

lab19: Pertussis Mini Project

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Pertussis (whooping cough) is a highly infectious lung infection caused by the bacteria *B. Pertussis*. The CDC tracks case numbers in the US and makes this data available online: https://www.cdc.gov/pertussis/php/surveillance/pertussis-cases-by-year.html?CDC_AAref_Val=https://www.cdc.gov/pertussis/surv-reporting/cases-by-year.html

1. Investigating pertussis cases by year - warm up

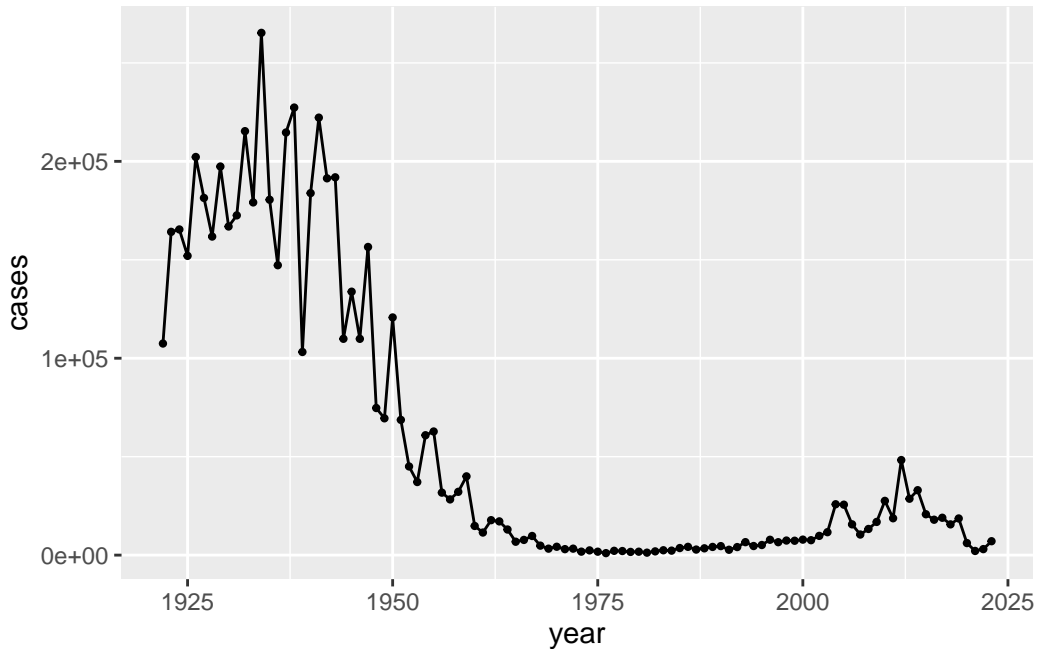
Q1. With the help of the R “addin” package datapasta assign the CDC pertussis case number data to a data frame called cdc and use ggplot to make a plot of cases numbers over time.

Theres no link to a csv file, so we need to scrape this data from the webpage. Use datapasta package. Copy the data table you want from a website, then click addins on the top menu, and paste as dataframe in the ‘datapasta’ section.

