

Pregnancy during respiratory pandemics: a comparison between 2009/10 H1N1 flu and 2020/21 COVID-19 pandemics in Brazil

Codes and outputs

10/01/2021

Description

This file presents the documentation of the analysis for the article “Pregnancy during respiratory pandemics: a comparison between 2009/10 H1N1 flu and 2020/21 COVID-19 pandemics in Brazil”.

R packages used, functions

The data are analyzed using the free-software R (<https://www.R-project.org>) in version 4.0.3. Next, we present and load the libraries used in the data analysis process.

```
loadlibrary <- function(x) {  
  if (!require(x, character.only = TRUE)) {  
    install.packages(x, dependencies = T)  
    if (!require(x, character.only = TRUE))  
      stop("Package not found")  
  }  
}  
  
packages <-  
c(  
  "dplyr",  
  "lubridate",  
  "readr",  
  "ggplot2",  
  "kableExtra",  
  "tables",  
  "questionr",  
  "car",  
  "data.table",  
  "magrittr",  
  "tidyverse",  
  "readxl",  
  "summarytools",  
  "zoo",  
  "grid",  
  "gridExtra",  
  "cowplot",
```

```

    "modelsummary",
    "effectsize",
    "rcompanion",
    "DescTools"
  )
lapply(packages, loadlibrary)

```

One can see below the functions that will be used in the data analysis.

```

#functions for summary measures
MEAN <- function(x) mean(x, na.rm = TRUE)
MEDIAN <- function(x) median(x, na.rm = TRUE)
SDev <- function(x) sd(x, na.rm = TRUE)
MIN <- function(x) base::min(x, na.rm = TRUE)
MAX <- function(x) base::max(x, na.rm = TRUE)
q25 <- function(x) stats::quantile(x, p=0.25, na.rm=TRUE)
q75 <- function(x) stats::quantile(x, p=0.75, na.rm=TRUE)
IQR <- function(x) round(q75(x)-q25(x), 2)
n <- function(x) sum(!is.na(x))

```

Function for Breslow-Day Test:

```

teste_breslowday <- function(dados_covid, dados_h1n1, var) {
  tab <- array(0, dim = c(2,2,2))
  tab[, ,1] <- table(dados_h1n1$pregnant_YN, dados_h1n1[[var]])
  tab[, ,2] <- table(dados_covid$pregnant_YN, dados_covid[[var]])
  a <- BreslowDayTest(tab, correct = TRUE)
  out <- data.frame(comp = c("h1n1-covid"),
    stat = c(a$statistic),
    p_valor = c(a$p.value)
  )
  return(out)
}

```

This research studies some demographic, clinical and mortality variables of H1N1 and COVID-19 pandemics aiming to compare pregnant and non-pregnant childbearing age women.

The Influenza Epidemiological Surveillance Information System, SIVEP-Gripe (Sistema de Informação de Vigilância Epidemiológica da Gripe), is a nationwide surveillance database used to monitor severe acute respiratory infections in Brazil.

The analyzed data set includes all female patients from SIVEP-Gripe at childbearing age (10 to 49 years) with H1N1 and COVID-19 disease diagnosis, confirmed, respectively, by positive RT-PCR H1N1 and positive RT-PCR SARS-CoV-2 from the first 13 months of each pandemic, this is, from May 2009 to April 2010 for H1N1 and from March 2020 to February 2021 for COVID-19. The data sets can be obtained at <https://drive.google.com/drive/folders/1qzXgHNjqNUdZ3SnnKRxpv6tQkZeRcpDv?usp=sharing>. The data are loaded next.

Selection of COVID-19 cases

The datasets from 2020 and 2021 are loaded and combined below:

```
##### loading the databases #####
#2021
dados_2021 <- read_delim(
  "INFLUD21-17-05-2021.csv",
  ";",
  escape_double = FALSE,
  locale = locale(encoding = "ISO-8859-2"),
  trim_ws = TRUE
)

#2020
dados_2020 <- read_delim(
  "INFLUD-17-05-2021.csv",
  ";",
  escape_double = FALSE,
  locale = locale(encoding = "ISO-8859-2"),
  trim_ws = TRUE
)

sem <- 19 #last epidemiological week considered of 2021

#### Concatenate 2020 and 2021 data #####
dados1 <- rbind(dados_2020, dados_2021)

# Year and month of the case
dados1 <- dados1 %>%
  dplyr::mutate(
    dt_sint = as.Date(DT_SIN_PRI, format = "%d/%m/%Y"), #date of first symptoms
    ano = lubridate::year(dt_sint), #year of the case
    mes = lubridate::month(dt_sint) #month of the case
  )
```

There are currently 2007693 observations in the database.

Filtering and data treatment

The first filtering consists of selecting the symptom epidemiological weeks of the analysis in 2020 and 2021.

```
#selection of the 2020 and 2021 epidemiological weeks - from March 2020 to February 2021.
dados2 <- dados1 %>%
  filter((ano==2020 & SEM_PRI >=8) | ano ==2021)

dados2 <- dados2 %>%
  mutate(ano = ifelse(ano ==2021 & SEM_PRI ==53, 2020, ano)) %>% filter(ano==2020 | (ano ==2021 & SEM_PRI <=52))

dados3 <- filter(dados2,
  (mes >=3 & ano == 2020) | (mes <=3 & ano == 2021))

with(dados3, ctable(SEM_PRI, ano))
```

```
## Cross-Tabulation, Row Proportions
```

```
## SEM_PRI * ano
## Data Frame: dados3
##
## -----
##      ano      2020      2021      Total
## SEM_PRI
##      1      0 ( 0.0%) 35407 (100.0%) 35407 (100.0%)
##      2      0 ( 0.0%) 34176 (100.0%) 34176 (100.0%)
##      3      0 ( 0.0%) 31415 (100.0%) 31415 (100.0%)
##      4      0 ( 0.0%) 29396 (100.0%) 29396 (100.0%)
##      5      0 ( 0.0%) 35312 (100.0%) 35312 (100.0%)
##      6      0 ( 0.0%) 38422 (100.0%) 38422 (100.0%)
##      7      0 ( 0.0%) 48352 (100.0%) 48352 (100.0%)
##      8      0 ( 0.0%) 51278 (100.0%) 51278 (100.0%)
##      9      0 ( 0.0%) 71029 (100.0%) 71029 (100.0%)
##     10     1984 ( 2.7%) 71533 ( 97.3%) 73517 (100.0%)
##     11     5139 ( 6.8%) 70292 ( 93.2%) 75431 (100.0%)
##     12    12825 (18.7%) 55824 ( 81.3%) 68649 (100.0%)
##     13    14978 (35.2%) 27559 ( 64.8%) 42537 (100.0%)
##     14    16298 (100.0%)      0 ( 0.0%) 16298 (100.0%)
##     15    19581 (100.0%)      0 ( 0.0%) 19581 (100.0%)
##     16    24877 (100.0%)      0 ( 0.0%) 24877 (100.0%)
##     17    30814 (100.0%)      0 ( 0.0%) 30814 (100.0%)
##     18    34864 (100.0%)      0 ( 0.0%) 34864 (100.0%)
##     19    34576 (100.0%)      0 ( 0.0%) 34576 (100.0%)
##     20    37150 (100.0%)      0 ( 0.0%) 37150 (100.0%)
##     21    33800 (100.0%)      0 ( 0.0%) 33800 (100.0%)
##     22    31235 (100.0%)      0 ( 0.0%) 31235 (100.0%)
##     23    35607 (100.0%)      0 ( 0.0%) 35607 (100.0%)
##     24    34139 (100.0%)      0 ( 0.0%) 34139 (100.0%)
##     25    36700 (100.0%)      0 ( 0.0%) 36700 (100.0%)
##     26    32968 (100.0%)      0 ( 0.0%) 32968 (100.0%)
##     27    37431 (100.0%)      0 ( 0.0%) 37431 (100.0%)
##     28    37026 (100.0%)      0 ( 0.0%) 37026 (100.0%)
##     29    34453 (100.0%)      0 ( 0.0%) 34453 (100.0%)
##     30    33718 (100.0%)      0 ( 0.0%) 33718 (100.0%)
##     31    32203 (100.0%)      0 ( 0.0%) 32203 (100.0%)
##     32    30043 (100.0%)      0 ( 0.0%) 30043 (100.0%)
##     33    31091 (100.0%)      0 ( 0.0%) 31091 (100.0%)
##     34    28286 (100.0%)      0 ( 0.0%) 28286 (100.0%)
##     35    26357 (100.0%)      0 ( 0.0%) 26357 (100.0%)
##     36    26499 (100.0%)      0 ( 0.0%) 26499 (100.0%)
##     37    24059 (100.0%)      0 ( 0.0%) 24059 (100.0%)
##     38    22244 (100.0%)      0 ( 0.0%) 22244 (100.0%)
##     39    21578 (100.0%)      0 ( 0.0%) 21578 (100.0%)
##     40    22454 (100.0%)      0 ( 0.0%) 22454 (100.0%)
##     41    21032 (100.0%)      0 ( 0.0%) 21032 (100.0%)
##     42    19028 (100.0%)      0 ( 0.0%) 19028 (100.0%)
##     43    19470 (100.0%)      0 ( 0.0%) 19470 (100.0%)
##     44    18727 (100.0%)      0 ( 0.0%) 18727 (100.0%)
##     45    23281 (100.0%)      0 ( 0.0%) 23281 (100.0%)
##     46    25803 (100.0%)      0 ( 0.0%) 25803 (100.0%)
##     47    29261 (100.0%)      0 ( 0.0%) 29261 (100.0%)
##     48    29161 (100.0%)      0 ( 0.0%) 29161 (100.0%)
```

```
##          49          33057 (100.0%)          0 ( 0.0%)          33057 (100.0%)
##          50          30608 (100.0%)          0 ( 0.0%)          30608 (100.0%)
##          51          28490 (100.0%)          0 ( 0.0%)          28490 (100.0%)
##          52          30470 (100.0%)          0 ( 0.0%)          30470 (100.0%)
##          53          21659 (100.0%)          0 ( 0.0%)          21659 (100.0%)
##      Total          1175024 ( 66.2%)          599995 ( 33.8%)          1775019 (100.0%)
## -----
```

