

Cardiovascular diseases worsen the maternal prognosis of COVID-19

Codes and outputs

06/08/2022

Description

This file presents the documentation of the analysis of article “Cardiovascular diseases worsen the maternal prognosis of COVID-19” with authors Carolina Testa, Luciana Godoi, Maria Rita Bortolotto, Nátaly Monroy, Bruna de Mattos, Agatha Rodrigues, and Rossana Francisco.

R packages used, functions and dataset import

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",  
  "MatchIt",  
  "lubridate",  
  "readr",  
  "readxl",  
  "ggplot2",  
  "kableExtra",  
  "tables",  
  "questionr",  
  "car",  
  "data.table",  
  "magrittr",  
  "tidyverse",  
  "readxl",  
  "summarytools",  
  "modelsummary",  
  "RColorBrewer",  
)
```

```

    "zoo",
    "WeightIt",
    "jtools",
    "cobalt",
    "weights",
    "psych"
  )
lapply(packages, loadlibrary)

```

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

```

#functions for summary measures
media <- function(x)
  mean(x, na.rm = TRUE)
mediana <- function(x)
  median(x, na.rm = TRUE)
DP <- function(x)
  sd(x, na.rm = TRUE)
minimo <- function(x)
  base::min(x, na.rm = TRUE)
maximo <- 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))

```

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.

Notification is mandatory for Influenza Syndrome (characterized by at least two of the following signs and symptoms: fever, even if referred, chills, sore throat, headache, cough, runny nose, olfactory or taste disorders) and who has dyspnea/respiratory discomfort or persistent pressure in the chest or O₂ saturation less than 95% in room air or bluish color of the lips or face. Asymptomatic individuals with laboratory confirmation by molecular biology or immunological examination for COVID-19 infection are also reported.

For notifications in Sivep-Gripe, hospitalized cases in both public and private hospitals and all deaths due to severe acute respiratory infections regardless of hospitalization must be considered.

The search was limited to the first notified case of COVID-19 in February 2020 until the 15th epidemiological week of 2021 (up to April 17, 2021). The datasets were obtained on May 5, 2021, on the site <https://opendatasus.saude.gov.br/dataset>. The first period (8th to 53rd epidemiological week of 2020) and the second period (1st to 15th epidemiological week of 2021) datasets can be obtained at <https://drive.google.com/file/d/1jts4h0ovdwFh86SdKyslMLSG9rOy3UjX/view?usp=sharing> and at https://drive.google.com/file/d/1gQSy_dcUkd1UrDEcsrDbyGl4gEvcI8z_/view?usp=sharing, respectively. The data are loaded below:

```

##### loading the datasets #####
#2021
data_2021 <- read_delim(

```

```

"INFLUD21-03-05-2021.csv",
",",
escape_double = FALSE,
locale = locale(encoding = "ISO-8859-2"),
trim_ws = TRUE
)

#2020
data_2020 <- read_delim(
  "INFLUD-03-05-2021.csv",
  ",",
  escape_double = FALSE,
  locale = locale(encoding = "ISO-8859-2"),
  trim_ws = TRUE
)

sem <- 15 #limit of epidemiological week of 2021

#memory.limit(999999)

#### Concatenating 2020 and 2021 data #####
data_all <- rbind(data_2020, data_2021)

#Creating the case year variable
data_all <- data_all %>%
  dplyr::mutate(
    dt_sint = as.Date(DT_SIN_PRI, format = "%d/%m/%Y"),
    year_case = lubridate::year(dt_sint),
  )

```

There are 1905854 observations. The case selection is presented in the following according to the flowchart presented in the article.

Case selection and data treatment

The first filter consists of selecting the cases from 8th epidemiological week of 2020 to 15th epidemiological week of 2021.

```

#Cases from the 8th epidemiological week of 2020 to 15th of 2021
data1 <- data_all %>%
  filter((year_case==2020 & SEM_PRI >=8) | year_case ==2021)

```

There are 12563 cases in 2021 in epidemiological week 53 of 2020. These are cases from the first two days of 2021, which are still part of the last epidemiological week of 2020 (<http://portalsinan.saude.gov.br/calendario-epidemiologico?layout=edit&id=168>). However, these cases belong to the 53rd week of 2020 and we corrected as follows:

```

data1 <- data1 %>%
  mutate(year_case = ifelse(year_case ==2021 & SEM_PRI ==53, 2020, year_case)) %>%
  filter(year_case==2020 | (year_case ==2021 & SEM_PRI <= sem))

```

There are 1876953 observations.

The next selection consists of selecting only confirmed cases of COVID-19:

```
##Filtering confirmed cases of COVID-19
data2 <- data1 %>%
  filter(CLASSI_FIN == 5)
```

There are 1174350 observations.

```
with(data2, table(PCR_SARS2, CRITERIO))
```

```
##          CRITERIO
## PCR_SARS2      1      2      3      4
##          1 755241  1546  2607  1344
```

The next step is to identify hospitalized cases (HOSPITAL=1) and then select only those cases.

```
##Filtering only hospitalized cases
data3 <- data2 %>%
  filter(HOSPITAL == 1)
```

Now we have 1114042 observations.

The next selection consists of selecting females cases:

```
##Filtering female notifications
data4 <- filter(data3, CS_SEX0 == "F")
```

There are 495698 observations.

The next selection consists of selecting women between 10 and 55 years old.

```
##Filtering women aged 10-55
data5 <- data4 %>%
  filter(NU_IDADE_N > 9 & NU_IDADE_N <= 55)
```

There are 174525 observations.

The next step is to identify pregnant and postpartum people (variable `classi_gesta_puerp`) and then select only those cases.

```
##Creating the classification variable if pregnant, postpartum and not (neither pregnant nor postpartum)
data5 <- data5 %>%
  mutate(
    classi_gesta_puerp = case_when(
      CS_GESTANT == 1 ~ "1tri", #1st trimester
      CS_GESTANT == 2 ~ "2tri", #2nd trimester
      CS_GESTANT == 3 ~ "3tri", #3rd trimester
      CS_GESTANT == 4 ~ "IG_ig", #ignored gestational Age
      CS_GESTANT == 5 &
        PUERPERA == 1 ~ "puerp", #puerperium
      CS_GESTANT == 9 & PUERPERA == 1 ~ "puerp", #puerperium
    )
  )
```

```

    TRUE ~ "no" #neither pregnant nor postpartum
  )
)

#Filtering only pregnant and postpartum women
data6 <- data5 %>%
  filter(classi_gesta_puerp != "no")

```

There are 10635 observations.

The variable identified as EVOLUCAO is categorized with 1 - cure, 2 - death by SARS, 3 - death by other cause, 9 - ignored.

```
with(data6, freq(EVOLUCAO))
```

```
## Frequencies
## data6$EVOLUCAO
## Type: Numeric
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##          1   8005    85.38      85.38    75.27     75.27
##          2    979    10.44      95.82     9.21     84.48
##          3     15     0.16      95.98     0.14     84.62
##          9    377     4.02     100.00     3.54     88.16
##         <NA>  1259          100.00    11.84    100.00
##         Total 10635    100.00     100.00   100.00    100.00
```

Now we are going to select only the finalized cases:

```

#Filtering only finalized cases
data7 <- data6 %>%
  filter((EVOLUCAO == 1 | EVOLUCAO == 2 | EVOLUCAO == 3) & !is.na(EVOLUCAO))

#Creating the evolution variable
data7 <- data7 %>%
  mutate(evolution = case_when(
    EVOLUCAO == 1 ~ "cure",
    EVOLUCAO == 2 ~ "death",
    EVOLUCAO == 3 ~ "death"
  ))

with(data7, freq(evolution))

```

```
## Frequencies
## data7$evolution
## Type: Character
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##         cure   8005    88.95      88.95    88.95     88.95
##        death    994    11.05     100.00    11.05    100.00
##         <NA>     0          100.00     0.00    100.00
##         Total  8999    100.00     100.00   100.00    100.00
```

There are 8999 confirmed and hospitalized cases of COVID-19 in pregnant and postpartum women aged 10 to 55 years. We identify 60.42% of these notifications without any information about the presence or absence of cardiovascular diseases (CVD). The next selection consists of selecting cases where the CVD variable (CARDIOPATI) indicates yes or no:

```
with(data7, freq(CARDIOPATI))
```

```
## Frequencies
## data7$CARDIOPATI
## Type: Numeric
##
##          Freq  % Valid  % Valid Cum.  % Total  % Total Cum.
## -----
##          1    602    16.55      16.55     6.69     6.69
##          2   2960    81.39     97.94    32.89    39.58
##          9     75     2.06    100.00     0.83    40.42
##         <NA>  5362    100.00    100.00    59.58   100.00
##         Total 8999    100.00    100.00   100.00   100.00
```

```
#Creating the CVD variable
data7 <- data7 %>%
  mutate(CVD = case_when(
    CARDIOPATI == 1 ~ "yes",
    CARDIOPATI == 2 ~ "no",
    TRUE ~ NA_character_
  ))
```

Now we present the final dataset.

```
#Filtering cases with information about CVD
data <- data7 %>%
  filter(!is.na(CVD))
```

```
questionr::freq(
  data$CVD,
  cum = FALSE,
  total = TRUE,
  na.last = FALSE,
  valid = FALSE
) %>%
  kable(caption = "Frequency of CVD", digits = 2) %>%
  kable_styling(latex_options = "HOLD_position")
```

Table 1: Frequency of CVD

| | n | % |
|-------|------|-------|
| no | 2960 | 83.1 |
| yes | 602 | 16.9 |
| Total | 3562 | 100.0 |

```

data7 <- data7 %>%
  mutate(pcr_covid_SN = case_when(
    (PCR_SARS2 == 1) |
    (
      str_detect(DS_PCR_OUT, "COVID|COVID 19|COVID-19")
    ) ~ "yes",
    TRUE ~ "no"
  ))

data7 <- data7 %>%
  mutate(ant_covid_SN = case_when(
    (AN_SARS2 == 1 & pcr_covid_SN != "yes") |
    (pcr_covid_SN != "yes" &
      str_detect(DS_AN_OUT, "COVID|COVID 19|COVID 19|COVID-19|COVID19|SARS COV 2|SARS COV-2|
      SARS COVID 19|SARS-COV-2|SARS-COV2|SARS-COV2 - TESTE RAPIDO|SARS-COVID2|SARS
      TR COVID IGM +"))
    ) ~ "yes",
    TRUE ~ "no"
  ))

data7 <- data7 %>%
  mutate(soro_SN = case_when(
    ((RES_IGG == 1 | RES_IGM == 1 | RES_IGA == 1) & (pcr_covid_SN != "yes") & (ant_covid_SN != "yes")
    ) ~ "yes",
    TRUE ~ "no"
  ))

data <- data7 %>%
  filter(!is.na(CVD))

```

The variable CRITERIO presents the criterion used for the final classification of the case, 1 - laboratory, 2 - clinical epidemiological, 3 - clinical and 4 - clinical by image (chest x-ray/tomography).