make graph - cases over time

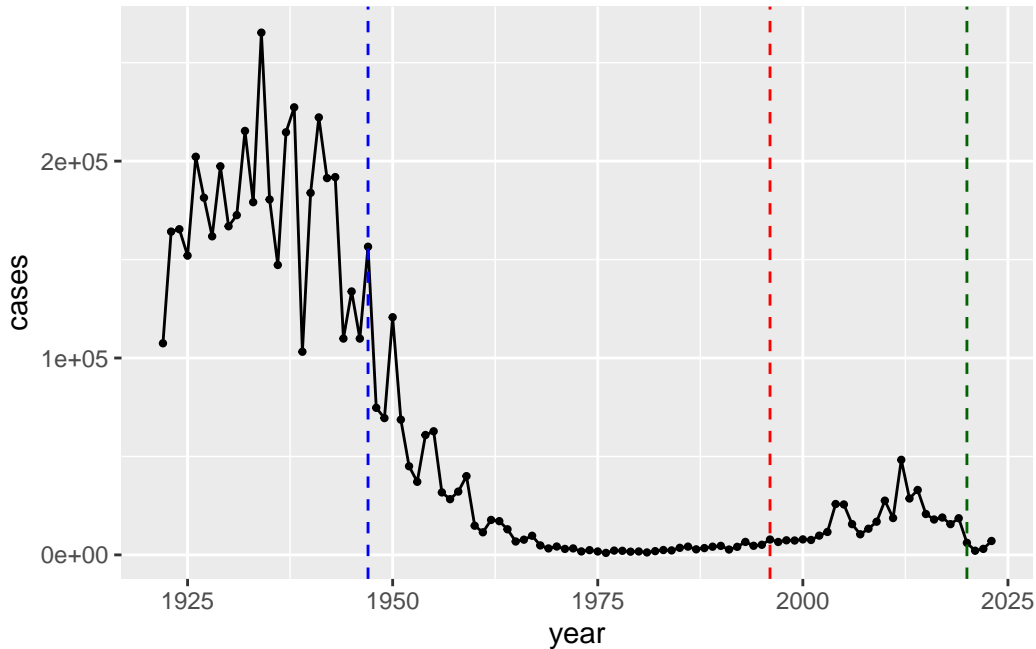
```
library(ggplot2)

ggplot(cdc, aes(year, cases))+
  geom_line()+
  geom_point(size=0.8)
```



Q2. Using the ggplot `geom_vline()` function add lines to your previous plot for the 1946 introduction of the wP (whole cell) vaccine, deployment in 1947, and the 1996 switch to aP vaccine (see example in the hint below). Add a line for 2020, also.

```
ggplot(cdc, aes(year, cases))+
  geom_line()+
  geom_point(size=0.8)+
  geom_vline(xintercept=1947, col="blue", linetype="dashed")+
  geom_vline(xintercept=1996, col="red", linetype="dashed")+
  geom_vline(xintercept=2020, col="darkgreen", linetype="dashed")
```



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

Why is there a spike in the mid-2000s? Anti-vaccine movement perhaps? Introduction of social media in the 2010s was able to spread anti-vaccine rhetoric. Maybe Ap and Wp vaccines have a fundamental difference in lasting immunity, Ap perhaps doesn't have as long-lasting of an immunity as Wp hence the need for boosters that not everyone may get.

Why does aP induced protection wane faster than Wp?

CMI-PB project

The CMI-Pertussis Boost (PB) project focusses on gathering data for this topic,. What is distinct between aP and wP individuals over time. Data is available in a JSON format, can be read in with `read_json()` in the **jsonlite** package.

```
library(jsonlite)

subject<-read_json("https://www.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

Q4. How many “subjects” are in this dataset

```
nrow(subject)
```

```
[1] 172
```

ans: 172 subjects

Q5. How many wP and aP primed subjects are there in this dataset

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

```
aP wP
87 85
```

There are 87 aP and 85 wP subjects in this dataset.

Q6. What is the biological sex and race breakdown of these subjects - is this representative of a population

```
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

overrepresentation of white females in this dataset - not representative of the US dataset.

Lets read more tables from the CBI-PB databse API. Specimen IDs stay consistent between dataframes

```
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)
```

Want to take subject and speciment table, and merge them using `inner_join()` or `full_join()`. inner join takes whats common between the two datasets, vs full join will just add everything even if data is missing form one dataset. We want to use inner join in `dplyr`

```
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) #notice it says joined by subject ID, since that is the common column between the 1
```

	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

```
#also want to join the antibody titer table
```

```
ab_data<-inner_join(meta,ab_titer) #this is quite a big dataframe now.
```

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

Q7. how many different antibody isotypes are there

```
unique(ab_data$isotype)
```

```
[1] "IgE" "IgG" "IgG1" "IgG2" "IgG3" "IgG4"
```

