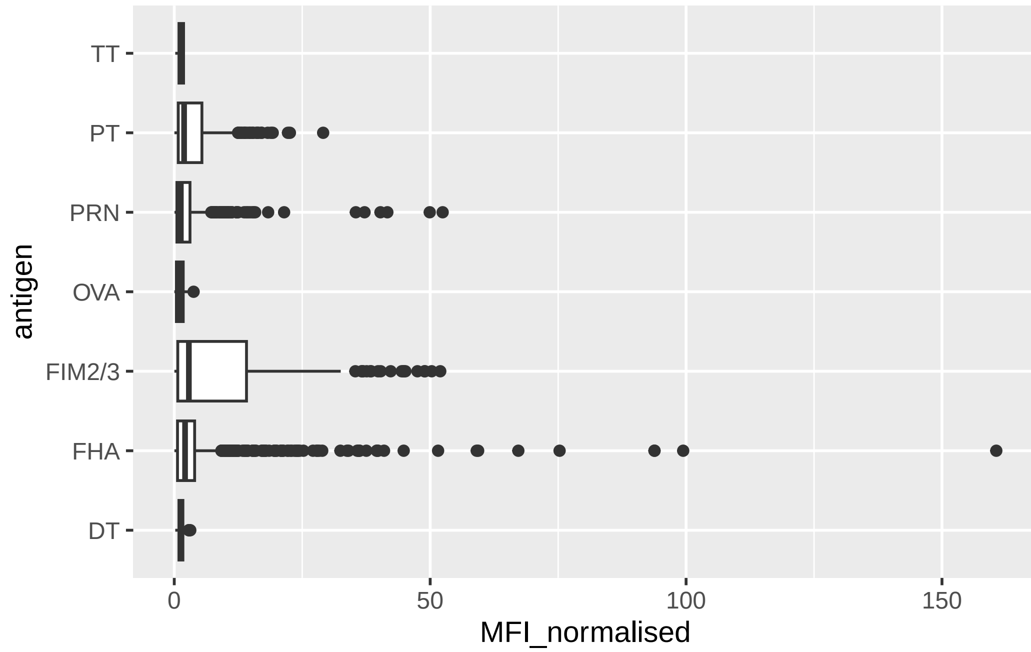
Examine IgG Ab titer levels

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

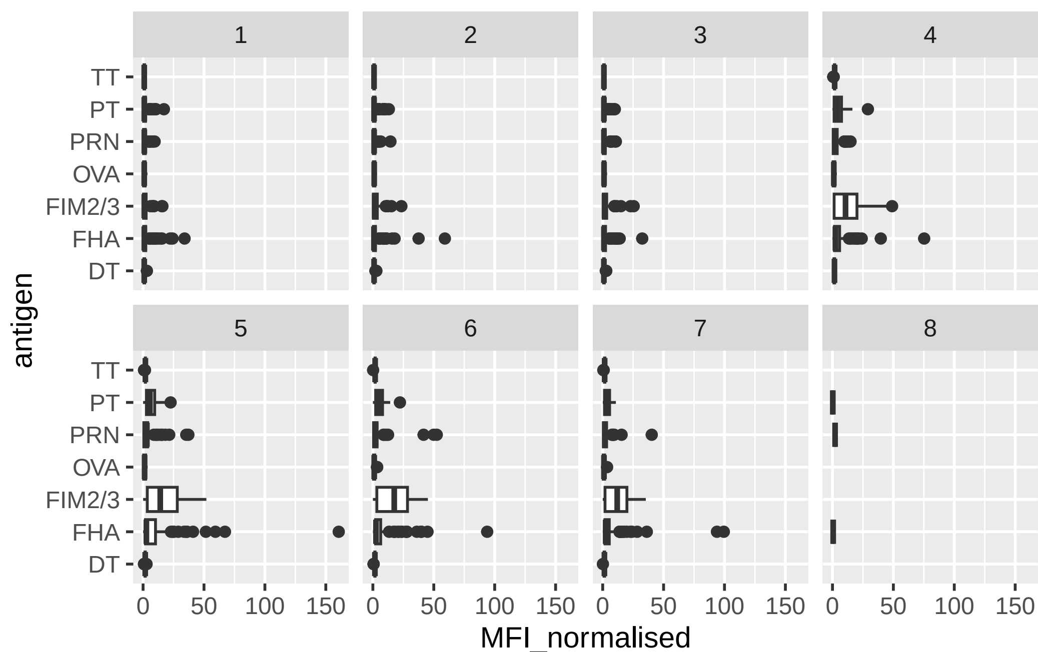
```
igg <- abdata %>% filter(isotype == "IgG")
head(igg)
```

```
  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
```

```
library(ggplot2)
base <- ggplot(igg) +
  aes(MFI_normalised,antigen) +
  geom_boxplot()
base
```




