Mini-Project: Investigating Pertussis Resurgence

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1. Investigating pertussis cases by year

Is Petussis on the rise?

The CDC track reported Petussis cases in US and mkae thier data available here:

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),
  No..Reported.Pertussis.Cases = c(107473,
                                     164191,165418,152003,202210,181411,
                                     161799,197371,166914,172559,215343,179135,
```

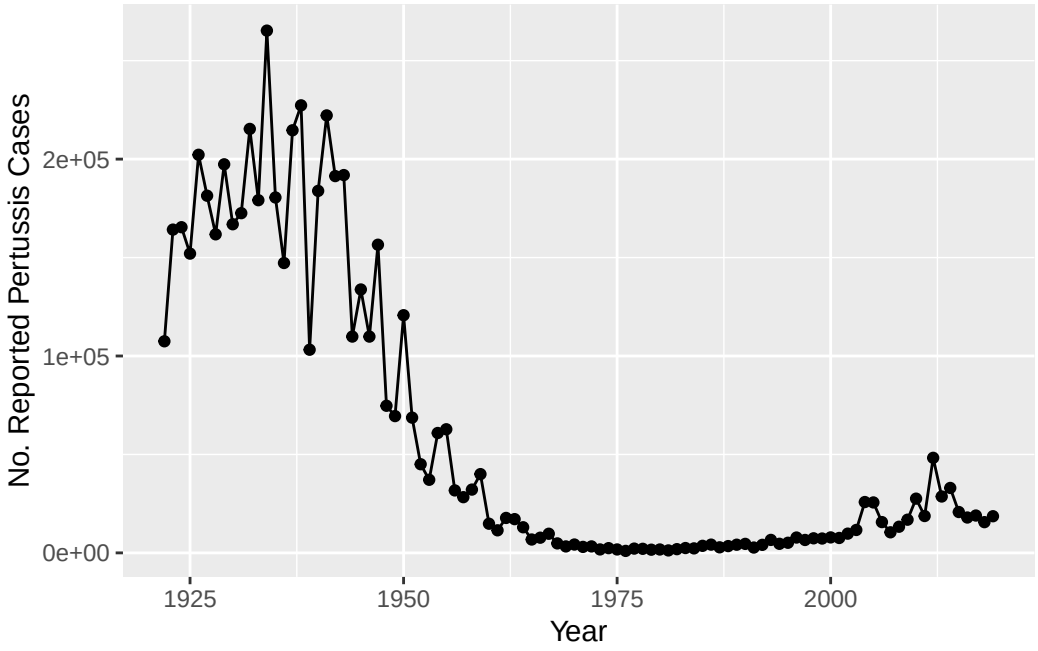
```
                                265269,180518,147237,214652,227319,103188,
                                183866,222202,191383,191890,109873,
                                133792,109860,156517,74715,69479,120718,
                                68687,45030,37129,60886,62786,31732,28295,
                                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)
)
```

```
head(cdc)
```

```
  Year No..Reported.Pertussis.Cases
1 1922                        107473
2 1923                        164191
3 1924                        165418
4 1925                        152003
5 1926                        202210
6 1927                        181411
```

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.

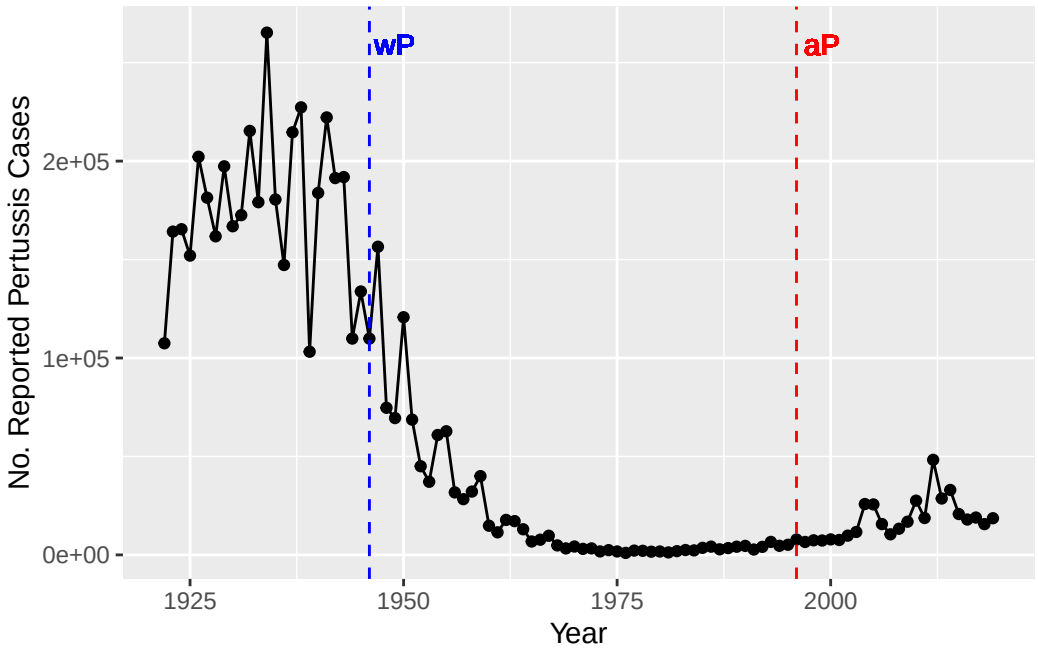
```
library(ggplot2)