There are 6 isotypes

Q8. How many different antigens are there

```
unique(ab_data$antigen)
```

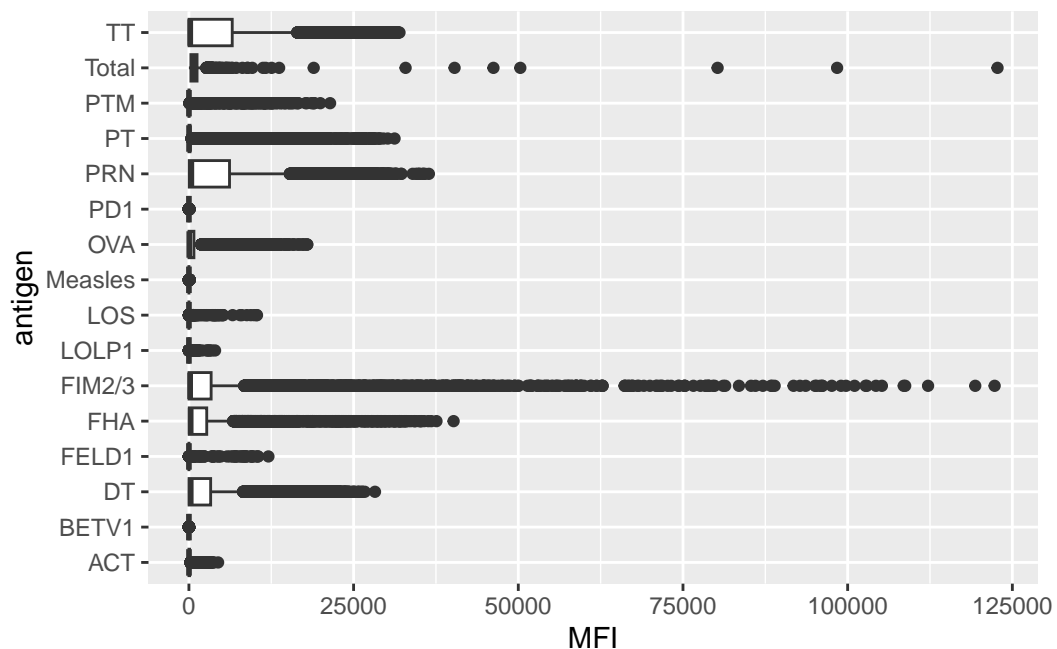
```
[1] "Total" "PT" "PRN" "FHA" "ACT" "LOS" "FELD1"  
[8] "BETV1" "LOLP1" "Measles" "PTM" "FIM2/3" "TT" "DT"  
[15] "OVA" "PD1"
```

There are 16 types of antigens. Measles can be considered a negative control?

Q9. Lets plot MFI vs. antigen

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

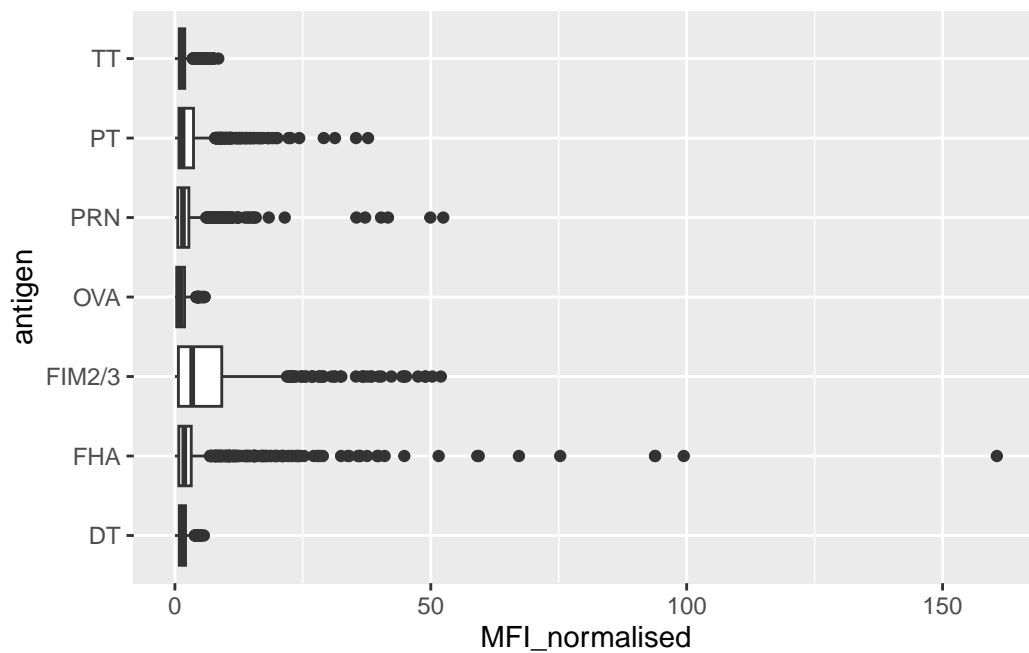
Warning: Removed 1 row containing non-finite outside the scale range
(`stat_boxplot()`).



