

Class 17: Investigating Pertussis

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Pertussis or whooping cough, is a highly contagious lung infection caused by a bacteria *B. pertussis*.

The CDC tracks reported cases in the U.S. since the 1920s.

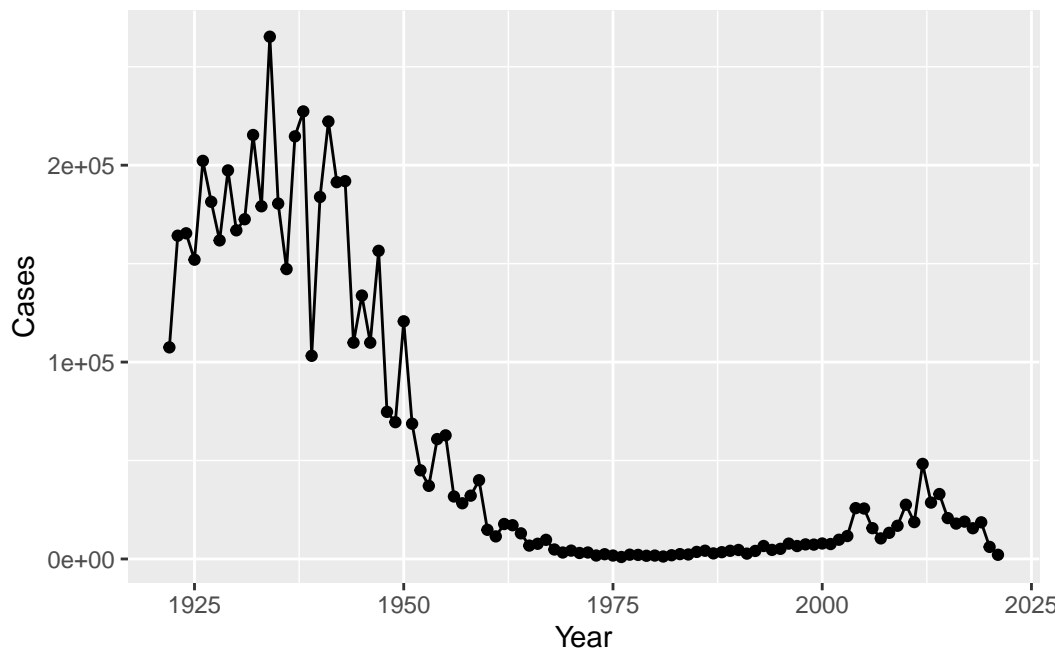
```
cdc <- data.frame(
  Year = c(1922L,1923L,1924L,1925L,
           1926L,1927L,1928L,1929L,1930L,1931L,
           1932L,1933L,1934L,1935L,1936L,
           1937L,1938L,1939L,1940L,1941L,1942L,
           1943L,1944L,1945L,1946L,1947L,
           1948L,1949L,1950L,1951L,1952L,
           1953L,1954L,1955L,1956L,1957L,1958L,
           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)
```

```
)
```

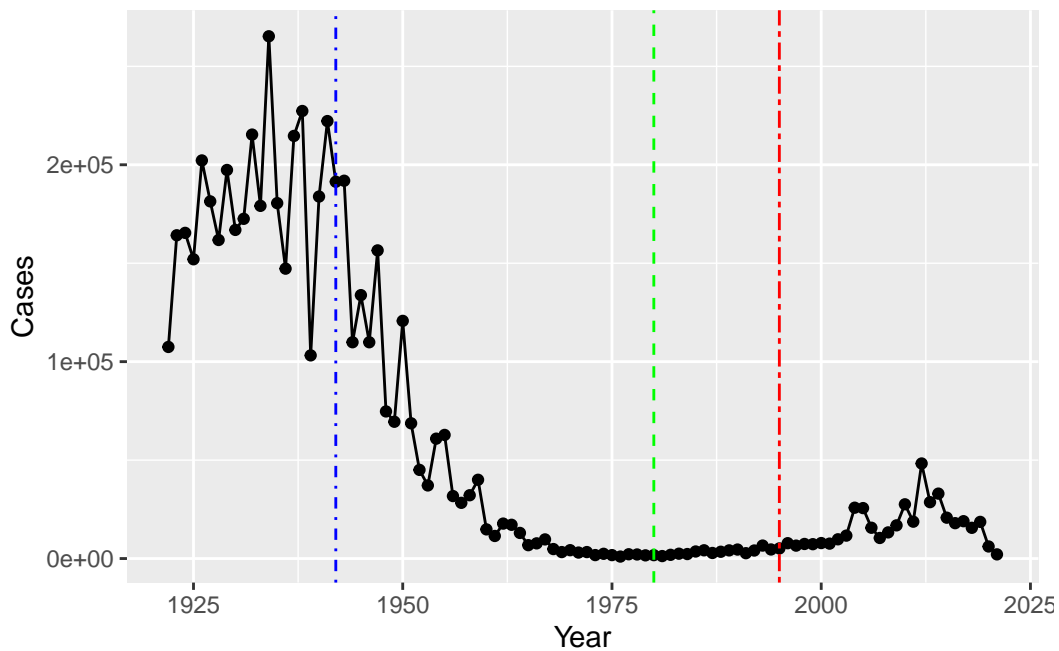
We can now plot the number of reported pertussis cases per year in the U.S.

```
library(ggplot2)
ggplot(cdc)+
  aes(Year,Cases) +
  geom_point() +
  geom_line()
```