There are 1775019 observations in the database.

The next selection of females cases:

```
#filtering F
dados4 <- filter(dados3, CS_SEXO == "F")
```

There are 813023 observations in the database.

The next step is to filter only women between 10 and 49 years old:

```
#filtering age
dados5 <- filter(dados4, NU_IDADE_N > 9 & NU_IDADE_N < 50)
```

There are 216608 observations in the database.

The next selection is the COVID-19 cases indicated by the CLASSI_FIN variable.

```
with(dados5, freq(CLASSI_FIN))
```

```
## Frequencies
## dados5$CLASSI_FIN
## Type: Numeric
##
##          Freq    % Valid    % Valid Cum.    % Total    % Total Cum.
## -----
##          1      372      0.19      0.19      0.17      0.17
##          2      714      0.36      0.55      0.33      0.50
##          3      507      0.26      0.81      0.23      0.74
##          4     65416     33.15     33.95     30.20     30.94
##          5    130340     66.05     100.00     60.17     91.11
##         <NA>     19259             8.89     100.00
##      Total    216608     100.00     100.00     100.00     100.00
```

```
dados6 <- dados5 %>%
  filter(CLASSI_FIN == 5)
```

There are 130340 observations in the database.

Now let's create the variable if CLASSI_FIN==5 by PCR or another type of diagnosis.

This variable is pcr_test, with the categories: pcr_sars2 if PCR_SARS2 == 1.

```
#create pcr_test variable by pcr variables
dados6 <- dados6 %>%
  mutate(pcr_test = case_when(PCR_SARS2 == 1 ~ "pcr_sars2",
                              TRUE ~ "não"
                              )
  )
```

```
with(dados6, freq(pcr_test))
```

```
## Frequencies
## dados6$pcr_test
## Type: Character
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##          não  44348    34.02        34.02    34.02        34.02
##      pcr_sars2  85992    65.98       100.00    65.98       100.00
##          <NA>      0      100.00        0.00     0.00       100.00
##          Total 130340   100.00       100.00   100.00       100.00
```

Now we will filter the cases with 'pcr_test == pcr_sars2' which are the cases where they can be COVID-19 only by PCR:

```
dados7 <- dados6 %>%
  filter(pcr_test == "pcr_sars2")
```

There are 85992 observations in the database.

Now let's select only pregnant or non-pregnant people:

```
with(dados7, freq(CS_GESTANT))
```

```
## Frequencies
## dados7$CS_GESTANT
## Type: Numeric
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##          0      1      0.0012      0.0012    0.0012      0.0012
##          1     484      0.5628      0.5640    0.5628      0.5640
##          2    1376      1.6001      2.1642    1.6001      2.1642
##          3    3271      3.8038      5.9680    3.8038      5.9680
##          4     252      0.2931      6.2610    0.2931      6.2610
##          5   64224     74.6860     80.9471   74.6860     80.9471
##          6    3430      3.9887     84.9358    3.9887     84.9358
##          9   12954     15.0642    100.0000   15.0642    100.0000
##          <NA>      0      100.0000      0.0000    0.0000    100.0000
##          Total 85992    100.0000    100.0000  100.0000    100.0000
```

```
dados7 <- dados7 %>%
  mutate(
    classi_gesta = case_when(
      CS_GESTANT == 1 ~ "1tri", #first trimester of pregnancy
      CS_GESTANT == 2 ~ "2tri", #second trimester of pregnancy
      CS_GESTANT == 3 ~ "3tri", #third trimester of pregnancy
      CS_GESTANT == 4 ~ "IG_ig", #ignored gestational age of pregnancy
      CS_GESTANT == 5 ~ "não", #not pregnancy
      TRUE ~ NA_character_
    )
  )
```

```
)

#filtering only pregnant or non-pregnant
dados8 <- dados7 %>%
  filter(!is.na(classi_gesta))

#creating the variable pregnant yes or no (gestante_SN)
dados8 <- dados8 %>%
  mutate(gestante_SN = ifelse(CS_GESTANT == 5, "não", "sim")) #não for no and sim for yes

freq(dados8$gestante_SN)
```

```
## Frequencies
## dados8$gestante_SN
## Type: Character
##
##           Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##      não  64224    92.27      92.27    92.27    92.27
##      sim   5383     7.73     100.00    7.73    100.00
##      <NA>     0
##      Total 69607   100.00    100.00  100.00   100.00
```

There is 69607 observations in the database.

```
dados_covid <- dados8
```

Selection of H1N1 cases

The datasets from 2009 and 2010 are loaded and combined below:

```
##### loading the databases #####
#2009 e 2010
dados2009 <- read_delim(
  "influd09_limpo-final.csv",
  ";",
  escape_double = FALSE,
  locale = locale(encoding = "ISO-8859-2"),
  trim_ws = TRUE
)

dados2010 <- read_delim(
  "influd10_limpo-final.csv",
  ";",
  escape_double = FALSE,
  locale = locale(encoding = "ISO-8859-2"),
  trim_ws = TRUE
)

dados_2009 <- dados2009 %>%
```

```

rename(SRAGFINAL = SRAG2009FINAL)

dados_2010 <- dados2010 %>%
  rename(SRAGFINAL = SRAG2010FINAL)

dados <- full_join(dados_2009, dados_2010)

#Create case year variable
dados <- dados %>%
  dplyr::mutate(
    dt_sint = as.Date(DT_SIN_PRI, format = "%d/%m/%Y"), #date of first symptoms
    ano = lubridate::year(dt_sint), #year of the case
    mes = lubridate::month(dt_sint) #month of the case
  )

```

There are currently 217167 observations in the database.

Filtering and data treatment

The first filtering consists of selecting cases from May 2009 to April 2010.

```

dados1 <- filter(dados,
  (mes >=5 & ano == 2009) | (mes <=5 & ano == 2010))

```

There are 212584 observations in the database.

The next selection of females:

```

#filtering F
dados2 <- filter(dados1, CS_SEXO == "F")

```

There are 115357 observations in the database.

The next step is to filter only women between 10 and 49 years old.

```

#Filtering by age range of interest
dados3 <- dados2 %>%
  filter(NU_IDADE_N > 4009 & NU_IDADE_N < 4050)

```

There are 75717 observations in the database.