```
table(data$CRITERIO, useNA="ifany")
```

```
##
##      1      2      3      4 <NA>
## 3327    16    51   128    40
```

We note that some observations with the variable CRITERIO as 2 - clinical epidemiological, 3 - clinical and 4 - clinical by image (chest x-ray/tomography) or empty cell had positive laboratory results. To evaluate this cases, we considered a new variable named as Final_criterion.

```

data$Final_criterion <- data$CRITERIO

a2 <- which(data$CRITERIO==2 & (data$soro_SN == "yes" | data$ant_covid_SN == "yes" | data$pcr_covid_SN
data$Final_criterion[a2] <- 1

a3 <- which(data$CRITERIO==3 & (data$soro_SN == "yes" | data$ant_covid_SN == "yes" | data$pcr_covid_SN
data$Final_criterion[a3] <- 1

a4 <- which(data$CRITERIO==4 & (data$soro_SN == "yes" | data$ant_covid_SN == "yes" | data$pcr_covid_SN

```

```
data$Final_criterion[a4] <- 1

a <- which(is.na(data$CRITERIO) & (data$soro_SN == "yes" | data$ant_covid_SN == "yes" | data$pcr_covid_
data$Final_criterion[a] <- 1

table(data$Final_criterion, useNA="ifany")
```

```
##
##      1      2      3      4 <NA>
## 3381      8     36    126     11
```

```
round(prop.table(table(data$Final_criterion, useNA="ifany"))*100, 2)
```

```
##
##      1      2      3      4 <NA>
## 94.92  0.22  1.01  3.54  0.31
```

These 0.31% cases of NA's corresponds to observations waiting the results of laboratory tests or observations with positive results of RT-PCR and/or antigen test without specification for COVID-19 or any other virus. Of the 126 observations with criteria defined by imaging, 54 (42.86%) of them are awaiting laboratory results (RES_AN== 5 and PCR_RESUL == 5).

Epidemiologic characteristics

Ethnicity

```
# Ethnicity
data <- data %>%
  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_
    )
  )
```

```
with(data, ctable(ethnicity, CVD, prop = "c", useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Column Proportions
```

```
## ethnicity * CVD
```

```
## Data Frame: data
```

```
##
```

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

```
##           CVD           no           yes           Total
```

```
## ethnicity
```



```
##          black          167 ( 6.5%)    46 ( 9.1%)    213 ( 6.9%)
##          brown         1375 (53.5%)   244 (48.1%)   1619 (52.6%)
##    indigenous          30 ( 1.2%)     1 ( 0.2%)    31 ( 1.0%)
##          white          975 (37.9%)   214 (42.2%)   1189 (38.6%)
##          yellow         24 ( 0.9%)     2 ( 0.4%)    26 ( 0.8%)
##          Total         2571 (100.0%)  507 (100.0%)  3078 (100.0%)
## -----
```

```
fisher.test(data$ethnicity, data$CVD)
```

```
##
## Fisher's Exact Test for Count Data
##
## data: data$ethnicity and data$CVD
## p-value = 0.007096
## alternative hypothesis: two.sided
```

Education

```
data <- data %>%
  mutate(education = case_when(CS_ESCOL_N == 0 ~ "No schooling",
                                CS_ESCOL_N == 1 ~ "1st to 5th grade",
                                CS_ESCOL_N == 2 ~ "6th to 9th grade",
                                CS_ESCOL_N == 3 ~ "Middle school",
                                CS_ESCOL_N == 4 ~ "Superior",
                                TRUE ~ NA_character_))
```

```
data$education <- factor(data$education,
  levels = c("No schooling", "1st to 5th grade", "6th to 9th grade",
             "Middle school", "Superior"))
```

```
with(data, ctable(education, CVD, prop = "c", useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Column Proportions
## education * CVD
## Data Frame: data
##
## -----
##          CVD          no          yes          Total
##    education
##    No schooling      11 ( 0.7%)      2 ( 0.7%)      13 ( 0.7%)
##    1st to 5th grade    123 ( 7.9%)     33 (12.2%)     156 ( 8.5%)
##    6th to 9th grade    307 (19.7%)     52 (19.2%)     359 (19.6%)
##    Middle school      857 (55.0%)    140 (51.7%)     997 (54.5%)
##    Superior          260 (16.7%)     44 (16.2%)     304 (16.6%)
##    Total            1558 (100.0%)    271 (100.0%)    1829 (100.0%)
## -----
```

```
fisher.test(data$education, data$CVD)
```

```
##
## Fisher's Exact Test for Count Data
##
## data: data$education and data$CVD
## p-value = 0.2405
## alternative hypothesis: two.sided
```

Age (Years)

```
datasummary((CVD) ~ NU_IDADE_N*(n+media+DP+mediana+minimo+maximo+q25+q75+IQR),
  data = data, output = 'markdown')
```

| CVD | n | media | DP | mediana | minimo | maximo | q25 | q75 | IQR |
|-----|------|-------|------|---------|--------|--------|-------|-------|-------|
| no | 2960 | 30.00 | 7.43 | 30.00 | 13.00 | 55.00 | 24.00 | 35.00 | 11.00 |
| yes | 602 | 34.76 | 8.52 | 34.00 | 15.00 | 55.00 | 29.00 | 39.75 | 10.75 |

```
t.test(NU_IDADE_N ~ CVD, data = data)
```

```
##
## Welch Two Sample t-test
##
## data: NU_IDADE_N by CVD
## t = -12.745, df = 797.4, p-value < 2.2e-16
## alternative hypothesis: true difference in means between group no and group yes is not equal to 0
## 95 percent confidence interval:
## -5.485124 -4.021042
## sample estimates:
## mean in group no mean in group yes
## 30.00439 34.75748
```

Age group

```
data <- data %>%
  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_
    )
  )
data$age_group <-
  factor(data$age_group, levels = c("<20", "20-34", ">=35"))
```

```
with(data, ctable(age_group, CVD, prop = "c", useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Column Proportions
## age_group * CVD
## Data Frame: data
##
## -----
##           CVD           no           yes           Total
## age_group
##   <20         237 ( 8.0%)    10 ( 1.7%)    247 ( 6.9%)
##   20-34       1895 ( 64.0%)   292 ( 48.5%)   2187 ( 61.4%)
##   >=35        828 ( 28.0%)   300 ( 49.8%)   1128 ( 31.7%)
##   Total       2960 (100.0%)   602 (100.0%)   3562 (100.0%)
## -----
```

```
with(data, fisher.test(age_group, CVD))
```

```
##
## Fisher's Exact Test for Count Data
##
## data: age_group and CVD
## p-value < 2.2e-16
## alternative hypothesis: two.sided
```

Now we consider a new grouping for the age variable by analyzing adolescents in more detail.

```
data <- data %>%
  mutate(
    age_group2 = case_when(
      NU_IDADE_N <= 13 ~ "<14",
      NU_IDADE_N <= 18 & NU_IDADE_N <= 14 ~ "14-18",
      NU_IDADE_N > 18
      & NU_IDADE_N <= 34 ~ "19-34",
      NU_IDADE_N > 34 ~ ">=35",
      TRUE ~ NA_character_
    )
  )
data$age_group2 <-
  factor(data$age_group2, levels = c("<14", "14-18", "19-34", ">=35"))
```

```
with(data, ctable(age_group2, CVD, prop = "c", useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Column Proportions
## age_group2 * CVD
## Data Frame: data
##
## -----
##           CVD           no           yes           Total
## age_group2
##   <14         1 ( 0.04%)    0 ( 0.0%)    1 ( 0.03%)
##   14-18        9 ( 0.32%)    0 ( 0.0%)    9 ( 0.26%)
```

```
##      19-34      1970 ( 70.16%)   300 ( 50.0%)   2270 ( 66.61%)
##      >=35      828 ( 29.49%)   300 ( 50.0%)   1128 ( 33.10%)
##      Total      2808 (100.00%)   600 (100.0%)   3408 (100.00%)
## -----
```

```
with(data, fisher.test(age_group2, CVD))
```

```
##
## Fisher's Exact Test for Count Data
##
## data: age_group2 and CVD
## p-value < 2.2e-16
## alternative hypothesis: two.sided
```

Residence area

```
data <- data %>%
  mutate(zone = case_when(CS_ZONA == 1 ~ "Urban",
                           CS_ZONA == 2 ~ "Rural",
                           CS_ZONA == 3 ~ "Periurban",
                           TRUE ~ NA_character_))
```

```
with(data, ctable( zone, CVD, prop = "c", useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Column Proportions
## zone * CVD
## Data Frame: data
##
## -----
##           CVD           no           yes           Total
##      zone
## Periurban      10 ( 0.4%)      3 ( 0.5%)      13 ( 0.4%)
##      Rural     159 ( 5.7%)     24 ( 4.4%)     183 ( 5.5%)
##      Urban    2618 (93.9%)    522 (95.1%)    3140 (94.1%)
##      Total    2787 (100.0%)    549 (100.0%)   3336 (100.0%)
## -----
```

```
fisher.test(data$zone, data$CVD)
```

```
##
## Fisher's Exact Test for Count Data
##
## data: data$zone and data$CVD
## p-value = 0.3673
## alternative hypothesis: two.sided
```

Gestational moment

```
ctable(data$classi_gesta_puerp, data$CVD, prop="c", OR=TRUE, useNA = "no", chisq = TRUE)
```