The first big whole-cell vaccine program started in 1942.

```
ggplot(cdc)+  
  aes(Year,Cases) +  
  geom_point() +  
  geom_line() +  
  geom_vline(xintercept = 1942, color = "blue", linetype = 4) +  
  geom_vline(xintercept = 1980, color = "green",linetype = 2) +  
  geom_vline(xintercept = 1995, color = "red",linetype = 6)
```



Something big is happening with pertussis cases and big outbreaks are once again a major public health concern!

One of the main hypothesis for the increasing case numbers is waning vaccine efficacy with the newer aP vaccine.

Enter the CMI-PB project, which is studying this problem on a large scale. Let's see what data they have. Their data is available in the JSON format ("key:value" pair style). We will use the "jsonlite" package to read their 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 many 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

Now let's read some more database tables from CMI-PB:

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

I want to “join” (a.k.a “merge”) the `subject` and `specimen` tables together. I will use the `**dplyr**` package for this

```
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	736	736	Blood
3	1	1	Blood
4	3	3	Blood
5	7	7	Blood
6	11	14	Blood

	visit
1	1
2	10
3	2
4	3
5	4
6	5

```
ab <- read_json("http://cmi-pb.org/api/ab_titer", simplifyVector = T)
```

```
head(ab)
```

	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

Now I can join the “meta” that we made above and contains all info about the subjects and sepcimens with this ab data

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

Joining with `by = join_by(specimen_id)`

```
dim(abdata)
```

```
[1] 32675    20
```

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

```

There are way less visit 8 specimens because the project is still ongoing and we do not have that data individual data yet.

Examine IgG1 Ab titer levels

We will use the `filter()` function from `dyplr` to focus on just IgG1 isotype and visits 1 to 7 (i.e. exclude visit 8 as there are not many specimens there yet).