Focus on IgG

IgG is crucial for long-term immunity and respondign to bacterial/viral infections

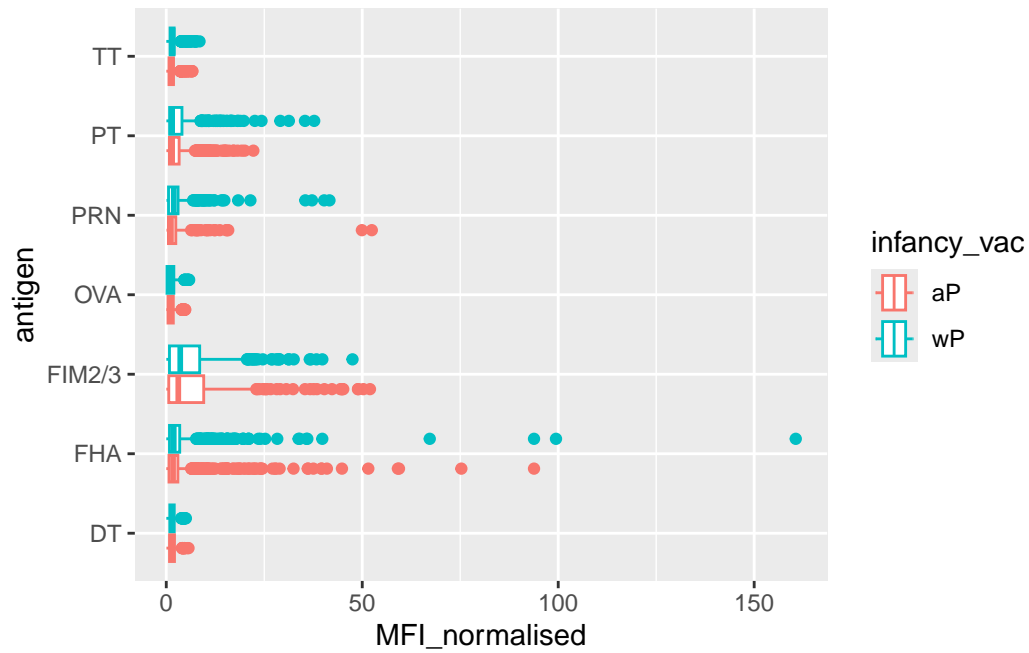
```
igg_ab<-ab_data %>%  
  filter(isotype=="IgG")  
  
ggplot(igg_ab,aes(MFI_normalised,antigen))+  
  geom_boxplot()
```



Difference between aP and wP?