Now let's select only pregnant or non-pregnant people.

```

with(dados3, freq(CS_GESTANT))

```

```

## Frequencies
## dados3$CS_GESTANT
## Type: Numeric
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##          1   2576     3.40         3.40     3.40         3.40

```


##	2	4782	6.32	9.72	6.32	9.72
##	3	4284	5.66	15.38	5.66	15.38
##	4	434	0.57	15.95	0.57	15.95
##	5	49663	65.59	81.54	65.59	81.54
##	6	5348	7.06	88.60	7.06	88.60
##	9	8630	11.40	100.00	11.40	100.00
##	<NA>	0			0.00	100.00
##	Total	75717	100.00	100.00	100.00	100.00

```
dados3 <- dados3 %>%
  mutate(
    classi_gesta = case_when(
      CS_GESTANT == 1 ~ "1tri", #first trimester of pregnancy
      CS_GESTANT == 2 ~ "2tri", #second trimester of pregnancy
      CS_GESTANT == 3 ~ "3tri", #third trimester of pregnancy
      CS_GESTANT == 4 ~ "IG_ig", #ignored gestational age of pregnancy
      CS_GESTANT == 5 ~ "nãoo", #not pregnancy
      TRUE ~ NA_character_
    )
  )

#filtering only pregnant or non-pregnant
dados4 <- dados3 %>%
  filter(!is.na(classi_gesta))

#creating the variable pregnant yes or no (gestante_SN)
dados4 <- dados4 %>%
  mutate(gestante_SN = ifelse(CS_GESTANT == 5, "nãoo", "sim")) # "nãoo" means 'no' and "sim" means 'yes'
```

There are 61739 observations in the database.

The next selection is the covid cases indicated by the CLASSI_FIN variable.

```
with(dados4, freq(CLASSI_FIN))
```

```
## Frequencies
## dados4$CLASSI_FIN
## Type: Numeric
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##          1  35214   59.842    59.842   57.037   57.037
##          2   1230    2.090    61.932    1.992   59.029
##          3  22351   37.983    99.915   36.202   95.232
##          4    24    0.041    99.956    0.039   95.270
##          9    26    0.044   100.000    0.042   95.313
##         <NA>  2894    0.000   100.000    4.687  100.000
##         Total 61739  100.000   100.000  100.000  100.000
```

```
dados5 <- dados4 %>%
  filter(CLASSI_FIN == 1)
```

There are 35214 observations in the database.

Now let's create the variable if CLASSI_FIN==1 by PCR or another type of diagnosis.

This variable is pcr_test, with the categories: pcr_pos if PCR positive.

```
#create pcr_test variable by pcr variables
dados5 <- dados5 %>%
  mutate(pcr_test = case_when(PCR_RES == 1 & #pcr positive
    PCR_ETIOL == 1 ~ "pcr_pos",
    TRUE ~ "não"))
```

Now we will filter the cases with pcr_test == "pcr_pos" that they are the cases where COVID-19 only by PCR:

```
dados6 <- dados5 %>%
  filter(pcr_test == "pcr_pos")
```

There are 8854 observations in the database.

```
dados_h1n1 <- dados6
```

Analysis

Creating a variable to identify pregnant and non-pregnant women:

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(pregnant_YN = ifelse(gestante_SN == "não", "no", "yes"))
```

```
dados_covid <- dados_covid %>%
  mutate(pregnant_YN = ifelse(gestante_SN == "não", "no", "yes"))
```

Epidemiologic characteristics

Age

H1N1

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(age = NU_IDADE_N - round(NU_IDADE_N, -2))
```

Descritiva :

```
datasummary((pregnant_YN) ~ age*(n+MEAN+SD+MEDIAN+MIN+MAX+q25+q75+IQR),
  data = dados_h1n1, output = 'markdown')
```

	n	MEAN	SD	MEDIAN	MIN	MAX	q25	q75	IQR
no	6070.00	26.87	10.67	26.00	10.00	49.00	18.00	35.00	17.00
yes	2784.00	25.15	6.12	25.00	10.00	49.00	21.00	29.00	8.00

```
#t test to compare ages of pregnant and non-pregnant women
t.test(age ~ pregnant_YN, data = dados_h1n1)
```

```
##
## Welch Two Sample t-test
##
## data: age by pregnant_YN
## t = 9.5691, df = 8435.1, p-value < 2.2e-16
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## 1.364875 2.068135
## sample estimates:
## mean in group no mean in group yes
## 26.86952 25.15302
```

```
#Cohen's effect size
c_h1n1 <- cohens_d(age ~ as.factor(pregnant_YN), data=dados_h1n1)
c_h1n1
```

```
## Cohen's d | 95% CI
## -----
## 0.18 | [0.14, 0.23]
##
## - Estimated using pooled SD.
```

```
interpret_d(c_h1n1$Cohens_d, rules="cohen1988")
```

```
## [1] "very small"
## (Rules: cohen1988)
```

COVID-19

```
dados_covid$age <- dados_covid$NU_IDADE_N
datasummary((pregnant_YN) ~ age*(n+MEAN+SD+MEDIAN+MIN+MAX+q25+q75+IQR),
  data = dados_covid, output = 'markdown')
```

	n	MEAN	SD	MEDIAN	MIN	MAX	q25	q75	IQR
no	64224.00	38.17	8.27	40.00	10.00	49.00	33.00	45.00	12.00
yes	5383.00	30.03	6.86	30.00	10.00	49.00	25.00	35.00	10.00

```
#t test to compare ages of pregnant and non-pregnant women
t.test(age ~ pregnant_YN, data = dados_covid)
```

```
##
## Welch Two Sample t-test
##
## data: age by pregnant_YN
## t = 82.22, df = 6767.5, p-value < 2.2e-16
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
## 7.945794 8.333941
## sample estimates:
## mean in group no mean in group yes
## 38.17442 30.03455
```

#Cohen's effect size

```
c_covid <- cohens_d(age ~ as.factor(pregnant_YN), data=dados_covid)
c_covid
```

```
## Cohen's d | 95% CI
## -----
## 1.00 | [1.10, 1.10]
##
## - Estimated using pooled SD.
```

```
interpret_d(c_covid$Cohens_d, rules="cohen1988")
```

```
## [1] "large"
## (Rules: cohen1988)
```

Age Group

H1N1

#Creating a variable to classify the age groups

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(
    age_group = case_when(
      NU_IDADE_N <= 4019 ~ "<20",
      NU_IDADE_N >= 4020
      & NU_IDADE_N <= 4034 ~ "20-34",
      NU_IDADE_N > 4034 ~ ">=35",
      TRUE ~ NA_character_
    )
  )
dados_h1n1$age_group <-
  factor(dados_h1n1$age_group, levels = c("<20", "20-34", ">=35"))
```

```
with(dados_h1n1, ctable(age_group, pregnant_YN, prop = "c", useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Column Proportions
## age_group * pregnant_YN
## Data Frame: dados_h1n1
```

```
##
##
## -----
##      pregnant_YN      no      yes      Total
## age_group
##   <20      1722 ( 28.4%)    499 ( 17.9%)    2221 ( 25.1%)
##   20-34     2783 ( 45.8%)    2052 ( 73.7%)    4835 ( 54.6%)
##   >=35     1565 ( 25.8%)     233 (  8.4%)    1798 ( 20.3%)
##   Total     6070 (100.0%)    2784 (100.0%)    8854 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##   639.2557    2    0
## -----
```

COVID-19

#Creating a variable to classify the age groups

```
dados_covid <- dados_covid %>%
  mutate(
    age_group = case_when(
      NU_IDADE_N <= 19 ~ "<20",
      NU_IDADE_N >= 20
      & NU_IDADE_N <= 34 ~ "20-34",
      NU_IDADE_N > 34 ~ ">=35",
      TRUE ~ NA_character_
    )
  )
dados_covid$age_group <-
  factor(dados_covid$age_group, levels = c("<20", "20-34", ">=35"))
```

```
with(dados_covid, ctable(age_group, pregnant_YN, prop = "c", useNA = "no", chisq = TRUE))
```

Cross-Tabulation, Column Proportions

age_group * pregnant_YN

Data Frame: dados_covid

##

##

```
## -----
##      pregnant_YN      no      yes      Total
## age_group
##   <20      1731 (  2.7%)    339 (  6.3%)    2070 (  3.0%)
##   20-34    17279 ( 26.9%)   3559 ( 66.1%)   20838 ( 29.9%)
##   >=35    45214 ( 70.4%)   1485 ( 27.6%)   46699 ( 67.1%)
##   Total    64224 (100.0%)   5383 (100.0%)   69607 (100.0%)
## -----
```

##

Chi.squared df p.value

Table 3: Frequency table for Ethnicity - H1N1 data

	n	%
Black	380	4.3
Brown	1495	16.9
Indigenous	27	0.3
White	6119	69.1
Yellow	70	0.8
NA	763	8.6
Total	8854	100.0