```
## Cross-Tabulation, Column Proportions
## classi_gesta_puerp * CVD
## Data Frame: data
##
## -----
##           CVD           no           yes           Total
## classi_gesta_puerp
##           1tri          161 ( 5.4%)          34 ( 5.6%)          195 ( 5.5%)
##           2tri          471 (15.9%)          120 (19.9%)          591 (16.6%)
##           3tri          1199 (40.5%)          248 (41.2%)          1447 (40.6%)
##           IG_ig           84 ( 2.8%)           30 ( 5.0%)          114 ( 3.2%)
##           puerp          1045 (35.3%)          170 (28.2%)          1215 (34.1%)
##           Total          2960 (100.0%)          602 (100.0%)          3562 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      19.4898     4     6e-04
## -----
```

Hospital-acquired infection

```
data <- data %>%
  mutate(hospital_infection = case_when(NOSOCOMIAL == 1 ~ "yes",
                                         NOSOCOMIAL == 2 ~ "no",
                                         TRUE ~ NA_character_))
```

```
with(data, ctable( hospital_infection, CVD, prop = "c", useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Column Proportions
## hospital_infection * CVD
## Data Frame: data
##
## -----
##           CVD           no           yes           Total
## hospital_infection
##           no          2551 ( 98.0%)          448 ( 98.0%)          2999 ( 98.0%)
##           yes           53 (  2.0%)           9 (  2.0%)           62 (  2.0%)
##           Total          2604 (100.0%)          457 (100.0%)          3061 (100.0%)
## -----
```

```
fisher.test(data$hospital_infection, data$CVD)
```

```
##
## Fisher's Exact Test for Count Data
```

```
##
## data: data$hospital_infection and data$CVD
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.4163122 1.9955578
## sample estimates:
## odds ratio
## 0.9669453
```

Symptoms

Fever

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

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

```
## Cross-Tabulation, Row Proportions
## CVD * fever
## Data Frame: data
##
## -----
##      fever      no      yes      Total
## CVD
## no      1289 (44.2%)  1625 (55.8%)  2914 (100.0%)
## yes      209 (38.3%)   337 (61.7%)   546 (100.0%)
## Total    1498 (43.3%)  1962 (56.7%)  3460 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      6.4048    1  0.0114
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.28      1.06    1.54
## -----
```

Cough

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

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

```
## Cross-Tabulation, Row Proportions
## CVD * cough
## Data Frame: data
##
## -----
##      cough      no      yes      Total
## CVD
## no      1002 (34.4%)  1913 (65.6%)  2915 (100.0%)
## yes      138 (24.6%)   424 (75.4%)   562 (100.0%)
## Total    1140 (32.8%)  2337 (67.2%)  3477 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      20.1693    1      0
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.61      1.31      1.98
## -----
```

Sore throat

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

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

```
## Cross-Tabulation, Row Proportions
## CVD * sore_throat
## Data Frame: data
##
## -----
##      sore_throat      no      yes      Total
## CVD
```

```
##      no                2245 (78.5%)    616 (21.5%)    2861 (100.0%)
##      yes                367 (74.7%)    124 (25.3%)     491 (100.0%)
##      Total              2612 (77.9%)    740 (22.1%)    3352 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      3.1648         1    0.0752
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.23          0.99        1.54
## -----
```

Dyspnea

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

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

```
## Cross-Tabulation, Row Proportions
## CVD * dyspnea
## Data Frame: data
##
## -----
##      dyspnea          no          yes          Total
##      CVD
##      no          1361 (46.7%)    1553 (53.3%)    2914 (100.0%)
##      yes          154 (27.7%)     401 (72.3%)     555 (100.0%)
##      Total        1515 (43.7%)    1954 (56.3%)    3469 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      67.3439         1      0
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      2.28          1.87        2.79
## -----
```


Respiratory distress

```
data <- data %>%
  mutate(resp_dist = case_when(DESC_RESP == 1 ~ "yes",
                                DESC_RESP == 2 ~ "no",
                                TRUE ~ NA_character_))
```

```
with(data, ctable(CVD, resp_dist, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

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

```
## CVD * resp_dist
```

```
## Data Frame: data
```

```
##
```

```
##
```

```
## -----
##      resp_dist      no      yes      Total
## CVD
## no      1541 (53.1%)  1361 (46.9%)  2902 (100.0%)
## yes      213 (40.3%)   316 (59.7%)   529 (100.0%)
## Total    1754 (51.1%)  1677 (48.9%)  3431 (100.0%)
## -----
```

```
##
```

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

```
## 28.9948      1      0
## -----
```

```
##
```

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

```
## 1.68      1.39      2.03
## -----
```

Saturation

```
data <- data %>%
  mutate(saturation = case_when(SATURACAO == 1 ~ "yes",
                                SATURACAO == 2 ~ "no",
                                TRUE ~ NA_character_))
```

```
with(data, ctable(CVD, saturation, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

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

```
## CVD * saturation
```

```
## Data Frame: data
```

```
##
```

```
##
```

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

```
##           saturation           no           yes           Total
##    CVD
##    no           1873 (65.1%)    1003 (34.9%)    2876 (100.0%)
##    yes           231 (43.4%)     301 (56.6%)     532 (100.0%)
##    Total         2104 (61.7%)    1304 (38.3%)    3408 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      88.612        1        0
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      2.43         2.02        2.94
## -----
```

Diarrhea

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

```
with(data, ctable(CVD, diarrhea, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * diarrhea
## Data Frame: data
##
## -----
##           diarrhea           no           yes           Total
##    CVD
##    no           2557 (88.8%)    324 (11.2%)    2881 (100.0%)
##    yes           421 (87.0%)     63 (13.0%)     484 (100.0%)
##    Total         2978 (88.5%)    387 (11.5%)    3365 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      1.1081        1    0.2925
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.18         0.88        1.58
## -----
```

Vomit

```
data <- data %>%
  mutate(vomit = case_when(VOMITO == 1 ~ "yes",
                            VOMITO == 2 ~ "no",
                            TRUE ~ NA_character_))

with(data, ctable(CVD, vomit, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * vomit
## Data Frame: data
##
## -----
##      vomit      no      yes      Total
## CVD
## no      2589 (90.2%)  282 ( 9.8%) 2871 (100.0%)
## yes      423 (87.9%)   58 (12.1%) 481 (100.0%)
## Total    3012 (89.9%)  340 (10.1%) 3352 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      2.021     1  0.1551
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.26      0.93    1.70
## -----
```

Abdominal pain

```
data <- data %>%
  mutate(abd_pain = case_when(DOR_ABD == 1 ~ "yes",
                              DOR_ABD == 2 ~ "no",
                              TRUE ~ NA_character_))

with(data, ctable(CVD, abd_pain, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * abd_pain
## Data Frame: data
##
## -----
```

```
##          abd_pain          no          yes          Total
##      CVD
##      no          1877 (91.1%)    183 ( 8.9%)    2060 (100.0%)
##      yes          291 (89.0%)     36 (11.0%)     327 (100.0%)
##      Total        2168 (90.8%)    219 ( 9.2%)    2387 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      1.2858         1    0.2568
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.27          0.87        1.85
## -----
```

Fatigue

```
data <- data %>%
  mutate(fatigue = case_when(FADIGA == 1 ~ "yes",
                             FADIGA == 2 ~ "no",
                             TRUE ~ NA_character_))
```

```
with(data, ctable(CVD, fatigue, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * fatigue
## Data Frame: data
##
## -----
##          fatigue          no          yes          Total
##      CVD
##      no          1609 (77.8%)    460 (22.2%)    2069 (100.0%)
##      yes          238 (69.6%)    104 (30.4%)     342 (100.0%)
##      Total        1847 (76.6%)    564 (23.4%)    2411 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      10.4972         1    0.0012
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.53          1.19        1.97
## -----
```

Loss of smell

```
data <- data %>%
  mutate(loss_smell = case_when(PERD_OLFT == 1 ~ "yes",
                                PERD_OLFT == 2 ~ "no",
                                TRUE ~ NA_character_))

with(data, ctable(CVD, loss_smell, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

## Cross-Tabulation, Row Proportions
## CVD * loss_smell
## Data Frame: data
##
## -----
##           loss_smell           no           yes           Total
## CVD
## no           1683 (81.4%)    384 (18.6%)    2067 (100.0%)
## yes           250 (74.2%)     87 (25.8%)     337 (100.0%)
## Total        1933 (80.4%)    471 (19.6%)    2404 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##    9.1828     1  0.0024
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##    1.53       1.17     1.99
## -----
```

Loss of taste

```
data <- data %>%
  mutate(loss_taste = case_when(PERD_PALA == 1 ~ "yes",
                                PERD_PALA == 2 ~ "no",
                                TRUE ~ NA_character_))

with(data, ctable(CVD, loss_taste, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))

## Cross-Tabulation, Row Proportions
## CVD * loss_taste
## Data Frame: data
##
## -----
```

```
##           loss_taste           no           yes           Total
## CVD
## no           1694 (82.1%)    369 (17.9%)    2063 (100.0%)
## yes           250 (74.0%)     88 (26.0%)     338 (100.0%)
## Total         1944 (81.0%)    457 (19.0%)    2401 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    11.9908     1    5e-04
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##     1.62       1.24     2.11
## -----
```

Any respiratory symptom

Now we are going to create the variable `resp_symp` indicating the presence of at least one respiratory symptom (Dyspnea, Fadigue, Saturation, Respiratory distress). Empty cells are considered missing data (<NA>). The variable `qt_resp_symp` indicates the number of respiratory symptoms of each case.