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

```

  subject_id infancy_vac biological_sex ethnicity race
1          1          1          wP      Female Not Hispanic or Latino White
2          1          1          wP      Female Not Hispanic or Latino White
3          1          1          wP      Female Not Hispanic or Latino White
4          1          1          wP      Female Not Hispanic or Latino White
5          1          1          wP      Female Not Hispanic or Latino White
6          1          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    IgG1             TRUE      ACT 274.355068    0.6928058 IU/ML

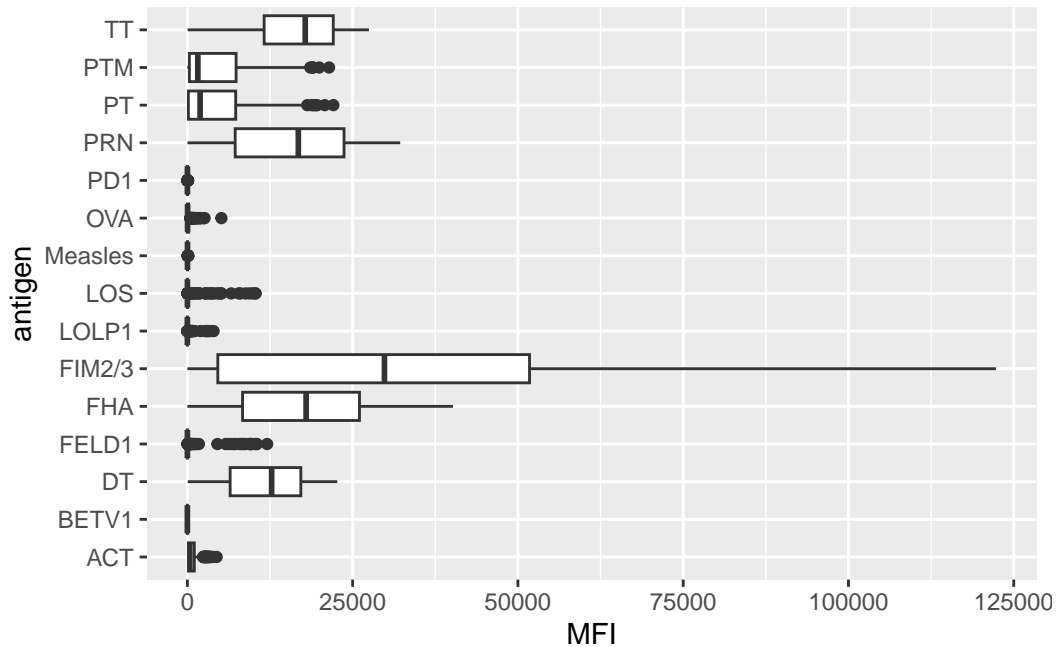
```


2	1	IgG1	TRUE	LOS	10.974026	2.1645083	IU/ML
3	1	IgG1	TRUE	FELD1	1.448796	0.8080941	IU/ML
4	1	IgG1	TRUE	BETV1	0.100000	1.0000000	IU/ML
5	1	IgG1	TRUE	LOLP1	0.100000	1.0000000	IU/ML
6	1	IgG1	TRUE	Measles	36.277417	1.6638332	IU/ML

	lower_limit_of_detection
1	3.848750
2	4.357917
3	2.699944
4	1.734784
5	2.550606
6	4.438966

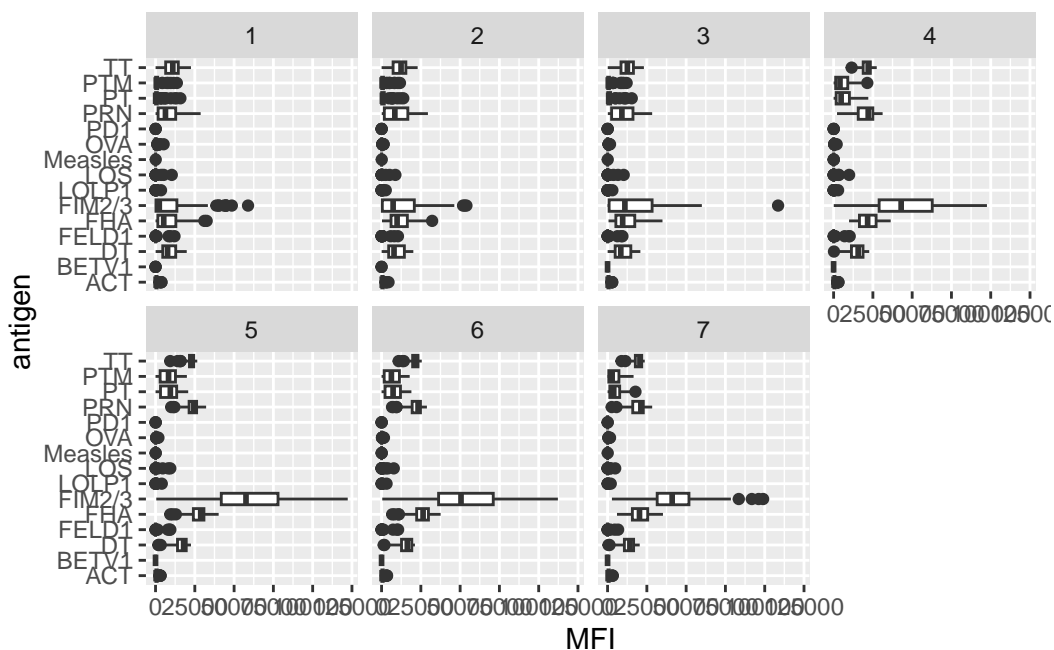
Box plot of antigen levels over time.

```
ggplot(ig1) +
  aes(MFI, antigen ) +
  geom_boxplot()
```



and facet by visit

```
ggplot(ig1) +
  aes(MFI, antigen ) +
  geom_boxplot() +
  facet_wrap(vars(visit), nrow=2)
```