```
##    4124.593      2      0
## -----
```

Ethnicity

H1N1

#Creating a variable to classify the ethnicity classes

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(ethnicity = case_when(CS_RACA == 1 ~ "White",
                                CS_RACA == 2 ~ "Black",
                                CS_RACA == 3 ~ "Yellow",
                                CS_RACA == 4 ~ "Brown",
                                CS_RACA == 5 ~ "Indigenous",
                                TRUE ~ NA_character_))
```

```
questionr::freq(
  dados_h1n1$ethnicity,
  cum = FALSE,
  total = TRUE,
  na.last = FALSE,
  valid = FALSE
) %>%
  kable(caption = "Frequency table for Ethnicity - H1N1 data", digits = 2)
```

```
with(dados_h1n1, ctable(ethnicity, pregnant_YN, prop="c", useNA = "no", chisq = FALSE))
```

Cross-Tabulation, Column Proportions

ethnicity * pregnant_YN

Data Frame: dados_h1n1

##

```
## -----
##      pregnant_YN      no      yes      Total
## ethnicity
##      Black      205 ( 3.7%)      175 ( 7.0%)      380 ( 4.7%)
##      Brown      872 (15.6%)      623 (25.0%)     1495 (18.5%)
##      Indigenous      21 ( 0.4%)       6 ( 0.2%)       27 ( 0.3%)
##      White     4446 (79.4%)     1673 (67.1%)     6119 (75.6%)
```

Table 4: Frequency table for Ethnicity - COVID-19 data

	n	%
Black	3132	4.5
Brown	22233	31.9
Indigenous	129	0.2
White	29743	42.7
Yellow	695	1.0
NA	13675	19.6
Total	69607	100.0

```
##      Yellow      53 ( 0.9%)      17 ( 0.7%)      70 ( 0.9%)
##      Total     5597 (100.0%)    2494 (100.0%)    8091 (100.0%)
## -----
```

The Exact's Fisher Test is applied considering that some frequencies are too small (less than 5).

```
fisher.test(dados_h1n1$ethnicity, dados_h1n1$pregnant_YN, simulate.p.value = TRUE)
```

```
##
## Fisher's Exact Test for Count Data with simulated p-value (based on
## 2000 replicates)
##
## data:  dados_h1n1$ethnicity and dados_h1n1$pregnant_YN
## p-value = 0.0004998
## alternative hypothesis: two.sided
```

COVID-19

```
#Creating a variable to classify the ethnicity classes
dados_covid <- dados_covid %>%
  mutate(ethnicity = case_when(CS_RACA == 1 ~ "White",
                               CS_RACA == 2 ~ "Black",
                               CS_RACA == 3 ~ "Yellow",
                               CS_RACA == 4 ~ "Brown",
                               CS_RACA == 5 ~ "Indigenous",
                               TRUE ~ NA_character_))
```

```
questionr::freq(
  dados_covid$ethnicity,
  cum = FALSE,
  total = TRUE,
  na.last = FALSE,
  valid = FALSE
) %>%
  kable(caption = "Frequency table for Ethnicity - COVID-19 data", digits = 2)
```

```
with(dados_covid, ctable(ethnicity, pregnant_YN, prop="c", useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Column Proportions
## ethnicity * pregnant_YN
## Data Frame: dados_covid
##
##
## -----
##      pregnant_YN      no      yes      Total
## ethnicity
##      Black      2839 ( 5.5%)      293 ( 6.7%)      3132 ( 5.6%)
##      Brown      20117 ( 39.0%)      2116 ( 48.0%)      22233 ( 39.8%)
##      Indigenous      112 ( 0.2%)      17 ( 0.4%)      129 ( 0.2%)
##      White      27815 ( 54.0%)      1928 ( 43.8%)      29743 ( 53.2%)
##      Yellow      643 ( 1.2%)      52 ( 1.2%)      695 ( 1.2%)
##      Total      51526 (100.0%)      4406 (100.0%)      55932 (100.0%)
## -----
##
## -----
##      Chi.squared      df      p.value
## -----
##      176.751      4      0
## -----
```

Displacement

Displacement: change city to access health care.

COVID-19

```
#Creating a variable to identify the need to move to another city other than where they live
dados_covid <- dados_covid %>%
  mutate(displacement = case_when((CO_MUN_RES == CO_MU_INTE) &
    !is.na(CO_MU_INTE) & !is.na(CO_MUN_RES) ~ "no",
    (CO_MUN_RES != CO_MU_INTE) & !is.na(CO_MU_INTE) &
    !is.na(CO_MUN_RES) ~ "yes",
    TRUE ~ NA_character_
  )
)
```

```
with(dados_covid, ctable(pregnant_YN, displacement, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * displacement
## Data Frame: dados_covid
##
##
## -----
##      displacement      no      yes      Total
## pregnant_YN
```

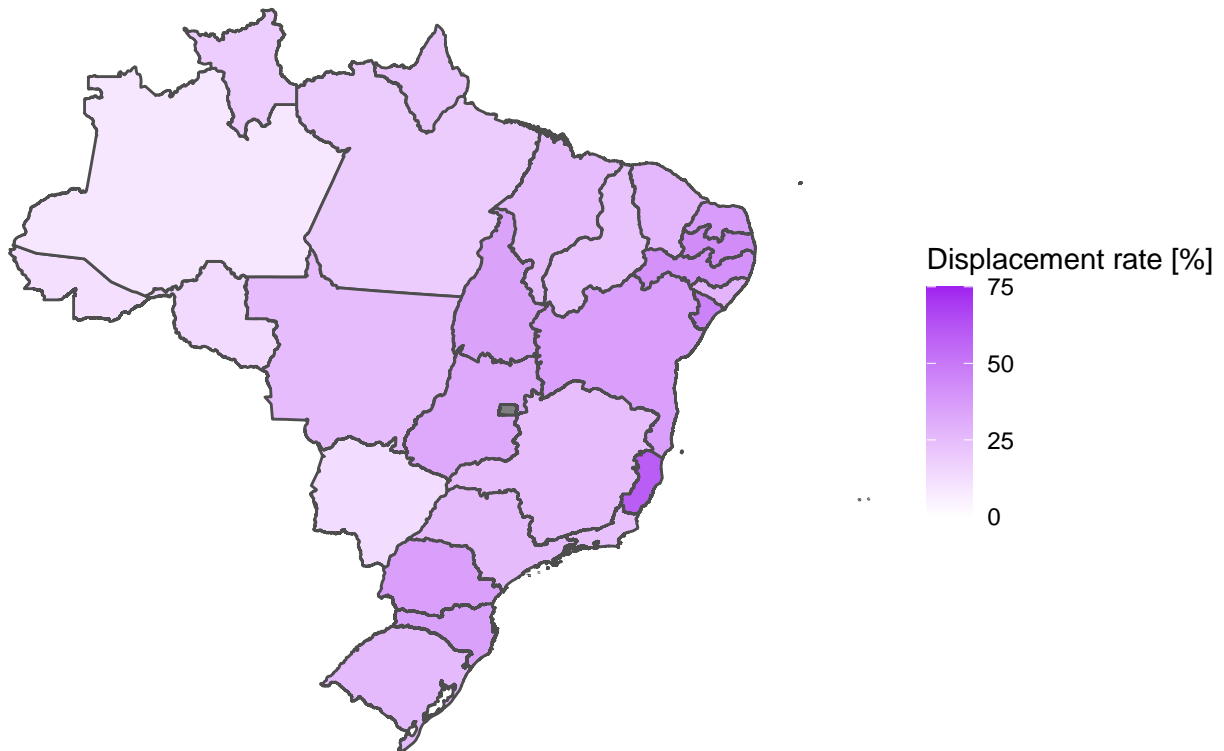


```
##           no           42351 (71.2%)   17109 (28.8%)   59460 (100.0%)
##           yes           3272 (63.5%)    1879 (36.5%)    5151 (100.0%)
##          Total          45623 (70.6%)   18988 (29.4%)   64611 (100.0%)
## -----
##
## -----
##  Chi.squared   df   p.value
## -----
##    135.2216     1       0
## -----
##
## -----
##  Odds Ratio   Lo - 95%   Hi - 95%
## -----
##     1.42       1.34     1.51
## -----
##
## -----
##  Risk Ratio   Lo - 0%   Hi - 0%
## -----
##     1.12       1.12     1.12
## -----
```