```
df <- select(data,dyspnea,fatigue,saturation,resp_dist )
soma <- function(x){
  if (sum(is.na(x))==4)
    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
data$qt_sintomas_resp_aux <- apply(df,1,soma)

data <- data %>%
  mutate(resp_symp = case_when(qt_sintomas_resp_aux >=1 ~ "yes",
                                qt_sintomas_resp_aux ==0 ~ "no",
                                TRUE ~ NA_character_))

with(data, ctable(CVD, resp_symp, prop="r", useNA = "no", chisq = TRUE, OR = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * resp_symp
## Data Frame: data
##
## -----
##           resp_symp           no           yes           Total
## CVD
## no           935 (31.9%)    1992 (68.1%)    2927 (100.0%)
## yes           94 (16.3%)     484 (83.7%)     578 (100.0%)
## Total         1029 (29.4%)    2476 (70.6%)    3505 (100.0%)
## -----
```

```
##
## -----
## Chi.squared   df   p.value
## -----
##      56.4759    1      0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      2.42      1.91      3.05
## -----
```

```
data <- data %>%
  mutate(qt_resp_symp = case_when(qt_sintomas_resp_aux == 4 ~ "4 symptoms",
                                   qt_sintomas_resp_aux == 3 ~ "3 symptoms",
                                   qt_sintomas_resp_aux == 2 ~ "2 symptoms",
                                   qt_sintomas_resp_aux == 1 ~ "1 symptom",
                                   qt_sintomas_resp_aux == 0 ~ "No respiratory symptom",
                                   TRUE ~ NA_character_))

with(data, ctable(qt_resp_symp, CVD, prop="c", useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Column Proportions
```

```
## qt_resp_symp * CVD
```

```
## Data Frame: data
```

```
##
## -----
##               CVD              no              yes              Total
## qt_resp_symp
##      1 symptom      640 ( 21.9%)    116 ( 20.1%)    756 ( 21.6%)
##      2 symptoms     528 ( 18.0%)    151 ( 26.1%)    679 ( 19.4%)
##      3 symptoms     615 ( 21.0%)    164 ( 28.4%)    779 ( 22.2%)
##      4 symptoms     209 (  7.1%)     53 (  9.2%)    262 (  7.5%)
## No respiratory symptom 935 ( 31.9%)     94 ( 16.3%)   1029 ( 29.4%)
##              Total    2927 (100.0%)    578 (100.0%)   3505 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      71.8703    4      0
## -----
```

Any symptom

```
df <- select(data, dyspnea, fatigue, saturation, resp_dist, fever, cough, sore_throat, diarrhea, vomit,

soma <- function(x){
  if (sum(is.na(x)) == 12)
```

```

    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
data$qt_symp_aux <- apply(df,1,soma)

data <- data %>%
  mutate(symp = case_when(qt_symp_aux >= 1 ~ "yes",
                          qt_symp_aux == 0 ~ "no",
                          TRUE ~ NA_character_))

with(data, ctable(CVD, symp, prop="r", useNA = "no", chisq = TRUE, OR=TRUE))

```

```

## Cross-Tabulation, Row Proportions
## CVD * symp
## Data Frame: data
##
## -----
##      symp      no      yes      Total
## CVD
## no      256 (8.7%) 2685 (91.3%) 2941 (100.0%)
## yes      22 (3.7%) 574 (96.3%) 596 (100.0%)
## Total    278 (7.9%) 3259 (92.1%) 3537 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##    16.513     1     0
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##     2.49      1.59     3.88
## -----

```

Comorbidities

```

#Hematologic
data <- data %>%
  mutate(hematologic = case_when(HEMATOLOGI == 1 ~ "yes",
                                HEMATOLOGI == 2 ~ "no",
                                TRUE ~ NA_character_))

#Immunodepression
data <- data %>%
  mutate(immunodepre = case_when(IMUNODEPRE == 1 ~ "yes",
                                IMUNODEPRE == 2 ~ "no",
                                TRUE ~ NA_character_))

```



```

#Hepatic
data <- data %>%
mutate(hepatic = case_when(HEPATICA == 1 ~ "yes",
                           HEPATICA== 2 ~ "no",
                           TRUE ~ NA_character_))

#Asthma
data <- data %>%
mutate(asthma = case_when(ASMA == 1 ~ "yes",
                          ASMA == 2 ~ "no",
                          TRUE ~ NA_character_))

#Diabetes
data <- data %>%
mutate(diabetes = case_when(DIABETES == 1 ~ "yes",
                            DIABETES == 2 ~ "no",
                            TRUE ~ NA_character_))

#Neurologic
data <- data %>%
mutate(neurologic = case_when(NEUROLOGIC == 1 ~ "yes",
                              NEUROLOGIC == 2 ~ "no",
                              TRUE ~ NA_character_))

#Pneumologic
data <- data %>%
mutate(pneumologic = case_when(PNEUMOPATI == 1 ~ "yes",
                                PNEUMOPATI == 2 ~ "no",
                                TRUE ~ NA_character_))

#Renal
data <- data %>%
mutate(renal = case_when(RENAL == 1 ~ "yes",
                         RENAL == 2 ~ "no",
                         TRUE ~ NA_character_))

#Obesity
data <- data %>%
mutate(obesity = case_when(OBESIDADE == 1 ~ "yes",
                           OBESIDADE == 2 ~ "no",
                           TRUE ~ NA_character_))

```

Hematologic

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

```

## Cross-Tabulation, Row Proportions
## CVD * hematologic
## Data Frame: data
##
## -----
##          hematologic          no          yes          Total
## CVD
## no          2919 (98.9%)    31 (1.1%)    2950 (100.0%)
## yes          428 (97.9%)     9 (2.1%)     437 (100.0%)
## Total        3347 (98.8%)    40 (1.2%)    3387 (100.0%)

```

```
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      2.5101      1  0.1131
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.98      0.94      4.19
## -----
```

Diabetes

```
ctable(data$CVD, data$diabetes, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * diabetes
## Data Frame: data
##
## -----
##          diabetes          no          yes          Total
## CVD
## no          2610 (88.6%)    337 (11.4%)    2947 (100.0%)
## yes          312 (66.4%)    158 (33.6%)    470 (100.0%)
## Total        2922 (85.5%)    495 (14.5%)    3417 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##    159.2143      1      0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      3.92      3.14      4.90
## -----
```

Obesity

```
ctable(data$CVD, data$obesity, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * obesity
```

```
## Data Frame: data
##
##
## -----
##      obesity      no      yes      Total
##      CVD
##      no      2651 (91.2%)  255 ( 8.8%)  2906 (100.0%)
##      yes      344 (76.6%)  105 (23.4%)   449 (100.0%)
##      Total    2995 (89.3%)  360 (10.7%)  3355 (100.0%)
## -----
##
## -----
##      Chi.squared  df  p.value
## -----
##      85.149      1    0
## -----
##
## -----
##      Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      3.17        2.46      4.09
## -----
```

Asthma

```
ctable(data$CVD, data$asthma, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * asthma
## Data Frame: data
##
##
## -----
##      asthma      no      yes      Total
##      CVD
##      no      2734 (93.2%)  199 (6.8%)  2933 (100.0%)
##      yes      396 (90.8%)   40 (9.2%)  436 (100.0%)
##      Total    3130 (92.9%)  239 (7.1%)  3369 (100.0%)
## -----
##
## -----
##      Chi.squared  df  p.value
## -----
##      2.9356      1    0.0866
## -----
##
## -----
##      Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.39        0.97      1.98
## -----
```

Hepatic

```
ctable(data$CVD, data$hepatic, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * hepatic
## Data Frame: data
##
## -----
##           hepatic           no           yes           Total
## CVD
## no           2921 ( 99.6%)    12 (0.4%)    2933 (100.0%)
## yes           426 ( 98.8%)     5 (1.2%)    431 (100.0%)
## Total        3347 ( 99.5%)    17 (0.5%)    3364 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      2.8535      1   0.0912
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      2.86      1.00      8.15
## -----
```

```
fisher.test(data$hepatic, data$CVD)
```

```
##
## Fisher's Exact Test for Count Data
##
## data:  data$hepatic and data$CVD
## p-value = 0.05627
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.7841874 8.7612195
## sample estimates:
## odds ratio
##  2.855734
```

Neurologic

```
ctable(data$CVD, data$neurologic, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * neurologic
```

```
## Data Frame: data
##
##
## -----
##      neurologic      no      yes      Total
## CVD
## no      2915 (99.0%)  28 (1.0%)  2943 (100.0%)
## yes      422 (97.9%)   9 (2.1%)   431 (100.0%)
## Total    3337 (98.9%)  37 (1.1%)  3374 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      3.4923      1  0.0617
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      2.22      1.04      4.74
## -----
```

```
fisher.test(data$neurologic, data$CVD)
```

```
##
## Fisher's Exact Test for Count Data
##
## data: data$neurologic and data$CVD
## p-value = 0.04511
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.9148775 4.8799321
## sample estimates:
## odds ratio
##  2.219605
```

Pneumologic

```
ctable(data$CVD, data$pneumologic, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * pneumologic
## Data Frame: data
##
## -----
##      pneumologic      no      yes      Total
## CVD
## no      2905 (98.9%)  31 (1.1%)  2936 (100.0%)
## yes      424 (97.0%)  13 (3.0%)   437 (100.0%)
```

```
##      Total                3329 (98.7%)    44 (1.3%)    3373 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      9.4404         1    0.0021
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      2.87          1.49        5.53
## -----
```

Immunodepression

```
ctable(data$CVD, data$imunodepre, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

```
## Cross-Tabulation, Row Proportions
## CVD * imunodepre
## Data Frame: data
##
## -----
##      imunodepre          no          yes          Total
##      CVD
##      no                2874 (98.0%)    58 (2.0%)    2932 (100.0%)
##      yes                418 (96.5%)    15 (3.5%)    433 (100.0%)
##      Total              3292 (97.8%)    73 (2.2%)    3365 (100.0%)
## -----
##
## -----
##      Chi.squared    df    p.value
## -----
##      3.2567         1    0.0711
## -----
##
## -----
##      Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.78          1.00        3.17
## -----
```

Renal

```
ctable(data$CVD, data$renal, chisq=TRUE, prop="r", OR=TRUE, useNA = "no")
```

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

```
## CVD * renal
## Data Frame: data
##
##
## -----
##          renal          no          yes          Total
##    CVD
##    no          2890 (98.8%)   36 (1.2%)   2926 (100.0%)
##    yes          414 (95.6%)   19 (4.4%)   433 (100.0%)
##    Total        3304 (98.4%)   55 (1.6%)   3359 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      21.431        1        0
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      3.68         2.09         6.48
## -----
```

The variable `comorb_group` indicates the number o comorbidities of each notification.