cdc_plot <- ggplot(cdc) +
  aes(cdc$Year, cdc$No..Reported.Pertussis.Cases) +
  geom_point() +
  geom_line() +
  labs(main = "Pertussis Cases by Year (1922-2019",
       x = "Year", y = "No. Reported Pertussis Cases")

print(cdc_plot)
```



2. A tale of two vaccines (wP & aP)

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?

```
cdc_plot +
  geom_vline(xintercept = 1946, color = "blue", linetype = 2) +
  geom_text(x = 1949, y = 259000, label = "wP", color = "blue") +
  geom_vline(xintercept = 1996, color = "red", linetype = 2) +
  geom_text(x = 1999, y = 259000, label = "aP", color = "red")
```



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

Ans: After the introduction of the aP vaccine in 1996, pertussis cases in the United States only stayed low for a short time and then increased once again. One of the possible explanations for this observed trend is the pertussis bacteria, Bordetella pertussis, underwent evolution pressure that helped them evolve new variants, which were able to escape from the new aP vaccine immunity.

3. Exploring CMI-PB data

The CMI-PB API returns JSON data

```
# Allows us to read, write and process JSON 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$race, subject$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

Side-Note: Working with dates

```
library(lubridate)
```

```
today()
```

```
[1] "2022-11-29"
```

Q7. Using this approach determine (i) the average age of wP individuals, (ii) the average age of aP individuals; and (iii) are they significantly different?

```
# Use today date to calculate age in days
subject$age <- today() - ymd(subject$year_of_birth)
```

```
library(dplyr)
```

```
# The average age of aP individuals
ap <- subject %>% filter(infancy_vac == "aP")
ap_age <- round(summary(time_length(ap$age, "years")))
print(ap_age)
```

```
 Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
   23      25      26      25      26      27
```

```
# The average age of wP individuals
wp <- subject %>% filter(infancy_vac == "wP")
wp_age <- round(summary(time_length(wp$age, "years")))
```

```
print(wp_age)
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
     28      32      35      36      40      55
```

```
# Perform Student's t-test to see if they are significantly different
t.test(ap_age, wp_age, paired = TRUE)
```

```
    Paired t-test

data:  ap_age and wp_age
t = -3.6457, df = 5, p-value = 0.01481
alternative hypothesis: true mean difference is not equal to 0
95 percent confidence interval:
 -21.029519  -3.637148
sample estimates:
mean difference
      -12.33333
```

Ans: Since the p-value = 0.01481 < 0.05, the average age of aP individuals and the average age of wP individuals are significantly different