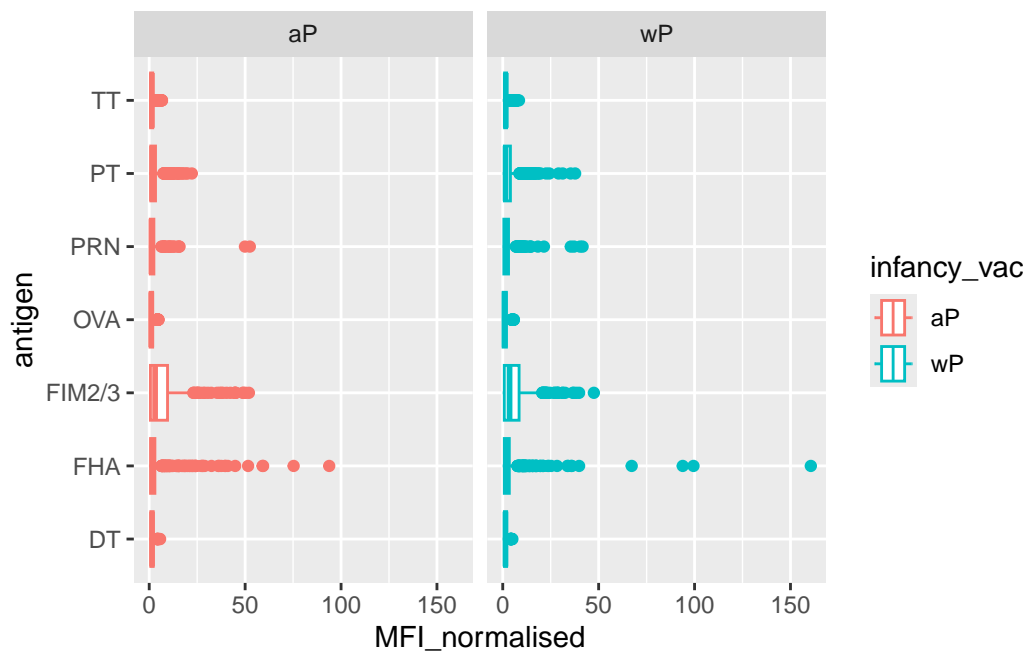
We can colour by infancy_vac

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



We can also facet by aP vs. wP column

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



Time course analysis

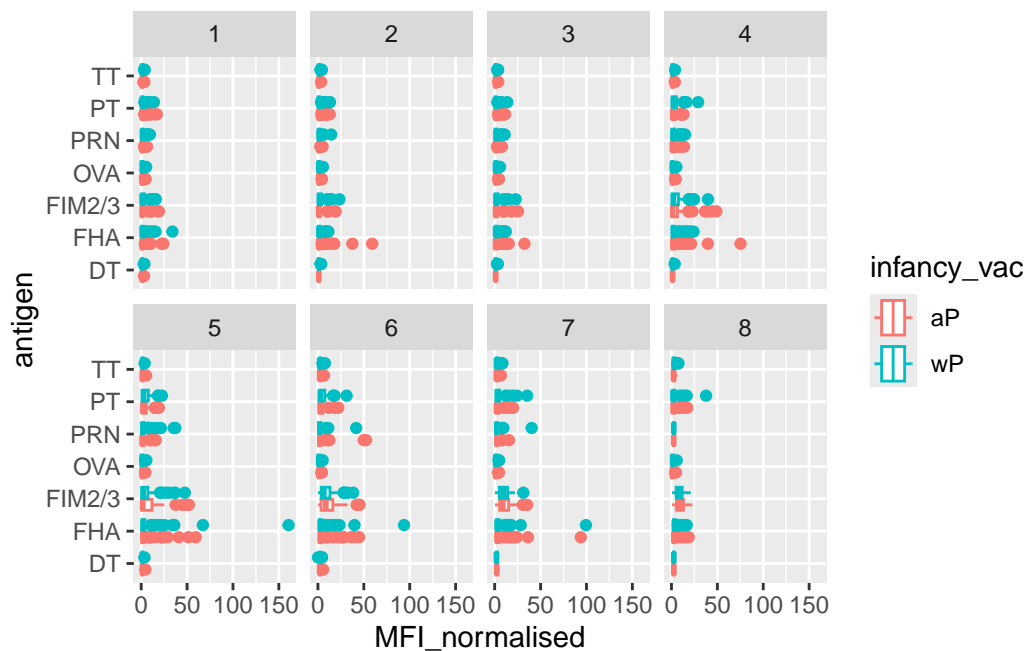
look at visits for each patient as a proxy for time. Will use visits 1-8 since some of the later ones aren't as complete

```
table(ab_data$visit)
```