Any comorbidity

```
df <- select(data,obesity,hematologic,hepatic,asthma,diabetes,neurologic,pneumologic,imunodepre,renal)
soma <- function(x){
  if (sum(is.na(x))==9)
    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
data$qt_comorb_aux <- apply(df,1,soma)

data <- data %>%
  mutate(qt_comorb = case_when(qt_comorb_aux== 9 ~ "9 comorbidities",
                                qt_comorb_aux == 7 ~ "7 comorbidities",
                                qt_comorb_aux== 6 ~ "6 comorbidities",
                                qt_comorb_aux == 5 ~ "5 comorbidities",
                                qt_comorb_aux== 4 ~ "4 comorbidities",
                                qt_comorb_aux == 3 ~ "3 comorbidities",
                                qt_comorb_aux == 2 ~ "2 comorbidities",
                                qt_comorb_aux == 1 ~ "1 comorbidity",
                                qt_comorb_aux == 0 ~ "No comorbidity",
                                TRUE ~ NA_character_))

data <- data %>%
  mutate(comorb_group = case_when(qt_comorb_aux == 0 ~ "No comorbidity",
                                    qt_comorb_aux == 1 ~ "1 comorbidity",
```

```

qt_comorb_aux == 2 ~ "2 comorbidities",
qt_comorb_aux > 2 ~ ">2 comorbidities",
TRUE ~ NA_character_)

data$comorb_group <-
  factor(data$comorb_group, levels = c("No comorbidity", "1 comorbidity", "2 comorbidities", ">2 comorbidity"))

with(data, ctable(comorb_group, CVD, prop="c", useNA = "no", chisq = TRUE, OR = TRUE))

## Cross-Tabulation, Column Proportions
## comorb_group * CVD
## Data Frame: data
##
## -----
##           CVD           no           yes           Total
## comorb_group
## No comorbidity      2126 ( 71.8%)      234 ( 46.8%)      2360 ( 68.2%)
## 1 comorbidity        701 ( 23.7%)       186 ( 37.2%)       887 ( 25.6%)
## 2 comorbidities       116 (  3.9%)        64 ( 12.8%)       180 (  5.2%)
## >2 comorbidities        17 (  0.6%)         16 (  3.2%)        33 (  1.0%)
## Total              2960 (100.0%)       500 (100.0%)      3460 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    165.5306     3         0
## -----

```

Outcome

```

# ICU
data <- data %>%
  mutate(icu = case_when(UTI == 1 ~ "yes",
                        UTI == 2 ~ "no",
                        TRUE ~ NA_character_))

# Ventilatory support
data <- data %>%
  mutate(ven_support = case_when(SUPPORT_VEN == 1 ~ "yes, invasive",
                                SUPPORT_VEN == 2 ~ "yes, noninvasive",
                                SUPPORT_VEN == 3 ~ "No",
                                TRUE ~ NA_character_))

```

ICU


```
#tabela cruzada de uti
with(data, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: data
##
##
## -----
##          icu          no          yes          Total
## CVD
## no      2043 (71.8%)    802 (28.2%)    2845 (100.0%)
## yes      356 (63.0%)    209 (37.0%)    565 (100.0%)
## Total    2399 (70.4%)   1011 (29.6%)   3410 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      17.0872    1       0
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##       1.50       1.24       1.81
## -----
```

1st trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "1tri")
with(df4, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df4
##
##
## -----
##          icu          no          yes          Total
## CVD
## no      121 (77.1%)    36 (22.9%)    157 (100.0%)
## yes      18 (58.1%)    13 (41.9%)    31 (100.0%)
## Total    139 (73.9%)    49 (26.1%)   188 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
```

```
## -----
##      3.9164      1      0.0478
## -----
##
## -----
## Odds Ratio      Lo - 95%      Hi - 95%
## -----
##      2.43      1.09      5.43
## -----
```

2nd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "2tri")

with(df4, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df4
##
## -----
##           icu           no           yes           Total
## CVD
## no      315 (68.8%)    143 (31.2%)    458 (100.0%)
## yes      66 (58.4%)     47 (41.6%)    113 (100.0%)
## Total    381 (66.7%)    190 (33.3%)    571 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      3.9355      1   0.0473
## -----
##
## -----
## Odds Ratio      Lo - 95%      Hi - 95%
## -----
##      1.57      1.03      2.39
## -----
```

3rd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "3tri")

with(df4, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

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

```
## CVD * icu
## Data Frame: df4
##
##
## -----
##          icu          no          yes          Total
##    CVD
##    no      883 (76.6%)   270 (23.4%)   1153 (100.0%)
##    yes      159 (68.2%)    74 (31.8%)    233 (100.0%)
##    Total   1042 (75.2%)   344 (24.8%)   1386 (100.0%)
## -----
##
## -----
##    Chi.squared   df   p.value
## -----
##      6.7894      1   0.0092
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.52        1.12        2.07
## -----
```

Puerperium

```
df4 <- data %>%
  filter(classi_gesta_puerp == "puerp")

with(df4, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df4
##
##
## -----
##          icu          no          yes          Total
##    CVD
##    no      678 (66.9%)   335 (33.1%)   1013 (100.0%)
##    yes      94 (58.4%)    67 (41.6%)    161 (100.0%)
##    Total   772 (65.8%)   402 (34.2%)   1174 (100.0%)
## -----
##
## -----
##    Chi.squared   df   p.value
## -----
##      4.1332      1   0.042
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
```

```
## -----
##      1.44      1.03      2.03
## -----
```

Duration of hospitalization in ICU

```
data <- data %>%
  dplyr::mutate(
    dt_entuti = as.Date(DT_ENTUTI, format = "%d/%m/%Y"),
    dt_saiduti = as.Date(DT_SAIDUTI, format = "%d/%m/%Y"),
    icu_days = as.numeric(dt_saiduti-dt_entuti)
  )
```

```
df <- data[data$icu== "yes" & !is.na(data$icu) & !is.na(data$icu_days),]

datasummary((CVD) ~ icu_days*(n+media+DP+mediana+minimo+maximo+q25+q75+IQR),
  data = df, output = 'markdown')
```

| CVD | n | media | DP | mediana | minimo | maximo | q25 | q75 | IQR |
|-----|-----|-------|-------|---------|--------|--------|------|-------|-------|
| no | 514 | 10.53 | 10.73 | 7.00 | 0.00 | 94.00 | 3.00 | 15.00 | 12.00 |
| yes | 114 | 13.46 | 14.49 | 10.50 | 0.00 | 105.00 | 4.00 | 17.00 | 13.00 |

```
wilcox.test(icu_days ~ CVD, data = df)
```

```
##
## Wilcoxon rank sum test with continuity correction
##
## data: icu_days by CVD
## W = 25486, p-value = 0.02941
## alternative hypothesis: true location shift is not equal to 0
```

Ventilatory support

```
with(data, ctable(CVD, ven_support, prop="r", useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * ven_support
## Data Frame: data
##
## -----
##      ven_support      No  yes, invasive  yes, noninvasive      Total
## CVD
## no      1470 (52.7%)    443 (15.9%)      877 (31.4%)    2790 (100.0%)
## yes      226 (40.7%)    110 (19.8%)      219 (39.5%)     555 (100.0%)
## Total    1696 (50.7%)    553 (16.5%)    1096 (32.8%)   3345 (100.0%)
```

```
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##    26.5268      2       0
## -----
```

Intubation

```
data <- data %>%
  mutate(intubation = case_when(SUPPORT_VEN == 1 ~ "yes",
                                SUPPORT_VEN == 2 ~ "no",
                                SUPPORT_VEN == 3 ~ "no",
                                TRUE ~ NA_character_)
  )
```

```
with(data, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

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

```
## CVD * intubation
```

```
## Data Frame: data
```

```
##
```

```
##
```

```
## -----
##           intubation           no           yes           Total
##   CVD
##   no           2347 (84.1%)    443 (15.9%)    2790 (100.0%)
##   yes           445 (80.2%)    110 (19.8%)    555 (100.0%)
##   Total        2792 (83.5%)    553 (16.5%)    3345 (100.0%)
## -----
```

```
##
```

```
## -----
##   Chi.squared   df   p.value
## -----
##    4.9304      1   0.0264
## -----
```

```
##
```

```
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##    1.31        1.04       1.65
## -----
```

1st trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "1tri")

with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
##
## -----
##          intubation          no          yes          Total
##    CVD
##    no          135 (88.8%)    17 (11.2%)    152 (100.0%)
##    yes          23 (79.3%)     6 (20.7%)     29 (100.0%)
##    Total        158 (87.3%)    23 (12.7%)    181 (100.0%)
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      2.07         0.74      5.80
## -----
```

```
fisher.test(df4$CVD, df4$intubation)
```

```
##
## Fisher's Exact Test for Count Data
##
## data: df4$CVD and df4$intubation
## p-value = 0.2182
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.601484 6.248095
## sample estimates:
## odds ratio
##  2.061721
```

2nd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "2tri")

with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
##
## -----
##          intubation          no          yes          Total
##    CVD
##    no          373 (85.0%)    66 (15.0%)    439 (100.0%)
##    yes          88 (79.3%)    23 (20.7%)    111 (100.0%)
##    Total        461 (83.8%)    89 (16.2%)    550 (100.0%)
```

```
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##     1.7139      1   0.1905
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##     1.48       0.87     2.51
## -----
```

3rd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "3tri")

with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
## -----
##           intubation           no           yes           Total
##   CVD
##   no           1007 (89.0%)    125 (11.0%)    1132 (100.0%)
##   yes           195 (84.4%)     36 (15.6%)     231 (100.0%)
##   Total         1202 (88.2%)    161 (11.8%)    1363 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##     3.3759      1   0.0662
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##     1.49       1.00     2.22
## -----
```

Puerperium

```
df4 <- data %>%
  filter(classi_gesta_puerp == "puerp")
```

```
with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
##
## -----
##          intubation          no          yes          Total
## CVD
##   no          778 (77.6%)    224 (22.4%)    1002 (100.0%)
##   yes          118 (75.2%)     39 (24.8%)     157 (100.0%)
## Total          896 (77.3%)    263 (22.7%)    1159 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      0.3468      1   0.5559
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.15      0.78      1.70
## -----
```

Outcome - cure x death

```
with(data, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: data
##
##
## -----
##          evolution          cure          death          Total
## CVD
##   no          2559 (86.5%)    401 (13.5%)    2960 (100.0%)
##   yes          488 (81.1%)    114 (18.9%)     602 (100.0%)
## Total          3047 (85.5%)    515 (14.5%)    3562 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##     11.3176      1   8e-04
## -----
##
```



```
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.49      1.19      1.88
## -----
```