Map to visualize the displacement rate by state:

```
d1 <- dados_covid
estado <- sort(unique(d1$SG_UF_NOT))
valor <- data.table(prop.table(table(d1$SG_UF_NOT,d1$displacement),1))
valor <- valor[valor$V2=="yes",]
dt1_estadual <- data.frame("uf"=valor$V1,"T1"=valor$N*100)
dt <- rbind(c("AC",12), c("AL",27), c("AP",16), c("AM",13), c("BA",29),
            c("CE",23), c("DF",53), c("ES",32), c("GO",52), c("MA",21),
            c("MT",51), c("MS",50), c("MG",31), c("PA",15), c("PB",25),
            c("PR",41), c("PE",26), c("PI",22), c("RN",24), c("RS",43),
            c("RJ",33), c("RO",11), c("RR",14), c("SC",42), c("SP",35),
            c("SE",28), c("TO",17)) %>% data.table %>% 'colnames<-'(c("uf","id"))
mapaUF <- readRDS("mapaUF.Rds")
dt1 <- full_join(dt, dt1_estadual, by = "uf")
ggplot(dt1) + geom_map(map = mapaUF, color = 'gray30', aes_string(map_id = "id", fill = "T1")) + geom_p
```

COVID-19 notifications



H1N1

#Creating a variable to identify the need to move to another city other than where they live

```
dados_h1n1 <- dados_h1n1 %>%
```

```
  mutate(displacement = case_when((ID_MN_RESI == CO_MU_INTE) &
    !is.na(CO_MU_INTE) & !is.na(ID_MN_RESI) ~ "no",
    (ID_MN_RESI != CO_MU_INTE) & !is.na(CO_MU_INTE) &
    !is.na(ID_MN_RESI) ~ "yes",
    TRUE ~ NA_character_
  )
)
```

```
with(dados_h1n1, ctable(pregnant_YN, displacement, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
```

```
## pregnant_YN * displacement
```

```
## Data Frame: dados_h1n1
```

```
##
```

```
##
```

```
## ----- displacement ----- no ----- yes ----- Total
```

```
## pregnant_YN
```

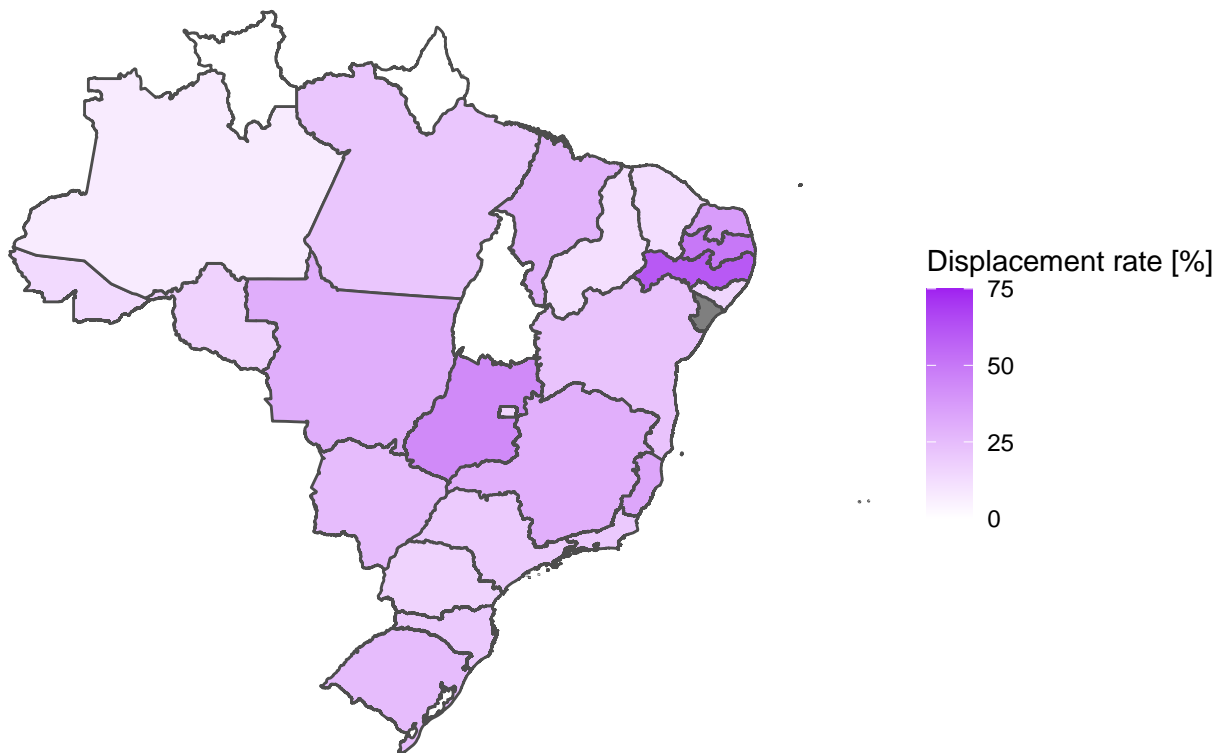
```
## no 2922 (79.7%) 745 (20.3%) 3667 (100.0%)
```

```
##           yes           1706 (78.4%)    471 (21.6%)    2177 (100.0%)
##           Total          4628 (79.2%)    1216 (20.8%)    5844 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      1.3632      1     0.243
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.08        0.95      1.23
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      1.02        1.02      1.02
## -----
```

Map to visualize the displacement rate by state:

```
#H1N1
d1 <- dados_h1n1
valor <- data.table(prop.table(table(d1$SG_UF_NOT,d1$displacement),1))
valor <- valor[valor$V2=="yes",]
dt1_estadual <- data.frame("id"=valor$V1,"T1"=valor$N*100)
dt <- rbind(c("AC",12), c("AL",27), c("AP",16), c("AM",13), c("BA",29),
            c("CE",23), c("DF",53), c("ES",32), c("GO",52), c("MA",21),
            c("MT",51), c("MS",50), c("MG",31), c("PA",15), c("PB",25),
            c("PR",41), c("PE",26), c("PI",22), c("RN",24), c("RS",43),
            c("RJ",33), c("RO",11), c("RR",14), c("SC",42), c("SP",35),
            c("SE",28), c("TO",17)) %>% data.table %>% 'colnames<-'(c("uf","id"))
mapaUF <- readRDS("mapaUF.Rds")
dt1 <- full_join(dt, dt1_estadual, by = "id")
ggplot(dt1) + geom_map(map = mapaUF, color = 'gray30', aes_string(map_id = "id", fill = "T1")) + geom_p
```

H1N1 Notifications



Breslow-Day Test to compare the displacement need in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"displacement")
```

```
##               comp      stat      p_valor
## X-squared h1n1-covid 13.96446 0.0001862991
```

Vaccine

Now the notifications where the case is identified as flu vaccinated will be analyzed.

H1N1

```
#Creating a variable to identify flu vaccinated
dados_h1n1 <- dados_h1n1 %>%
  mutate(vaccine = case_when(VACINA == 1 ~ "Yes",
                             VACINA == 2 ~ "No",
                             TRUE ~ NA_character_)
)
```

```
with(dados_h1n1, ctable(pregnant_YN, vaccine, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * vaccine
## Data Frame: dados_h1n1
##
##
## -----
##      vaccine           No           Yes           Total
## pregnant_YN
##      no           4448 (89.0%)    549 (11.0%)    4997 (100.0%)
##      yes           2074 (95.0%)    110 ( 5.0%)    2184 (100.0%)
##      Total           6522 (90.8%)    659 ( 9.2%)    7181 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      63.84         1      0
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.43          0.35        0.53
## -----
##
## -----
##      Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.94          0.94        0.94
## -----
```

COVID-19

```
#Creating a variable to identify flu vaccinated
dados_covid <- dados_covid %>%
  mutate(vaccine = case_when(VACINA == 1 ~ "Yes",
                             VACINA == 2 ~ "No",
                             TRUE ~ NA_character_)
  )
```

```
with(dados_covid, ctable(pregnant_YN, vaccine, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * vaccine
## Data Frame: dados_covid
##
##
## -----
##      vaccine           No           Yes           Total
## pregnant_YN
##      no           23450 (76.8%)    7080 (23.2%)    30530 (100.0%)
##      yes           1539 (62.9%)     906 (37.1%)     2445 (100.0%)
```

```
##           Total           24989 (75.8%)    7986 (24.2%)    32975 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    236.3533    1     0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.95      1.79      2.13
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      1.22      1.22      1.22
## -----
```

Breslow-Day Test to compare the effect of flu vaccine in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"vaccine")
```

```
##           comp      stat p_valor
## X-squared h1n1-covid 185.9719      0
```