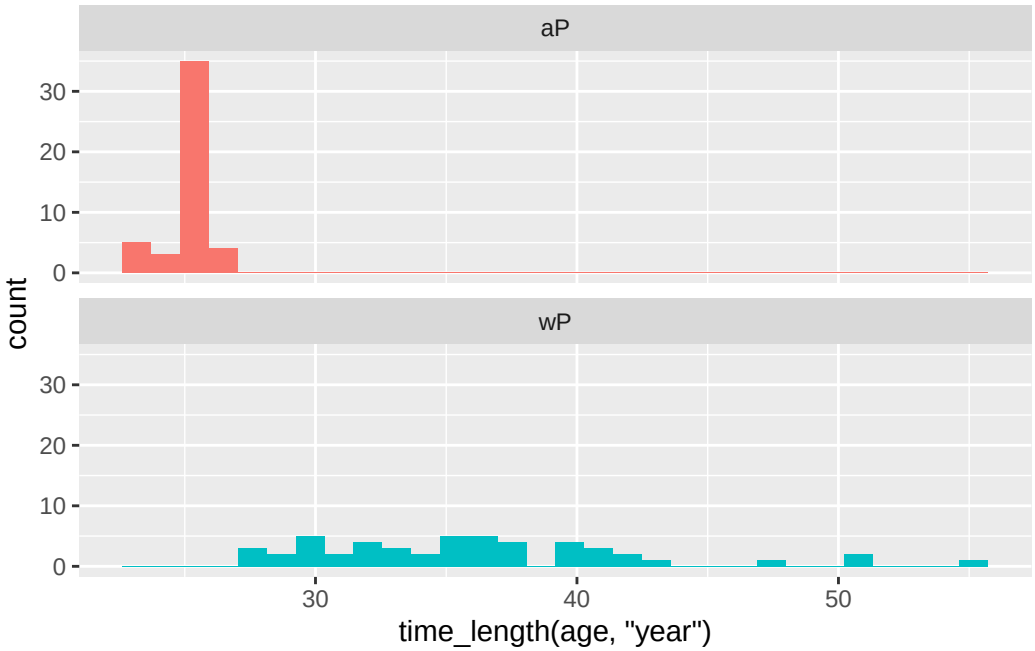
Q8. Determine the age of all individuals at time of boost?

```
int <- ymd(subject$date_of_boost) - ymd(subject$year_of_birth)
age_at_boost <- round(time_length(int, "year"))
head(age_at_boost)
```

```
[1] 31 51 34 29 26 29
```

Q9. With the help of a faceted boxplot (see below), do you think these two groups are significantly different?

```
ggplot(subject) +
  aes(time_length(age, "year"),
      fill = as.factor(infancy_vac)) +
  geom_histogram(show.legend = FALSE) +
  facet_wrap(vars(infancy_vac), nrow = 2)
```



Joining multiple tables

```
# Complete the API URLs...

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

titer <- read_json("https://www.cmi-pb.org/api/ab_titer", 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
```

```
head(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
```

Q9. Complete the code to join 'specimen' and 'subject' tables to make a new merged data frame containing all specimen records along with their associated subject details:

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

```
Joining, by = "subject_id"
```

```
dim(meta)
```

```
[1] 729  14
```

```
head(meta)
```

```
  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 infancy_vac biological_sex
1                             0         Blood     1          wP         Female
2                           736         Blood    10          wP         Female
3                             1         Blood     2          wP         Female
4                             3         Blood     3          wP         Female
5                             7         Blood     4          wP         Female
6                            14         Blood     5          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
         age
1 13481 days
2 13481 days
3 13481 days
4 13481 days
5 13481 days
6 13481 days
```

Q10. Now using the same procedure join 'meta' with 'titer' data so we can further analyze this data in terms of time of visit aP/wP, male/female etc.

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

```
Joining, by = "specimen_id"
```

```
dim(abdata)
```

```
[1] 32675    21
```

```
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 actual_day_relative_to_boost
1 UG/ML                 2.096133          1                           -3
2 IU/ML                29.170000          1                           -3
3 IU/ML                 0.530000          1                           -3
4 IU/ML                 6.205949          1                           -3
5 IU/ML                 4.679535          1                           -3
6 IU/ML                 2.816431          1                           -3
  planned_day_relative_to_boost specimen_type visit infancy_vac biological_sex
1                             0         Blood     1          wP         Female
2                             0         Blood     1          wP         Female
3                             0         Blood     1          wP         Female
4                             0         Blood     1          wP         Female
5                             0         Blood     1          wP         Female
6                             0         Blood     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
        age
1 13481 days
2 13481 days
3 13481 days
4 13481 days
5 13481 days
6 13481 days
```