1st trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "1tri")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = FALSE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##      evolution      cure      death      Total
## CVD
## no      146 (90.7%)   15 ( 9.3%)   161 (100.0%)
## yes      30 (88.2%)    4 (11.8%)   34 (100.0%)
## Total    176 (90.3%)   19 ( 9.7%)   195 (100.0%)
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.30      0.40      4.18
## -----
```

```
fisher.test(df4$CVD, df4$evolution)
```

```
##
## Fisher's Exact Test for Count Data
##
## data: df4$CVD and df4$evolution
## p-value = 0.7494
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##  0.2926084 4.4639958
## sample estimates:
## odds ratio
##  1.295924
```

2nd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "2tri")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##           evolution      cure      death      Total
## CVD
## no           410 (87.0%)    61 (13.0%)    471 (100.0%)
## yes           90 (75.0%)    30 (25.0%)    120 (100.0%)
## Total        500 (84.6%)    91 (15.4%)    591 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      9.753      1  0.0018
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      2.24      1.37    3.67
## -----
```

3rd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "3tri")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##           evolution      cure      death      Total
## CVD
## no           1071 (89.3%)    128 (10.7%)    1199 (100.0%)
## yes           212 (85.5%)     36 (14.5%)     248 (100.0%)
## Total        1283 (88.7%)    164 (11.3%)    1447 (100.0%)
## -----
##
```

```
## -----
## Chi.squared  df  p.value
## -----
##      2.6461    1  0.1038
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.42      0.95     2.12
## -----
```

Puerperium

```
df4 <- data %>%
  filter(classi_gesta_puerp == "puerp")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##      evolution      cure      death      Total
## CVD
## no      856 (81.9%)  189 (18.1%)  1045 (100.0%)
## yes     133 (78.2%)   37 (21.8%)   170 (100.0%)
## Total   989 (81.4%)  226 (18.6%)  1215 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      1.0751    1  0.2998
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.26      0.85     1.87
## -----
```

Time elapsed between the start of symptoms and the outcome (days)

```
data <- data %>%
  dplyr::mutate(
    dt_sin_pri = as.Date(DT_SIN_PRI, format = "%d/%m/%Y"),
    dt_evoluca = as.Date(DT_EVOLUCA, format = "%d/%m/%Y"),
```

```

    days_symp_evol = as.numeric(dt_evoluca-dt_sin_pri)
)

df <- data[!is.na(data$days_symp_evol) & !is.na(data$CVD),]

datasummary((CVD) ~ days_symp_evol*(n+media+DP+mediana+minimo+maximo+q25+q75+IQR),
  data = df, output = 'markdown')

```

| CVD | n | media | DP | mediana | minimo | maximo | q25 | q75 | IQR |
|-----|------|-------|-------|---------|--------|--------|------|-------|-------|
| no | 2863 | 16.00 | 15.80 | 13.00 | 0.00 | 244.00 | 8.00 | 19.00 | 11.00 |
| yes | 586 | 17.10 | 12.80 | 14.00 | 0.00 | 113.00 | 9.00 | 20.75 | 11.75 |

```

wilcox.test(days_symp_evol ~ CVD, data = df)

##
## Wilcoxon rank sum test with continuity correction
##
## data: days_symp_evol by CVD
## W = 751451, p-value = 6.809e-05
## alternative hypothesis: true location shift is not equal to 0

```

Considering only death cases

```

df <- data[!is.na(data$days_symp_evol) & !is.na(data$CVD),]

df <- df %>%
  filter(evolution == "death")

datasummary((CVD) ~ days_symp_evol*(n+media+DP+mediana+minimo+maximo+q25+q75+IQR),
  data = df, output = 'markdown')

```

| CVD | n | media | DP | mediana | minimo | maximo | q25 | q75 | IQR |
|-----|-----|-------|-------|---------|--------|--------|-------|-------|-------|
| no | 399 | 20.34 | 13.86 | 18.00 | 0.00 | 158.00 | 12.00 | 27.00 | 15.00 |
| yes | 114 | 20.04 | 14.11 | 17.00 | 0.00 | 113.00 | 11.00 | 26.75 | 15.75 |

```

wilcox.test(days_symp_evol ~ CVD, data = df)

##
## Wilcoxon rank sum test with continuity correction
##
## data: days_symp_evol by CVD
## W = 23410, p-value = 0.6331
## alternative hypothesis: true location shift is not equal to 0

```

Considering only cure cases

```
df <- data[!is.na(data$days_symp_evol) & !is.na(data$CVD),]

df <- df %>%
  filter(evolution == "cure")

datasummary((CVD) ~ days_symp_evol*(n+media+DP+mediana+minimo+maximo+q25+q75+IQR),
  data = df, output = 'markdown')
```

| CVD | n | media | DP | mediana | minimo | maximo | q25 | q75 | IQR |
|-----|------|-------|-------|---------|--------|--------|------|-------|-------|
| no | 2464 | 15.30 | 15.99 | 12.00 | 0.00 | 244.00 | 7.00 | 18.00 | 11.00 |
| yes | 472 | 16.39 | 12.37 | 13.00 | 0.00 | 93.00 | 9.00 | 19.00 | 10.00 |

```
wilcox.test(days_symp_evol ~ CVD, data = df)
```

```
##
## Wilcoxon rank sum test with continuity correction
##
## data: days_symp_evol by CVD
## W = 513735, p-value = 5.814e-05
## alternative hypothesis: true location shift is not equal to 0
```

Distribution of number of hospitalizations due to COVID-19 infection by month of first symptoms, stratified by groups with and without CVD

```
# Date of the first symptoms
data <- data %>%
mutate(dt_first_symp = as.Date(DT_SIN_PRI, format = "%d/%m/%Y")
)
```

The next graph presents the temporal evolution of hospitalizations by month of first symptoms, stratified by groups with and without cardiovascular disease.

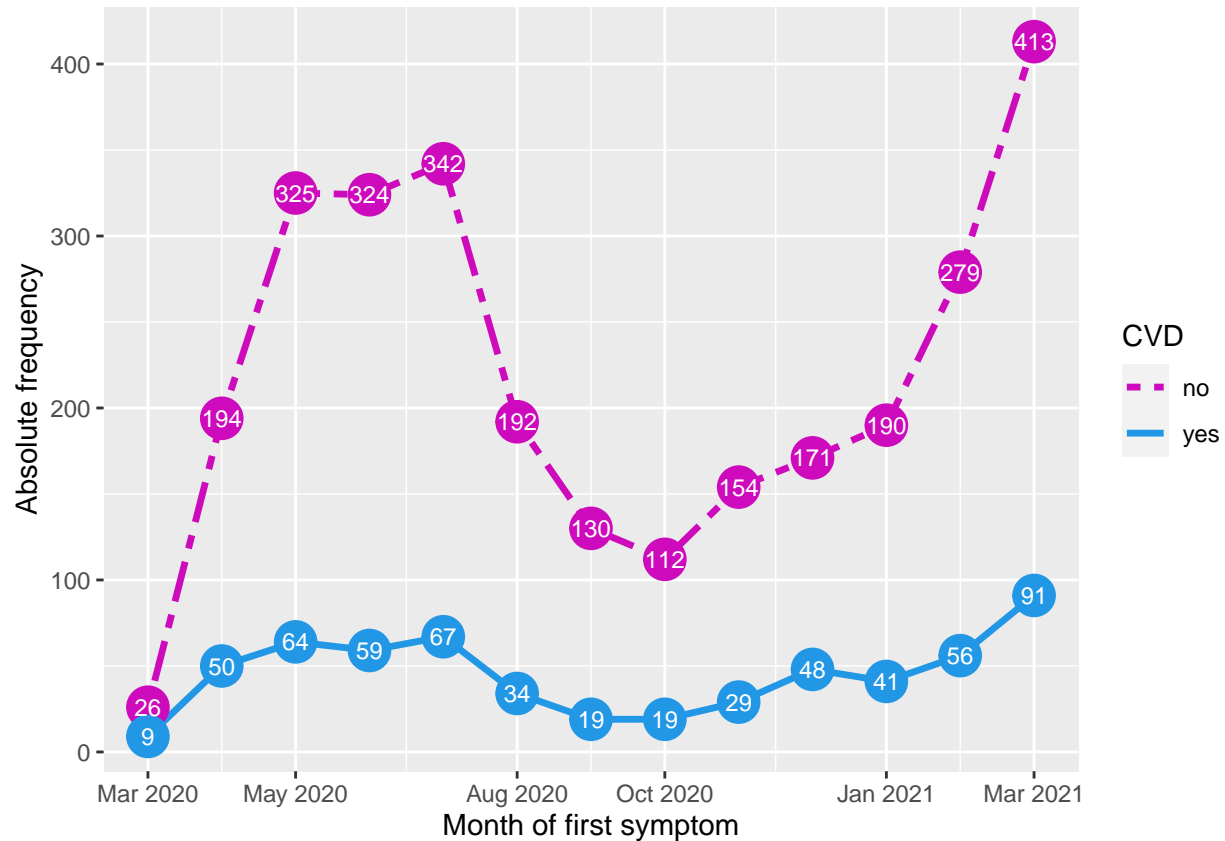
```
## Creating the variable month_year
d1 <- data[data$dt_first_symp < as.Date("01/04/2021",format="%d/%m/%Y"),]
d1 <- d1 %>%
mutate(month_year = paste(formatC(month(dt_first_symp), width=2, format="d", flag="0"),year(dt_first_symp))

d<- table(factor(d1$month_year, levels = c("03/2020", "04/2020", "05/2020", "06/2020", "07/2020", "08/2020"))
G <- data.table(d)
Sys.setlocale("LC_TIME","C")
```

```
## [1] "C"
```

```
G$V1 <- as.yearmon(G$V1, format = "%m/%Y")
ggplot(G, aes(x=V1, y=N, colour=factor(V2), linetype=factor(V2), group(V2))) +
  geom_line(size=1.2) + geom_point(size=7, show.legend = FALSE) +
  geom_text(color="white", size=3, aes(label=N)) +
```

```
# theme(legend.position="bottom", legend.box = "horizontal")+
scale_linetype_manual(values=c("twodash", "solid"))+
scale_color_manual(values = c(6,4))+
labs(x="Month of first symptom", y="Absolute frequency", linetype = "CVD", color = "CVD")
```



Frequency table of number of hospitalizations due to COVID-19 infection by month of first symptoms, stratified by groups with and without CVD.