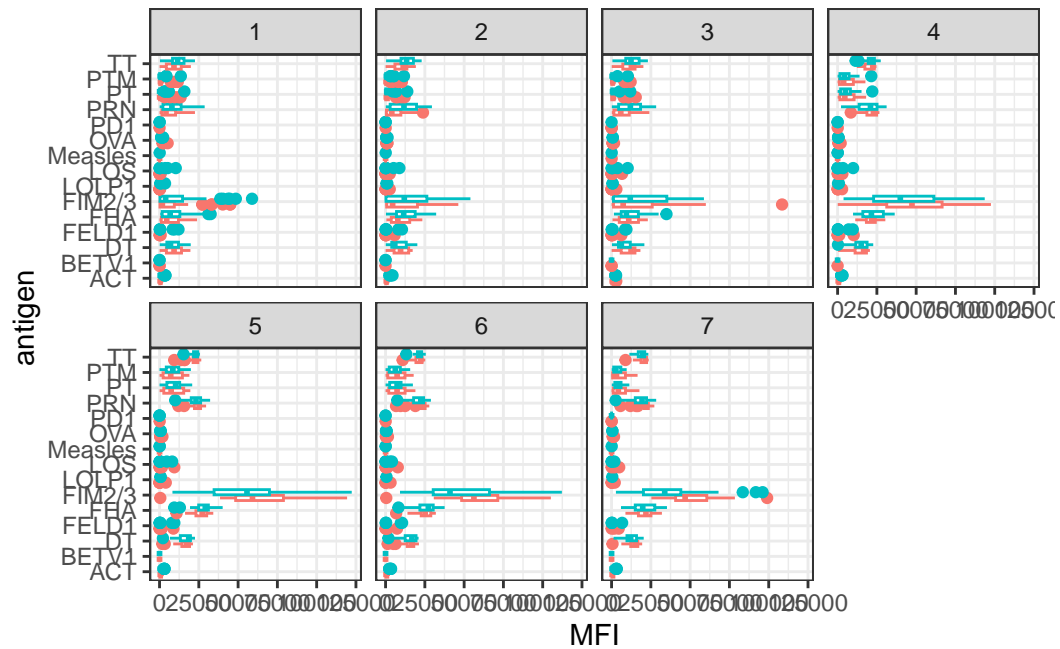


Clearly FIM2/3 changes. This is the “Fimbrial protein” that makes the bacteria pilis and is involved in cell adhesion.

PT: Pertussis toxin

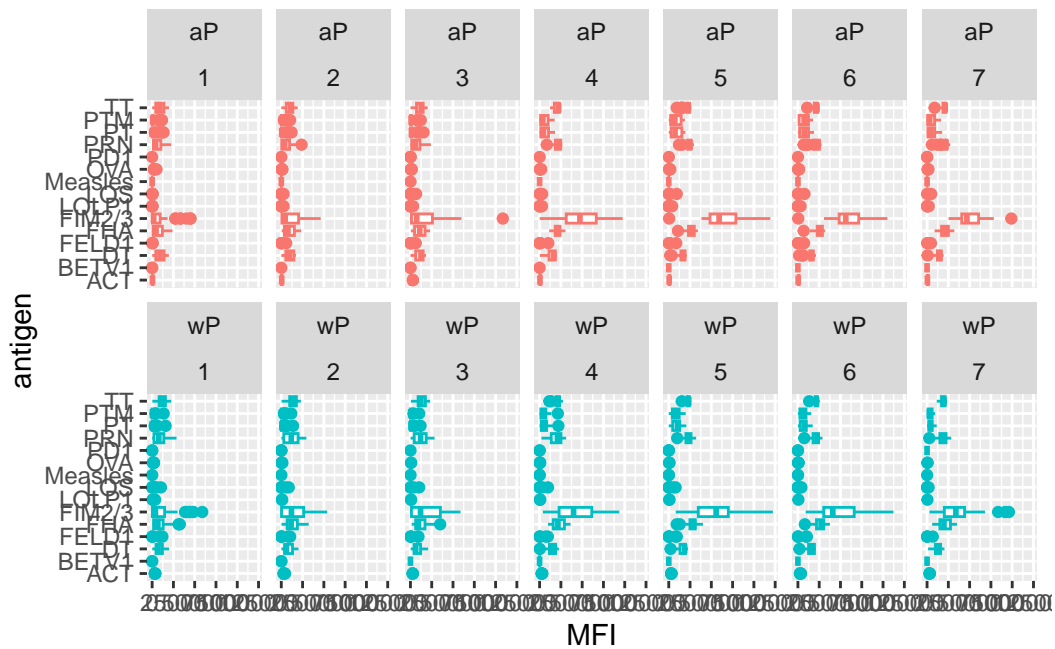
FHA: Filamentus Hemagglutinin surface associated adherence protein of Bordetella pertussis.

```
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(visit), nrow=2) +
  theme_bw()
```