Comorbidities

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(cardiac = case_when(CARDIOPATI == 1 ~ "Yes",
                             CARDIOPATI == 2 ~ "No",
                             TRUE ~ NA_character_))

dados_h1n1 <- dados_h1n1 %>%
  mutate(pneumologic = case_when(PNEUMOPATI == 1 ~ "Yes",
                                  PNEUMOPATI == 2 ~ "No",
                                  TRUE ~ NA_character_))

dados_h1n1 <- dados_h1n1 %>%
  mutate(renal = case_when(RENAL == 1 ~ "Yes",
                           RENAL == 2 ~ "No",
                           TRUE ~ NA_character_))

dados_h1n1 <- dados_h1n1 %>%
  mutate(imuno = case_when(IMUNODEPRE == 1 ~ "Yes",
                           IMUNODEPRE == 2 ~ "No",
                           TRUE ~ NA_character_))

dados_h1n1 <- dados_h1n1 %>%
```

```

mutate(hematologic = case_when(HEMOGLOBI == 1 ~ "Yes",
                                HEMOGLOBI == 2 ~ "No",
                                TRUE ~ NA_character_))

dados_covid <- dados_covid %>%
  mutate(cardiac = case_when(CARDIOPATI == 1 ~ "Yes",
                              CARDIOPATI == 2 ~ "No",
                              TRUE ~ NA_character_))

dados_covid <- dados_covid %>%
  mutate(pneumologic = case_when((PNEUMOPATI == 1 | ASMA == 1) ~ "Yes",
                                   (PNEUMOPATI == 2 | ASMA == 2) ~ "No",
                                   TRUE ~ NA_character_))

dados_covid <- dados_covid %>%
  mutate(renal = case_when(RENAL == 1 ~ "Yes",
                            RENAL == 2 ~ "No",
                            TRUE ~ NA_character_))

dados_covid <- dados_covid %>%
  mutate(imuno = case_when(IMUNODEPRE == 1 ~ "Yes",
                            IMUNODEPRE == 2 ~ "No",
                            TRUE ~ NA_character_))

dados_covid <- dados_covid %>%
  mutate(hematologic = case_when(HEMATOLOGI == 1 ~ "Yes",
                                   HEMATOLOGI == 2 ~ "No",
                                   TRUE ~ NA_character_))

```

Cardiac disease

H1N1:

```
with(dados_h1n1, ctable(pregnant_YN, cardiac, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```

## Cross-Tabulation, Row Proportions
## pregnant_YN * cardiac
## Data Frame: dados_h1n1
##
## -----
##           cardiac           No           Yes           Total
## pregnant_YN
##      no           5429 (97.1%)    163 (2.9%)    5592 (100.0%)
##      yes           2432 (98.5%)     38 (1.5%)    2470 (100.0%)
##      Total           7861 (97.5%)    201 (2.5%)    8062 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----

```

```
##      12.7914      1      3e-04
## -----
##
## -----
## Odds Ratio      Lo - 95%      Hi - 95%
## -----
##      0.52      0.36      0.74
## -----
##
## -----
## Risk Ratio      Lo - 0%      Hi - 0%
## -----
##      0.99      0.99      0.99
## -----
```

COVID-19:

```
with(dados_covid, ctable(pregnant_YN, cardiac, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * cardiac
## Data Frame: dados_covid
##
## -----
##      cardiac      No      Yes      Total
## pregnant_YN
##      no      13141 (57.2%)      9825 (42.8%)      22966 (100.0%)
##      yes      1421 (81.3%)      327 (18.7%)      1748 (100.0%)
##      Total      14562 (58.9%)      10152 (41.1%)      24714 (100.0%)
## -----
##
## -----
## Chi.squared      df      p.value
## -----
##      387.941      1      0
## -----
##
## -----
## Odds Ratio      Lo - 95%      Hi - 95%
## -----
##      0.31      0.27      0.35
## -----
##
## -----
## Risk Ratio      Lo - 0%      Hi - 0%
## -----
##      0.70      0.70      0.70
## -----
```

Breslow-Day Test to compare the effect cardiac morbidity in both pandemics


```
teste_breslowday(dados_covid,dados_h1n1,"cardiac")
```

```
##                comp      stat      p_valor
## X-squared h1n1-covid 7.573643 0.005922794
```

Pneumologic

H1N1:

```
with(dados_h1n1, ctable(pregnant_YN, pneumologic, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * pneumologic
## Data Frame: dados_h1n1
##
##
## -----
##                pneumologic      No      Yes      Total
## pregnant_YN
##      no      5185 (92.6%)    417 (7.4%)    5602 (100.0%)
##      yes      2346 (95.3%)    116 (4.7%)    2462 (100.0%)
##      Total      7531 (93.4%)    533 (6.6%)    8064 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      20.2427    1      0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      0.61      0.50      0.76
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##      0.97      0.97      0.97
## -----
```

COVID-19:

```
with(dados_covid, ctable(pregnant_YN, pneumologic, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * pneumologic
```

```
## Data Frame: dados_covid
##
##
## -----
##          pneumologic          No          Yes          Total
## pregnant_YN
##          no          17015 (82.0%)    3728 (18.0%)    20743 (100.0%)
##          yes          1500 (86.6%)     233 (13.4%)     1733 (100.0%)
##          Total          18515 (82.4%)    3961 (17.6%)    22476 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    22.2714     1     0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##    0.71       0.61       0.82
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##    0.95       0.95       0.95
## -----
```

Breslow-Day Test to compare the effect of pneumologic morbidity in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"pneumologic")
```

```
##          comp      stat   p_valor
## X-squared h1n1-covid 1.199801 0.2733615
```

Renal

H1N1:

```
with(dados_h1n1, ctable(pregnant_YN, renal, prop = "r", useNA = "no", chisq = FALSE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * renal
## Data Frame: dados_h1n1
##
##
## -----
##          renal          No          Yes          Total
## pregnant_YN
##          no          5521 ( 98.8%)    66 (1.2%)    5587 (100.0%)
```

```
##           yes           2456 ( 99.6%)   10 (0.4%)   2466 (100.0%)
##          Total           7977 ( 99.1%)   76 (0.9%)   8053 (100.0%)
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      0.34      0.17      0.66
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##      0.99      0.99      0.99
## -----
```

```
fisher.test(dados_h1n1$renal, dados_h1n1$pregnant_YN)
```

```
##
## Fisher's Exact Test for Count Data
##
## data:  dados_h1n1$renal and dados_h1n1$pregnant_YN
## p-value = 0.0006227
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.1558760 0.6680346
## sample estimates:
## odds ratio
##  0.3406406
```

COVID-19:

```
with(dados_covid, ctable(pregnant_YN, renal, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * renal
## Data Frame: dados_covid
##
## -----
##           renal           No           Yes           Total
## pregnant_YN
##      no      18233 (92.1%)   1563 (7.9%)   19796 (100.0%)
##      yes      1614 (97.9%)    35 (2.1%)   1649 (100.0%)
##      Total     19847 (92.5%)   1598 (7.5%)   21445 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      72.7285    1      0
```

```
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.25      0.18      0.35
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.94      0.94      0.94
## -----
```

Breslow-Day Test to compare the effect of renal morbidity in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"renal")
```

```
##                comp    stat    p_valor
## X-squared h1n1-covid 0.61435 0.4331546
```

Imunossupression

H1N1:

```
with(dados_h1n1, ctable(pregnant_YN, imuno, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * imuno
## Data Frame: dados_h1n1
##
## -----
##          imuno          No          Yes          Total
## pregnant_YN
##      no          5414 (96.8%)    177 (3.2%)    5591 (100.0%)
##      yes          2423 (98.1%)     47 (1.9%)    2470 (100.0%)
##      Total          7837 (97.2%)    224 (2.8%)    8061 (100.0%)
## -----
##
## -----
## Chi.squared    df    p.value
## -----
##      9.6528      1    0.0019
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.59      0.43      0.82
## -----
```

```
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.99      0.99      0.99
## -----
```

COVID-19:

```
with(dados_covid, ctable(pregnant_YN, imuno, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * imuno
## Data Frame: dados_covid
##
## -----
##      imuno      No      Yes      Total
## pregnant_YN
##      no      18059 (90.5%)  1885 (9.5%)  19944 (100.0%)
##      yes      1602 (96.9%)   52 (3.1%)   1654 (100.0%)
##      Total      19661 (91.0%)  1937 (9.0%)  21598 (100.0%)
## -----
##
## -----
## Chi.squared    df    p.value
## -----
##      73.6598      1      0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.31      0.23      0.41
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.93      0.93      0.93
## -----
```

Breslow-Day Test to compare the effect of immunosuppression in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"imuno")
```

```
##      comp      stat      p_valor
## X-squared h1n1-covid 9.009579 0.002685683
```