```
d1$mes_ano <- factor(d1$month_year, levels = c("03/2020", "04/2020", "05/2020", "06/2020", "07/2020", "08/2020", "09/2020", "10/2020", "11/2020", "12/2020", "01/2021", "02/2021", "03/2021"))
ctable(d1$month_year, d1$CVD, prop="c", useNA = "no")
```

```
## Cross-Tabulation, Column Proportions
```

```
## month_year * CVD
```

```
## Data Frame: d1
```

```
##
```

```
## -----
##      CVD      no      yes      Total
## month_year
## 01/2021      190 ( 6.7%)      41 ( 7.0%)      231 ( 6.7%)
## 02/2021      279 ( 9.8%)      56 ( 9.6%)      335 ( 9.7%)
## 03/2020       26 ( 0.9%)       9 ( 1.5%)       35 ( 1.0%)
## 03/2021      413 (14.5%)      91 (15.5%)      504 (14.7%)
## 04/2020      194 ( 6.8%)      50 ( 8.5%)      244 ( 7.1%)
## 05/2020      325 (11.4%)      64 (10.9%)      389 (11.3%)
## 06/2020      324 (11.4%)      59 (10.1%)      383 (11.1%)
```

| | | | | |
|----|---------|---------------|--------------|---------------|
| ## | 07/2020 | 342 (12.0%) | 67 (11.4%) | 409 (11.9%) |
| ## | 08/2020 | 192 (6.7%) | 34 (5.8%) | 226 (6.6%) |
| ## | 09/2020 | 130 (4.6%) | 19 (3.2%) | 149 (4.3%) |
| ## | 10/2020 | 112 (3.9%) | 19 (3.2%) | 131 (3.8%) |
| ## | 11/2020 | 154 (5.4%) | 29 (4.9%) | 183 (5.3%) |
| ## | 12/2020 | 171 (6.0%) | 48 (8.2%) | 219 (6.4%) |
| ## | Total | 2852 (100.0%) | 586 (100.0%) | 3438 (100.0%) |
| ## | ----- | ----- | ----- | ----- |

Now, to understand better the monthly growth rate of hospitalized cases by COVID-19, we present the following graph:

```
D1<- table(d1$month_year, d1$CVD) %>%
  data.table()
D1$V1 <- as.yearmon(D1$V1, format = "%m/%Y")

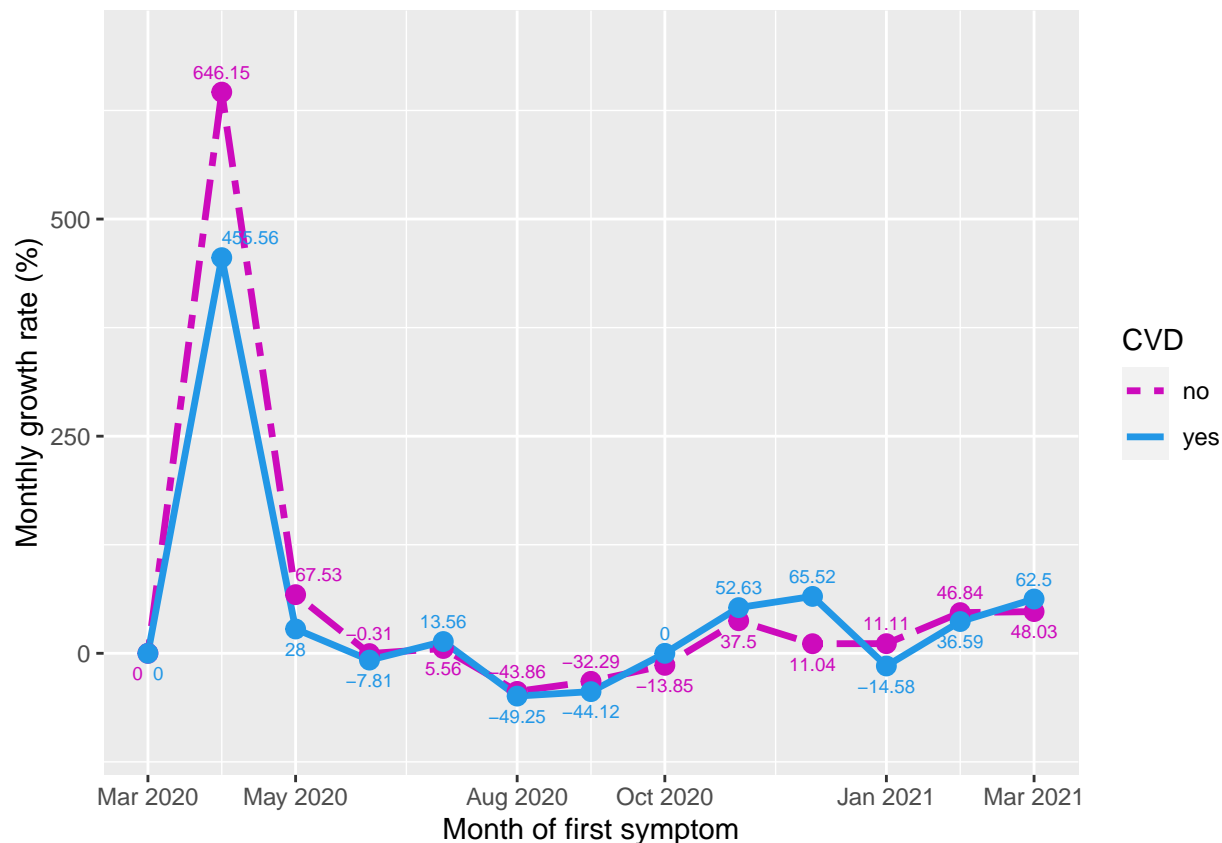
# Calculating the monthly growth rate
D1 <- D1 %>%
  arrange(D1)

dif<-c()
dif[1:2]<-0
for(i in 1:nrow(D1)){
  if( i %% 2 == 0){
    dif[i]<-D1$N[i+2]-D1$N[i]
  }
  else{
    dif[i]<-D1$N[i+2]-D1$N[i]
  }
}
D1$dif<-dif

taxa_cresc<-c()
taxa_cresc[1:2]<-0
for(i in 1:(nrow(D1)-2)){
  if( i %% 2 == 0){
    taxa_cresc[i+2]<-(dif[i])/(D1$N[i])
  }
  else{
    taxa_cresc[i+2]<-(dif[i])/(D1$N[i])
  }
}

D1$growth_rate <-taxa_cresc*100

ggplot(D1, aes(x=V1, y = growth_rate, color = V2, linetype=factor(V2))) +
  geom_line(size=1.2) + geom_point(size=3, show.legend = FALSE) +
  geom_text(size = 2.5, aes(label = round(growth_rate, 2)), vjust = c(2, 2, -1.0, -1.0, -1, 2, -1, 2, 2, 2),
    hjust = c(1.5, -0.5, 0.5, 0, 0, 0.5, rep(0.5,20)), show.legend = FALSE) +
  # theme(legend.position="bottom", legend.box = "horizontal")+
  scale_linetype_manual(values=c("twodash", "solid"))+
  scale_color_manual(values = c(6,4))+
  labs( x="Month of first symptom", y="Monthly growth rate (%)", linetype = "CVD", color = "CVD") +
  scale_y_continuous(limits = c(-100, 700))
```



The average growth rate of COVID-19 cases related to the CVD and non-CVD groups in each wave of infection is calculated below. For the first we considered the period between March to October 2020 and for the second wave from October 2020 to April 2021.

```
#####
### First wave
#####

D1_FW = D1[3:16,]

### CVD group

rate <- ((D1_FW[V2=="yes"]$growth_rate)+100)/100
rate_CVD_FW <- geometric.mean(rate)
rate_CVD_FW
```

```
## [1] 1.11265
```

```
### non-CVD group

rate <- ((D1_FW[V2=="no"]$growth_rate)+100)/100
rate_non_CVD_FW <- geometric.mean(rate)
rate_non_CVD_FW
```

```
## [1] 1.231988
```



```
#####
### Second wave
#####

D1_SW = D1[17:26,]

### CVD group

rate <- ((D1_SW[V2=="yes"]$growth_rate)+100)/100
rate_CVD_SW <- geometric.mean(rate)
rate_CVD_SW
```

```
## [1] 1.36791
```

```
### non-CVD group

rate <- ((D1_SW[V2=="no"]$growth_rate)+100)/100
rate_non_CVD_SW <- geometric.mean(rate)
rate_non_CVD_SW
```

```
## [1] 1.298214
```

Proportion of deaths in the CVD and non-CVD groups, fixed the month of the first symptom.

```
# Proportion of deaths in the group with presence of CVD
d1 <- data
d1 <- d1 %>%
  filter(CVD == 'yes')
d1 <- d1 %>%
  mutate(month_year = paste(formatC(month(dt_first_symp), width=2, format="d", flag="0"),year(dt_first_symp)))

d<- prop.table(table(d1$month_year, d1$evolution),1)
G3 <- as.data.frame(d)
G3 <- G3[G3$Var2 == "death",]
G3$Freq <- round((G3$Freq)*100, 2)
G3$Var1 <- as.yearmon(G3$Var1, format = "%m/%Y")