visit	count
1	8280
2	8280
3	8420
4	8420
5	8420
6	8100
7	7700
8	2670
9	770
10	686
11	105
12	105

```
vis<-igg_ab%>%
  filter(visit%in% 1:8)

ggplot(vis,aes(MFI_normalised,antigen,col=infancy_vac))+
  geom_boxplot()+
  facet_wrap(~visit,nrow=2)
```

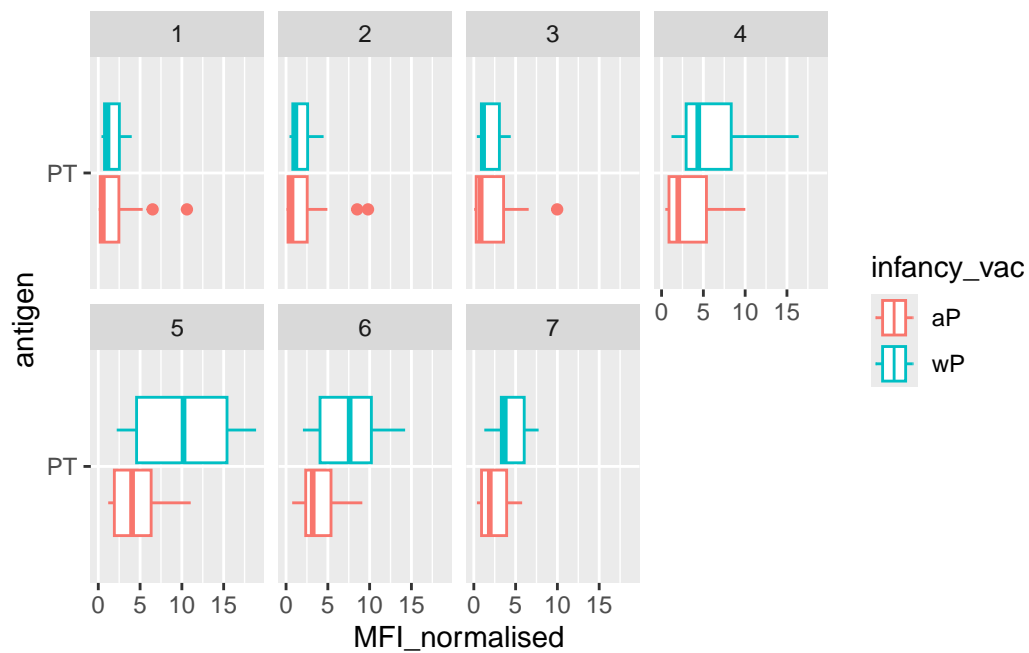


Some antigens like FIM2/3 appears to increase over time, FIM2/3 refers to Fimbriae 2 and 3 which are antigens derived from *B. Pertussis* bacterium - causative agent of whooping cough. These are delivered in the vaccines.