Hematologic

H1N1:

```
with(dados_h1n1, ctable(pregnant_YN, hematologic, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * hematologic
## Data Frame: dados_h1n1
##
## -----
##           hematologic           No           Yes           Total
## pregnant_YN
##           no           5556 (99.5%)    28 (0.5%)    5584 (100.0%)
##           yes           2447 (99.4%)    14 (0.6%)    2461 (100.0%)
##           Total           8003 (99.5%)    42 (0.5%)    8045 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      0.0479      1   0.8267
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.14      0.60      2.16
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##      1.00      1.00      1.00
## -----
```

COVID-19:

```
with(dados_covid, ctable(pregnant_YN, hematologic, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * hematologic
## Data Frame: dados_covid
##
## -----
##           hematologic           No           Yes           Total
## pregnant_YN
##           no           19050 (97.2%)    557 (2.8%)    19607 (100.0%)
```

```
##           yes           1632 (98.4%)    26 (1.6%)    1658 (100.0%)
##          Total          20682 (97.3%)   583 (2.7%)   21265 (100.0%)
## -----
##
## -----
##  Chi.squared    df    p.value
## -----
##    8.8149       1     0.003
## -----
##
## -----
## Odds Ratio     Lo - 95%    Hi - 95%
## -----
##    0.54         0.37       0.81
## -----
##
## -----
## Risk Ratio     Lo - 0%     Hi - 0%
## -----
##    0.99         0.99       0.99
## -----
```

Breslow-Day Test to compare the effect of hematologic issues in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"hematologic")
```

```
##           comp      stat    p_valor
## X-squared h1n1-covid 3.748672 0.05284947
```

Severity

For the analysis of severity, all cases where hospitalization occurred were considered as serious cases. The cases where hospitalization was not necessary were considered as less serious cases.

```
#H1N1
dados_h1n1 <- dados_h1n1 %>%
  mutate(severity = factor(case_when(HOSPITAL == 1 ~ "hospitalized",
                                     HOSPITAL == 2 ~ "non-hospitalized",
                                     TRUE ~ NA_character_)))
dados_h1n1$severity <- relevel(
  dados_h1n1$severity,
  ref = "non-hospitalized"
)

#COVID-19
dados_covid <- dados_covid %>%
  mutate(severity = factor(case_when(HOSPITAL == 1 ~ "hospitalized",
                                     HOSPITAL == 2 ~ "non-hospitalized",
                                     TRUE ~ NA_character_)))
dados_covid$severity <- relevel(
  dados_covid$severity,
```

```

    ref = "non-hospitalized"
)

```

H1N1

```

with(dados_h1n1, ctable(pregnant_YN, severity, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

```

```

## Cross-Tabulation, Row Proportions
## pregnant_YN * severity
## Data Frame: dados_h1n1
##
##
## -----
##          severity  non-hospitalized  hospitalized      Total
## pregnant_YN
##          no          2166 (36.9%)    3698 (63.1%)    5864 (100.0%)
##          yes          535 (19.6%)    2190 (80.4%)    2725 (100.0%)
##          Total        2701 (31.4%)    5888 (68.6%)    8589 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##    257.6111    1      0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      2.40      2.15      2.67
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##      1.88      1.88      1.88
## -----

```

COVID-19

```

with(dados_covid, ctable(pregnant_YN, severity, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

```

```

## Cross-Tabulation, Row Proportions
## pregnant_YN * severity
## Data Frame: dados_covid
##
##
## -----
##          severity  non-hospitalized  hospitalized      Total

```



```
## pregnant_YN
##          no          3406 (5.4%)    59463 (94.6%)    62869 (100.0%)
##          yes          163 (3.1%)     5151 (96.9%)     5314 (100.0%)
##          Total        3569 (5.2%)    64614 (94.8%)    68183 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    54.0889     1     0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##    1.81         1.54         2.12
## -----
##
## -----
## Risk Ratio     Lo - 0%     Hi - 0%
## -----
##    1.77         1.77         1.77
## -----
```

Breslow-Day Test to compare the severity of both pandemics.

```
teste_breslowday(dados_covid,dados_h1n1,"severity")
```

```
##                comp      stat      p_valor
## X-squared h1n1-covid 8.097947 0.004431541
```

In sequence, we analyze only hospitalized cases:

```
#H1N1
dados_h1n1 <- dados_h1n1 %>%
  filter(severity == "hospitalized")

#COVID-19
dados_covid <- dados_covid %>%
  filter(severity == "hospitalized")
```

Symptoms

Fever

H1N1

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(fever = case_when(FEBRE == 1 ~ "yes",
                           FEBRE == 2 ~ "no",
                           TRUE ~ NA_character_))
```

```
with(dados_h1n1, ctable(pregnant_YN, fever, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * fever
## Data Frame: dados_h1n1
##
## -----
##          fever          no          yes          Total
## pregnant_YN
##      no      114 (3.1%)  3557 (96.9%)  3671 (100.0%)
##      yes      120 (5.5%)  2048 (94.5%)  2168 (100.0%)
##      Total    234 (4.0%)  5605 (96.0%)  5839 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      20.2889   1      0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      0.55      0.42      0.71
## -----
##
## -----
## Risk Ratio   Lo - 0%    Hi - 0%
## -----
##      0.56      0.56      0.56
## -----
```

COVID-19

```
dados_covid <- dados_covid %>%
  mutate(fever = case_when(FEBRE == 1 ~ "yes",
                           FEBRE == 2 ~ "no",
                           TRUE ~ NA_character_))
```

```
with(dados_covid, ctable(pregnant_YN, fever, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * fever
## Data Frame: dados_covid
##
## -----
##          fever          no          yes          Total
## pregnant_YN
```

```
##           no           14652 (27.9%)   37842 (72.1%)   52494 (100.0%)
##           yes           1420 (31.6%)    3076 (68.4%)    4496 (100.0%)
##          Total           16072 (28.2%)   40918 (71.8%)   56990 (100.0%)
## -----
##
## -----
##  Chi.squared   df   p.value
## -----
##    27.3945     1     0
## -----
##
## -----
##  Odds Ratio   Lo - 95%   Hi - 95%
## -----
##    0.84        0.79      0.90
## -----
##
## -----
##  Risk Ratio   Lo - 0%   Hi - 0%
## -----
##    0.88        0.88      0.88
## -----
```

Breslow-Day Test to compare the effect of fever in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"fever")
```

```
##           comp      stat      p_valor
## X-squared h1n1-covid 9.725931 0.001816863
```

Cough

H1N1

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(cough = case_when(TOSSE == 1 ~ "yes",
                           TOSSE == 2 ~ "no",
                           TRUE ~ NA_character_))
```

```
with(dados_h1n1, ctable(pregnant_YN, cough, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * cough
## Data Frame: dados_h1n1
```

```
##
## -----
##           cough           no           yes           Total
##  pregnant_YN
##           no           136 (3.7%)   3538 (96.3%)   3674 (100.0%)
```

```
##           yes           81 (3.7%)   2091 (96.3%)   2172 (100.0%)
##           Total          217 (3.7%)   5629 (96.3%)   5846 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##           0           1           1
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##           0.99          0.75          1.31
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##           0.99          0.99          0.99
## -----
```

COVID-19

```
dados_covid <- dados_covid %>%
  mutate(cough = case_when(TOSSE == 1 ~ "yes",
                           TOSSE == 2 ~ "no",
                           TRUE ~ NA_character_))
```

```
with(dados_covid, ctable(pregnant_YN, cough, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * cough
## Data Frame: dados_covid
##
## -----
##           cough           no           yes           Total
## pregnant_YN
##           no           10197 (18.9%)   43622 (81.1%)   53819 (100.0%)
##           yes           1003 (21.5%)    3668 (78.5%)    4671 (100.0%)
##           Total          11200 (19.1%)   47290 (80.9%)   58490 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##           17.5519    1       0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
```

```
## -----
##      0.85      0.79      0.92
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##      0.88      0.88      0.88
## -----
```

Breslow-Day Test to compare the effect of cough in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"cough")
```