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



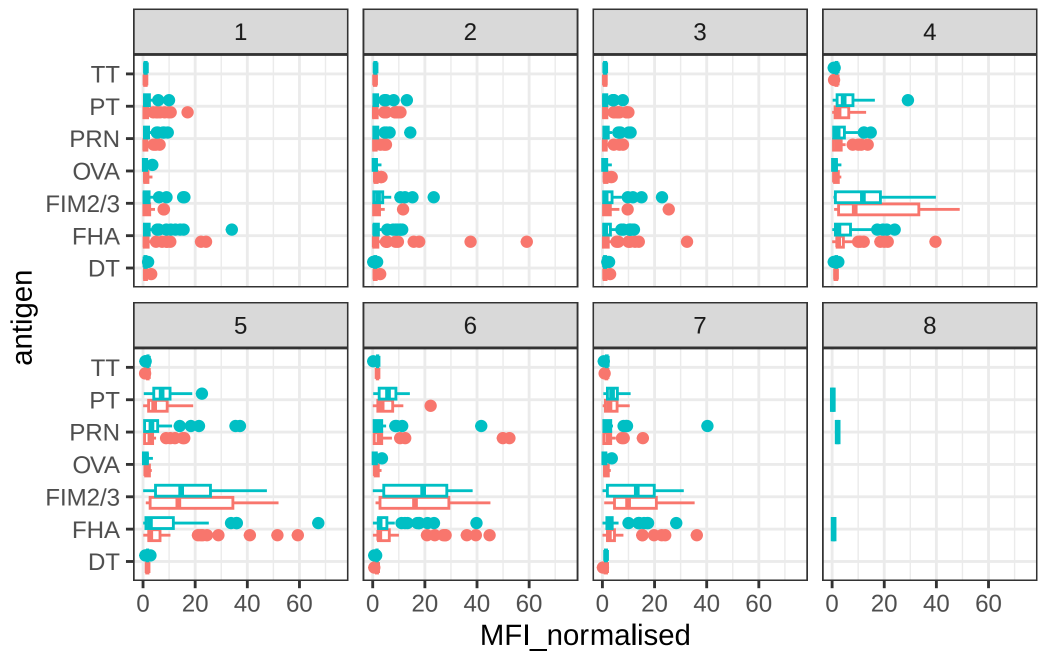
```r
table(igg$visit)
```

```

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

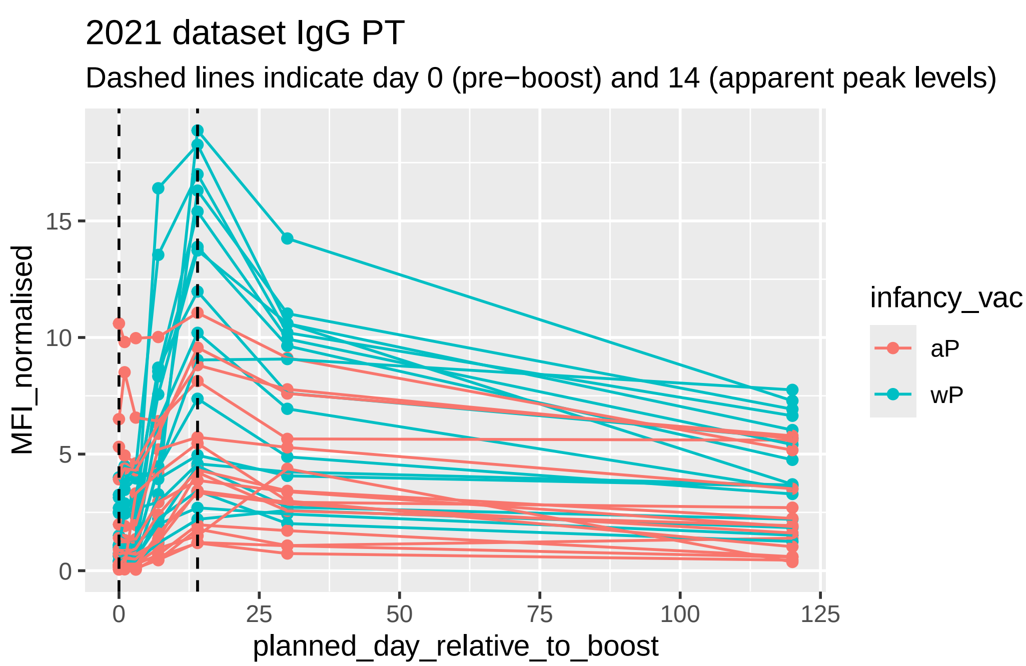
Let's dig in a little bit more...

```r
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()`).
```



```r
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)")
```




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

```

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