Time course of PT

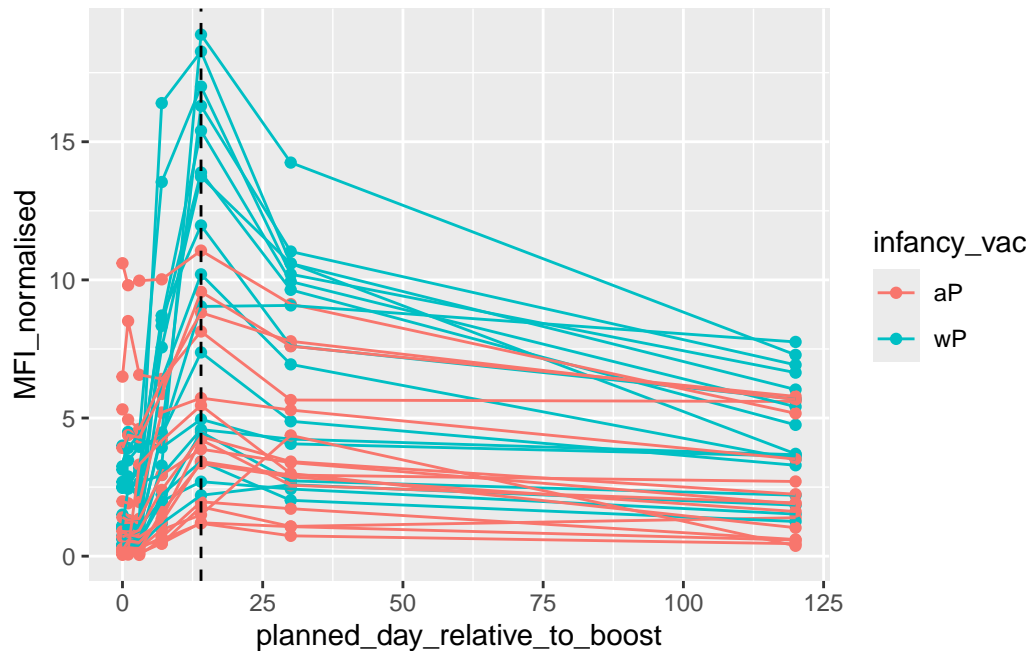
```
PT_ab<-ab_data %>%
  filter(isotype=="IgG")%>%
  filter(antigen=="PT")%>%
  filter(dataset=="2021_dataset")

ggplot(PT_ab,aes(MFI_normalised,antigen,col=infancy_vac))+
  geom_boxplot()+
  facet_wrap(~visit,nrow=2)
```



Over time, wP PT antigen levels appear to take over aP, indicating that the effects of wP are longer lasting than aP.

```
ggplot(PT_ab,aes(planned_day_relative_to_boost,MFI_normalised,
                  col=infancy_vac,
                  group=subject_id))+
  geom_point()+
  geom_line()+
  geom_vline(xintercept = 14,linetype="dashed")
```



This plot shows that around 14 days post booster shot, immunity peaks for both vaccine types. Over time, aP immunity degrades faster than wP. It also appears that wP MFI peaks much higher than aP MFI.

System setup - prints out information about my setup to run this analysis.

```
sessionInfo()
```

```
R version 4.2.3 (2023-03-15)
Platform: x86_64-apple-darwin17.0 (64-bit)
Running under: macOS Big Sur ... 10.16

Matrix products: default
BLAS:   /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRlapack.dylib

locale:
 [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8

attached base packages:
 [1] stats      graphics  grDevices  utils      datasets  methods   base
```

other attached packages:

[1] dplyr_1.1.4 jsonlite_1.8.8 ggplot2_4.0.0 datapasta_3.1.0

loaded via a namespace (and not attached):

[1] rstudioapi_0.17.1	knitr_1.50	magrittr_2.0.4	tidyselect_1.2.1
[5] R6_2.6.1	rlang_1.1.6	fastmap_1.2.0	tools_4.2.3
[9] grid_4.2.3	gtable_0.3.6	xfun_0.54	cli_3.6.5
[13] withr_3.0.2	htmltools_0.5.8.1	yaml_2.3.10	digest_0.6.33
[17] tibble_3.3.0	lifecycle_1.0.4	S7_0.2.0	RColorBrewer_1.1-3
[21] farver_2.1.2	vctrs_0.6.5	glue_1.8.0	evaluate_1.0.5
[25] rmarkdown_2.30	labeling_0.4.3	pillar_1.11.1	compiler_4.2.3
[29] generics_0.1.4	scales_1.4.0	pkgconfig_2.0.3	