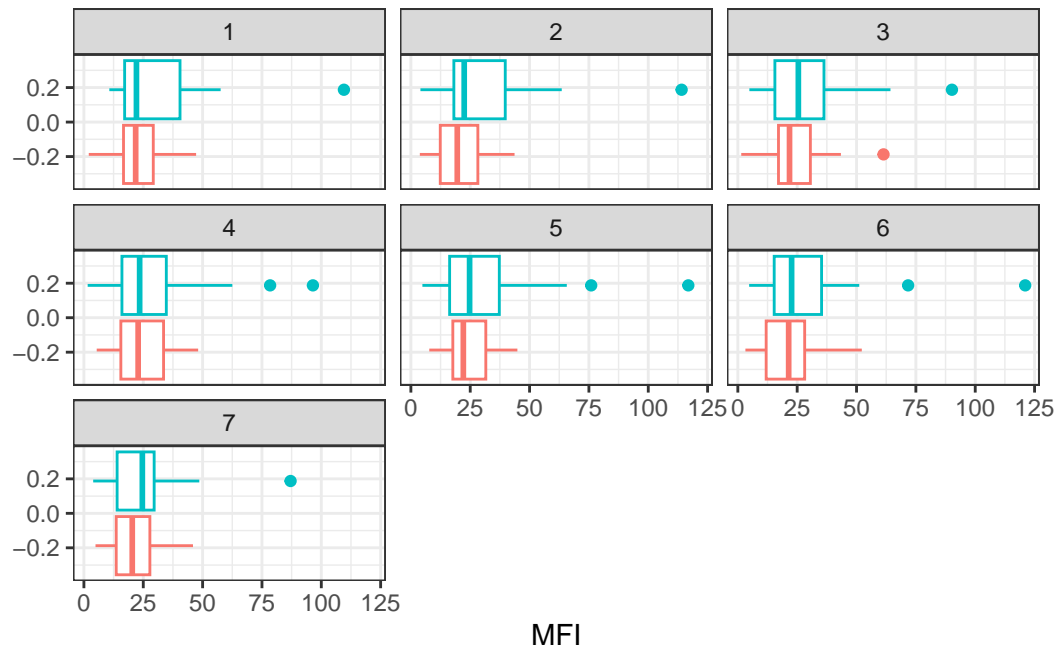


Another version of this plot adding infancy_vac to the faceting.

```
ggplot(ig1) +
  aes(MFI, antigen, col=infancy_vac ) +
  geom_boxplot(show.legend = FALSE) +
  facet_wrap(vars(infancy_vac, visit), nrow=2)
```



```
filter(ig1, antigen=="Measles") %>%
  ggplot() +
  aes(MFI, col=infancy_vac) +
  geom_boxplot(show.legend = F) +
  facet_wrap(vars(visit)) +
  theme_bw()
```



```
filter(ig1, antigen=="FIM2/3") %>%
  ggplot() +
  aes(MFI, col=infancy_vac) +
  geom_boxplot(show.legend = F) +
  facet_wrap(vars(visit)) +
  theme_bw()
```