```
##              comp      stat      p_valor
## X-squared h1n1-covid 1.01891 0.3127776
```

Dyspnea

H1N1

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(dyspnea = case_when(DISPNEIA == 1 ~ "yes",
                             DISPNEIA == 2 ~ "no",
                             TRUE ~ NA_character_))
```

```
with(dados_h1n1, ctable(pregnant_YN, dyspnea, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * dyspnea
## Data Frame: dados_h1n1
##
## -----
##      dyspnea      no      yes      Total
## pregnant_YN
##      no      667 (18.3%)  2972 (81.7%)  3639 (100.0%)
##      yes      514 (24.1%)  1618 (75.9%)  2132 (100.0%)
##      Total    1181 (20.5%)  4590 (79.5%)  5771 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      27.2362   1      0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
```

```
##      0.71      0.62      0.80
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.76      0.76      0.76
## -----
```

COVID-19

```
dados_covid <- dados_covid %>%
  mutate(dyspnea = case_when(DISPNEIA == 1 ~ "yes",
                             DISPNEIA == 2 ~ "no",
                             TRUE ~ NA_character_))
```

```
with(dados_covid, ctable(pregnant_YN, dyspnea, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * dyspnea
## Data Frame: dados_covid
##
## -----
##      dyspnea      no      yes      Total
## pregnant_YN
##      no      11018 (20.7%)  42214 (79.3%)  53232 (100.0%)
##      yes      1568 (34.7%)   2946 (65.3%)   4514 (100.0%)
##      Total      12586 (21.8%)  45160 (78.2%)  57746 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      480.2859    1      0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.49      0.46      0.52
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.60      0.60      0.60
## -----
```

Breslow-Day Test to compare the effect of dyspnea in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"dyspnea")
```

```
##                comp      stat      p_valor
## X-squared h1n1-covid 24.35352 8.018016e-07
```

Sore throat

H1N1

```
dados_h1n1 <- dados_h1n1 %>%
  mutate(sore_throat = case_when(GARGANTA == 1 ~ "yes",
                                GARGANTA == 2 ~ "no",
                                TRUE ~ NA_character_))
```

```
with(dados_h1n1, ctable(pregnant_YN, sore_throat, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
```

```
## pregnant_YN * sore_throat
```

```
## Data Frame: dados_h1n1
```

```
##
```

```
##
```

```
## ----- sore_throat ----- no ----- yes ----- Total
## pregnant_YN
##      no      1661 (46.8%)  1890 (53.2%)  3551 (100.0%)
##      yes      1043 (50.4%)  1027 (49.6%)  2070 (100.0%)
##      Total      2704 (48.1%)  2917 (51.9%)  5621 (100.0%)
## -----
```

```
##
```

```
##
```

```
## -----
```

```
## Chi.squared  df  p.value
```

```
## -----
```

```
##      6.6862      1      0.0097
```

```
## -----
```

```
##
```

```
## -----
```

```
## Odds Ratio  Lo - 95%  Hi - 95%
```

```
## -----
```

```
##      0.87      0.78      0.96
```

```
## -----
```

```
##
```

```
## -----
```

```
## Risk Ratio  Lo - 0%  Hi - 0%
```

```
## -----
```

```
##      0.93      0.93      0.93
```

```
## -----
```

```
##
```

COVID-19

```

dados_covid <- dados_covid %>%
  mutate(sore_throat = case_when(GARGANTA == 1 ~ "yes",
                                GARGANTA == 2 ~ "no",
                                TRUE ~ NA_character_))

with(dados_covid, ctable(pregnant_YN, sore_throat, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

## Cross-Tabulation, Row Proportions
## pregnant_YN * sore_throat
## Data Frame: dados_covid
##
##
## -----
##      sore_throat      no      yes      Total
## pregnant_YN
##      no      31319 (69.5%)  13765 (30.5%)  45084 (100.0%)
##      yes      2868 (72.6%)   1084 (27.4%)   3952 (100.0%)
##      Total    34187 (69.7%)  14849 (30.3%)  49036 (100.0%)
## -----
##
## -----
##      Chi.squared  df  p.value
## -----
##      16.4221      1  1e-04
## -----
##
## -----
##      Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      0.86        0.80      0.92
## -----
##
## -----
##      Risk Ratio  Lo - 0%  Hi - 0%
## -----
##      0.96        0.96      0.96
## -----

```

Breslow-Day Test to compare the effect of sore throat in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"sore_throat")
```

```

##              comp      stat  p_valor
## X-squared h1n1-covid 0.008784959 0.9253251

```

Diarrhea

H1N1


```

dados_h1n1 <- dados_h1n1 %>%
  mutate(diarrhea = case_when(DIARREIA == 1 ~ "yes",
                              DIARREIA == 2 ~ "no",
                              TRUE ~ NA_character_))

with(dados_h1n1, ctable(pregnant_YN, diarrhea, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

## Cross-Tabulation, Row Proportions
## pregnant_YN * diarrhea
## Data Frame: dados_h1n1
##
## -----
##           diarrhea           no           yes           Total
## pregnant_YN
##           no           2918 (84.2%)    548 (15.8%)    3466 (100.0%)
##           yes           1814 (90.8%)    184 ( 9.2%)    1998 (100.0%)
##           Total          4732 (86.6%)    732 (13.4%)    5464 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      47.0393    1       0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      0.54      0.45      0.64
## -----
##
## -----
## Risk Ratio   Lo - 0%   Hi - 0%
## -----
##      0.93      0.93      0.93
## -----

```

COVID-19

```

dados_covid <- dados_covid %>%
  mutate(diarrhea = case_when(DIARREIA == 1 ~ "yes",
                              DIARREIA == 2 ~ "no",
                              TRUE ~ NA_character_))

with(dados_covid, ctable(pregnant_YN, diarrhea, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

## Cross-Tabulation, Row Proportions
## pregnant_YN * diarrhea
## Data Frame: dados_covid

```

```
##
##
## -----
##           diarrhea           no           yes           Total
## pregnant_YN
##           no           34139 (77.2%)   10106 (22.8%)   44245 (100.0%)
##           yes           3287 (85.7%)    549 (14.3%)    3836 (100.0%)
##           Total        37426 (77.8%)   10655 (22.2%)   48081 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    148.3761    1     0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.56      0.51      0.62
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.90      0.90      0.90
## -----
```

Breslow-Day Test to compare the effect of diarrhea in both pandemics

```
teste_breslowday(dados_covid,dados_h1n1,"diarrhea")
```

```
##           comp      stat   p_valor
## X-squared h1n1-covid 0.1830762 0.6687429
```

Outcome

```
#H1N1
dados_h1n1 <- dados_h1n1 %>%
  mutate(progression = case_when(EVOLUCAO == 1 ~ "cure",
                                EVOLUCAO == 2 ~ "death",
                                EVOLUCAO == 3 ~ "death",
                                EVOLUCAO == 4 ~ "death",
                                TRUE ~ NA_character_))

#COVID-19
dados_covid <- dados_covid %>%
  mutate(progression = case_when(EVOLUCAO == 1 ~ "cure",
                                EVOLUCAO == 2 ~ "death",
                                EVOLUCAO == 3 ~ "death",
                                TRUE ~ NA_character_))
```

H1N1

```
with(dados_h1n1, ctable(pregnant_YN, progression, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * progression
## Data Frame: dados_h1n1
##
## -----
##      progression      cure      death      Total
## pregnant_YN
##      no      3024 (87.4%)    437 (12.6%)    3461 (100.0%)
##      yes      1806 (90.3%)    195 ( 9.7%)    2001 (100.0%)
##      Total      4830 (88.4%)    632 (11.6%)    5462 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      10.0078        1    0.0016
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      0.75          0.62        0.89
## -----
##
## -----
##      Risk Ratio    Lo - 0%    Hi - 0%
## -----
##      0.97          0.97        0.97
## -----
```

COVID-19

```
with(dados_covid, ctable(pregnant_YN, progression, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## pregnant_YN * progression
## Data Frame: dados_covid
##
## -----
##      progression      cure      death      Total
## pregnant_YN
##      no      44075 (82.6%)    9276 (17.4%)    53351 (100.0%)
##      yes      4124 (90.3%)     445 ( 9.7%)     4569 (100.0%)
##      Total      48199 (83.2%)    9721 (16.8%)    57920 (100.0%)
```

```
## -----
##
## -----
## Chi.squared  df  p.value
## -----
## 175.6697      1      0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
## 0.51          0.46        0.57
## -----
##
## -----
## Risk Ratio    Lo - 0%    Hi - 0%
## -----
## 0.92          0.92        0.92
## -----
```

Breslow-Day Test to compare the progression for both pandemics.

```
teste_breslowday(dados_covid,dados_h1n1,"progression")
```

```
##              comp      stat      p_valor
## X-squared h1n1-covid 13.09378 0.0002962787
```