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
```

Ans: The number of visit 8 specimens is much lower compared to other visits

4. Examine IgG1 Ab titer levels

In 'abdata' dataset, filter() for IgG1 'isotype' and exclude the small number of visit 8 entries.

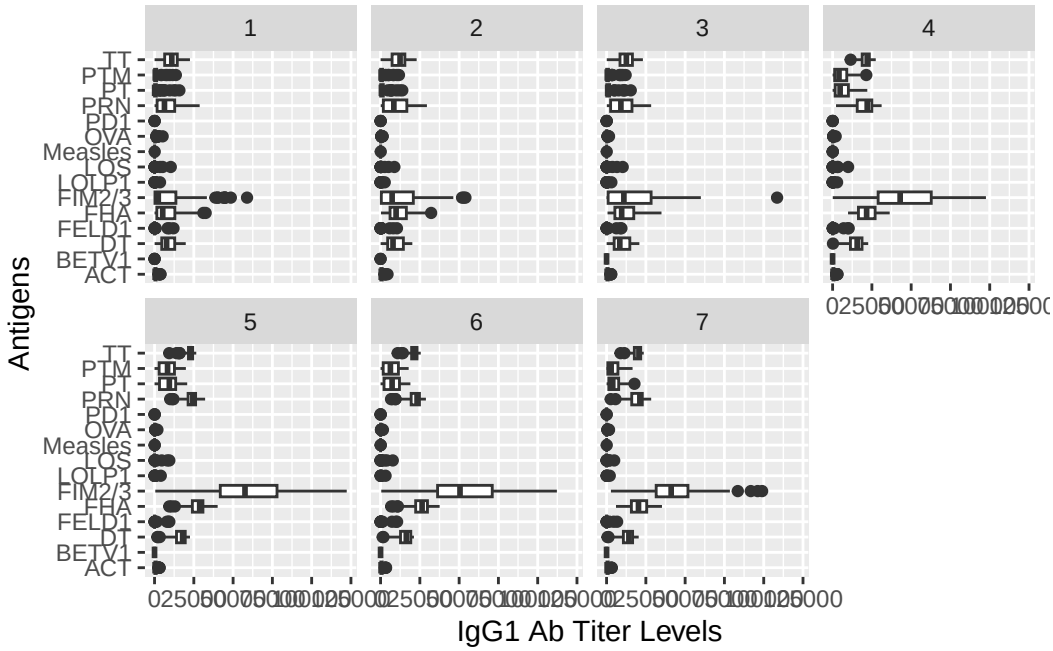
```
ig1 <- abdata %>% filter(isotype == "IgG1", visit!=8)
head(ig1)
```

```
  specimen_id isotype is_antigen_specific antigen        MFI MFI_normalised
1           1    IgG1                TRUE     ACT 274.355068      0.6928058
2           1    IgG1                TRUE     LOS  10.974026      2.1645083
3           1    IgG1                TRUE   FELD1   1.448796      0.8080941
4           1    IgG1                TRUE   BETV1   0.100000      1.0000000
5           1    IgG1                TRUE   LOLP1   0.100000      1.0000000
6           1    IgG1                TRUE Measles  36.277417      1.6638332
   unit lower_limit_of_detection subject_id actual_day_relative_to_boost
1 IU/ML                3.848750          1                           -3
2 IU/ML                4.357917          1                           -3
3 IU/ML                2.699944          1                           -3
4 IU/ML                1.734784          1                           -3
5 IU/ML                2.550606          1                           -3
6 IU/ML                4.438966          1                           -3
  planned_day_relative_to_boost specimen_type visit infancy_vac biological_sex
1                             0         Blood     1          wP         Female
2                             0         Blood     1          wP         Female
```

```
3                            0         Blood     1          wP         Female
4                            0         Blood     1          wP         Female
5                            0         Blood     1          wP         Female
6                            0         Blood     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
         age
1 13481 days
2 13481 days
3 13481 days
4 13481 days
5 13481 days
6 13481 days
```

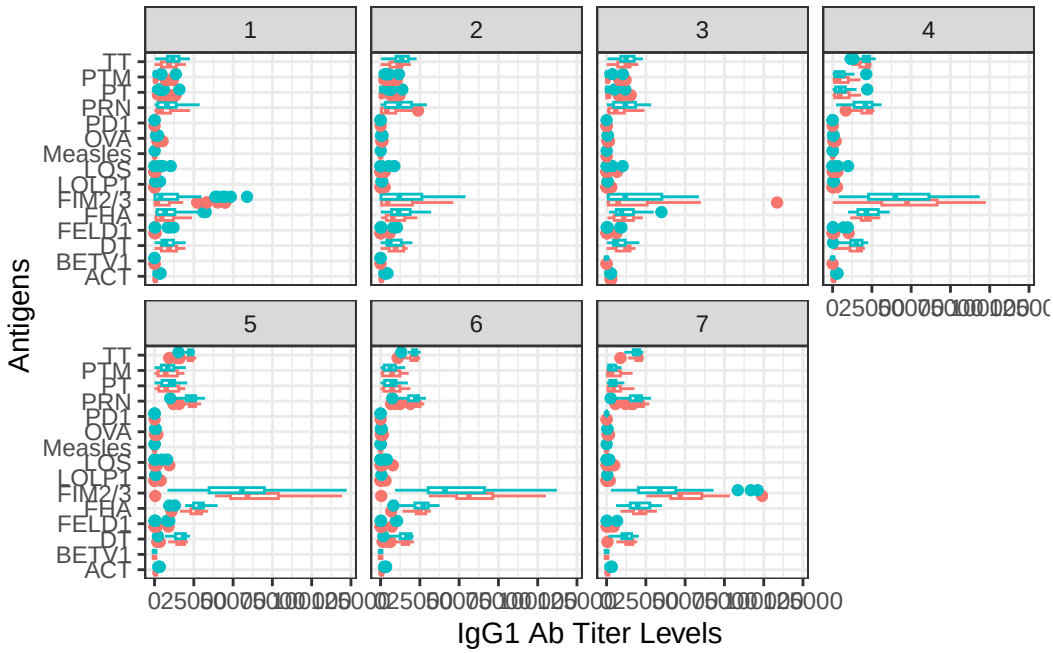
Q13. Complete the following code to make a summary boxplot of Ab titer levels for all antigens:

```
ggplot(ig1) +
  aes(ig1$MFI, ig1$antigen) +
  geom_boxplot() +
  labs(x = "IgG1 Ab Titer Levels", y = "Antigens") +
  facet_wrap(vars(visit), nrow = 2)
```



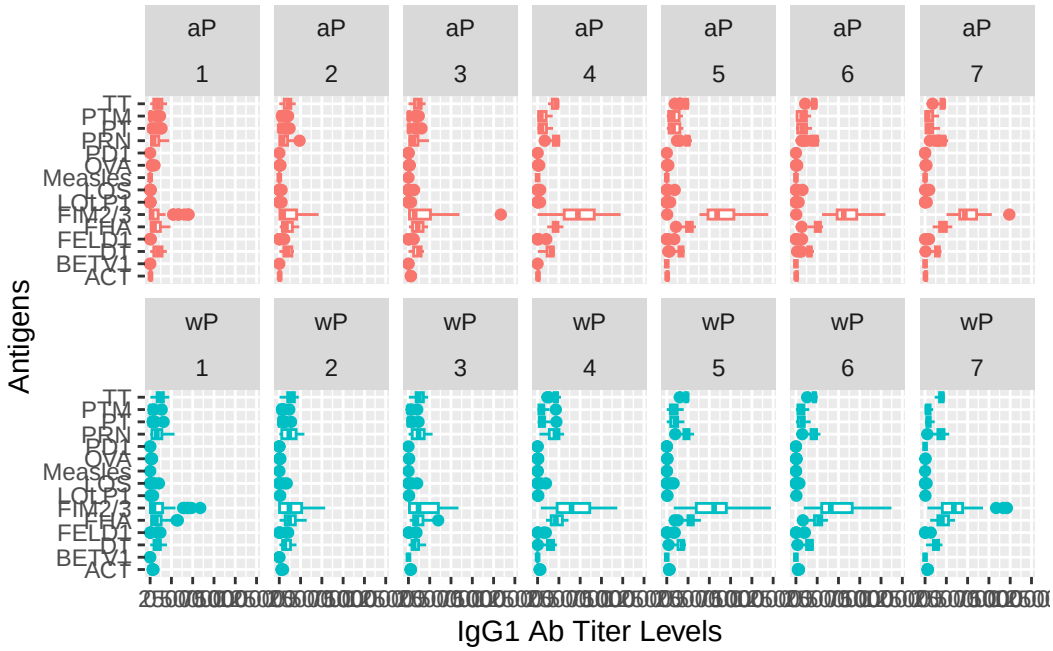
Examine differences between 'wP' and 'aP' by setting color and/or facet values of the plot to include infancy_vac status

```
ggplot(ig1) +
  aes(ig1$MFI, ig1$antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  labs(x = "IgG1 Ab Titer Levels", y = "Antigens") +
  facet_wrap(vars(visit), nrow=2) +
  theme_bw()
```



Another version of this plot adding infancy_vac to the faceting:

```
ggplot(ig1) +
  aes(ig1$MFI, ig1$antigen, col = infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  labs(x = "IgG1 Ab Titer Levels", y = "Antigens") +
  facet_wrap(vars(infancy_vac, visit), nrow = 2)
```


aP
1
2
3
4
5
6
7
wP
Antigens
TT
PTM
PT
PRN
PD1
OVA
Measles
LOS
LOtP1
FIM2/3
FHA
FELD1
DT
BETV1
ACT
IgG1 Ab Titer Levels