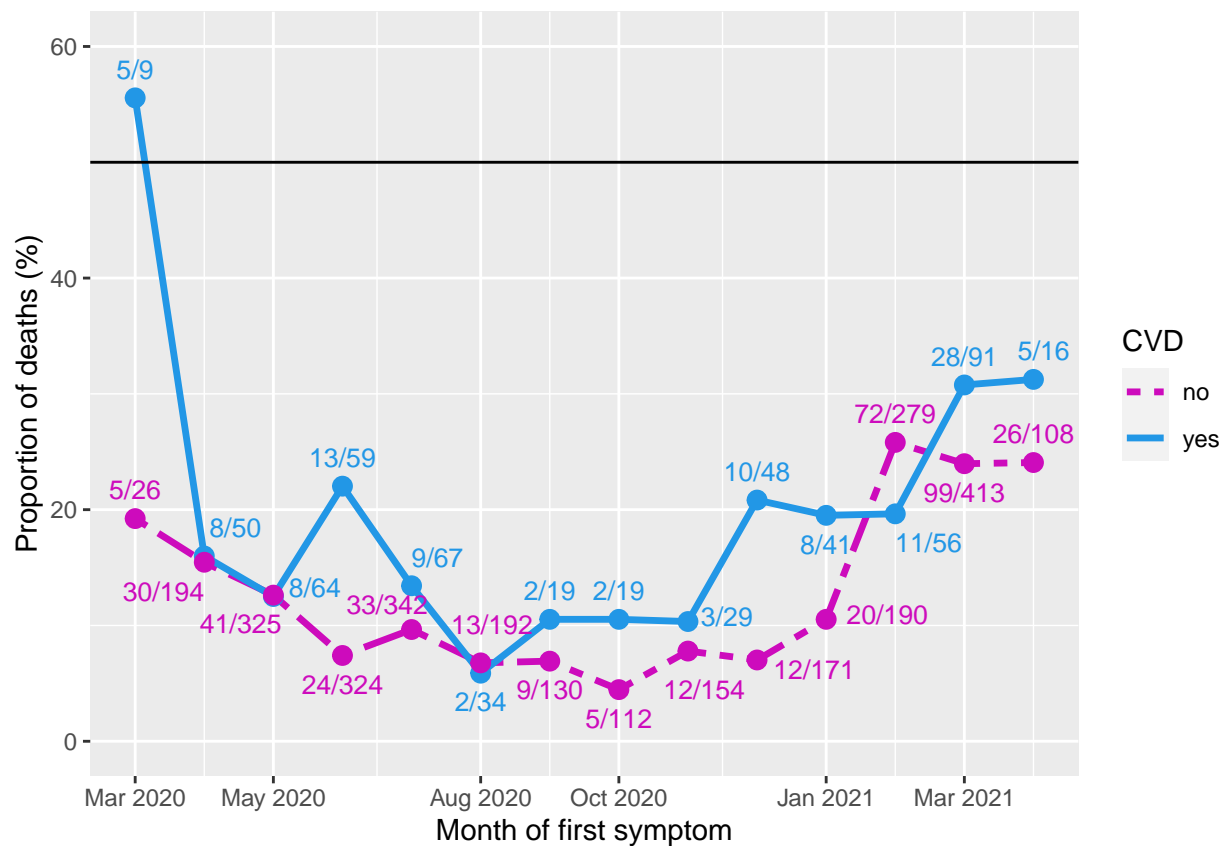
# Proportion of deaths in the group with absence of CVD
d2 <- data
d2 <- d2 %>%
  filter(CVD == 'no')
d2 <- d2 %>%
  mutate(month_year = paste(formatC(month(dt_first_symp), width=2, format="d", flag="0"),year(dt_first_symp)))

d2<- prop.table(table(d2$month_year, d2$evolution),1)
G32 <- as.data.frame(d2)
G32 <- G32[G32$Var2 == "death",]
G32$Freq <- round((G32$Freq)*100, 2)
G32$Var1 <- as.yearmon(G32$Var1, format = "%m/%Y")

# Concatening the proportion of deaths in both groups, with and without CVD
```

```
G33 <- rbind(G3, G32)
cardio <- c(rep("yes", nrow(G3)), rep("no", nrow(G32)))
G33 <- cbind(G33, cardio)

ggplot(data=G33,aes(x = Var1, y=Freq, color = cardio, linetype=cardio)) + geom_line(size=1.2) +
  geom_point(size=3, show.legend = FALSE) +
  geom_text(size = 3.5, aes(label = c("8/41", "11/56", "5/9", "28/91", "8/50", "5/16", "8/64", "13/59",
                                     hjust = c(0.5, 0, 0.5, 0.5, -0.1, 0.3, -0.3, 0.5, 0, 0.5, 0.5, 0.5, -0.25, 0.5,
                                     show.legend = FALSE)+
  geom_hline(yintercept = 50) +
  scale_linetype_manual(values=c("twodash", "solid"))+
  scale_color_manual(values = c(6,4))+
  scale_y_continuous(limits = c(0, 60)) +
  labs( x="Month of first symptom", y="Proportion of deaths (%)", color = "CVD", linetype = "CVD")
```



Propensity Score Matching (PSM):

The analysis that will be made in this section aims to understand the effect of having cardiovascular disease or not on some variables of interest such as symptoms and outcome. In order to make the CVD and non-CVD groups similar with respect to the distribution of some variables that may bring confusion to the study, we will make use of the Propensity Score Matching (PSM) technique. The variables we will control in the analysis are: age, race, diabetes and obesity.

First, we present the difference result between the groups regarding the control variables before the PSM. We consider as “balanced” the cases with mean difference greater than 0.05. As we can see, for most categories

of control variables the groups are not balanced before the matching.

```
data$cardio <- ifelse(data$CVD=="yes",1,0)

bal.tab(cardio ~ NU_IDADE_N + ethnicity + diabetes + obesity, data = data, estimand = "ATE", m.threshold = 0.05)

## Balance Measures
##
##      Type Diff.Un      M.Threshold.Un
## NU_IDADE_N      Contin.  0.5949 Not Balanced, >0.05
## ethnicity_black      Binary  0.0258      Balanced, <0.05
## ethnicity_brown      Binary -0.0535 Not Balanced, >0.05
## ethnicity_indigenous      Binary -0.0097      Balanced, <0.05
## ethnicity_white      Binary  0.0429      Balanced, <0.05
## ethnicity_yellow      Binary -0.0054      Balanced, <0.05
## ethnicity:<NA>      Binary  0.0264      Balanced, <0.05
## diabetes_yes      Binary  0.2218 Not Balanced, >0.05
## diabetes:<NA>      Binary  0.2149 Not Balanced, >0.05
## obesity_yes      Binary  0.1461 Not Balanced, >0.05
## obesity:<NA>      Binary  0.2359 Not Balanced, >0.05
##
## Balance tally for mean differences
##
##      count
## Balanced, <0.05      5
## Not Balanced, >0.05      6
##
## Variable with the greatest mean difference
##      Variable Diff.Un      M.Threshold.Un
## NU_IDADE_N  0.5949 Not Balanced, >0.05
##
## Sample sizes
##      Control Treated
## All      2960      602
```

As one can see, all variables categories are balanced after PSM.

```
## Estimating the weights of each sampling unit
fit <- weightit(cardio ~ NU_IDADE_N + ethnicity + diabetes + obesity, use.mlogit = FALSE, data = data,
               method = "ps", estimand = "ATE")

data$weight <- fit$weights

bal.tab(fit, m.threshold = 0.05, disp.v.ratio = TRUE)

## Call
## weightit(formula = cardio ~ NU_IDADE_N + ethnicity + diabetes +
## obesity, data = data, method = "ps", estimand = "ATE", use.mlogit = FALSE)
##
## Balance Measures
##
##      Type Diff.Adj      M.Threshold V.Ratio.Adj
## prop.score      Distance  0.0394 Balanced, <0.05      1.3504
## NU_IDADE_N      Contin.  0.0041 Balanced, <0.05      0.9849
## ethnicity_black      Binary -0.0003 Balanced, <0.05      .
## ethnicity_brown      Binary -0.0088 Balanced, <0.05      .
```

```
## ethnicity_indigenous    Binary    0.0056 Balanced, <0.05    .
## ethnicity_white         Binary    0.0088 Balanced, <0.05    .
## ethnicity_yellow        Binary   -0.0052 Balanced, <0.05    .
## ethnicity:<NA>           Binary    0.0144 Balanced, <0.05    .
## diabetes_yes            Binary   -0.0036 Balanced, <0.05    .
## diabetes:<NA>           Binary    0.0117 Balanced, <0.05    .
## obesity_yes             Binary    0.0064 Balanced, <0.05    .
## obesity:<NA>            Binary    0.0133 Balanced, <0.05    .
##
## Balance tally for mean differences
##               count
## Balanced, <0.05     12
## Not Balanced, >0.05    0
##
## Variable with the greatest mean difference
##      Variable Diff.Adj    M.Threshold
## ethnicity:<NA>  0.0144 Balanced, <0.05
##
## Effective sample sizes
##           Control Treated
## Unadjusted  2960.    602.
## Adjusted    2332.6  331.15
```

Symptom analysis after PSM:

```
with(data, ctable(CVD, fever, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Fever

```
## Cross-Tabulation, Row Proportions
## CVD * fever
## Data Frame: data
##
## -----
##           fever              no              yes              Total
## CVD
## no          1535.7 (44.5%)    1914.5 (55.5%)    3450.2 (100.0%)
## yes          1510.0 (43.0%)    1997.8 (57.0%)    3507.8 (100.0%)
## Total        3045.8 (43.8%)    3912.2 (56.2%)    6958.0 (100.0%)
## -----
##
## -----
## Chi.squared  df    p.value
## -----
##      1.4564    1    0.2275
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
```

```
##      1.06      0.97      1.17
## -----
```

```
with(data, ctable(CVD, cough, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Cough

```
## Cross-Tabulation, Row Proportions
## CVD * cough
## Data Frame: data
##
## -----
##      cough      no      yes      Total
## CVD
## no      1161.8 (33.7%)  2290.8 (66.3%)  3452.6 (100.0%)
## yes      1124.8 (32.0%)  2395.0 (68.0%)  3519.8 (100.0%)
## Total    2286.6 (32.8%)  4685.8 (67.2%)  6972.4 (100.0%)
## -----
##
## -----
##      Chi.squared  df  p.value
## -----
##      2.1957      1  0.1384
## -----
##
## -----
##      Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.08      0.98      1.19
## -----
```

```
with(data, ctable(CVD, sore_throat, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Sore throat

```
## Cross-Tabulation, Row Proportions
## CVD * sore_throat
## Data Frame: data
##
## -----
##      sore_throat      no      yes      Total
## CVD
## no      2651.6 (78.2%)  738.2 (21.8%)  3389.8 (100.0%)
## yes      2588.7 (76.6%)  790.8 (23.4%)  3379.6 (100.0%)
## Total    5240.3 (77.4%)  1529.0 (22.6%)  6769.3 (100.0%)
```

```
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##      2.4586      1   0.1169
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.10      0.98      1.23
## -----
```

```
with(data, ctable(CVD, dyspnea, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Dyspnea

```
## Cross-Tabulation, Row Proportions
## CVD * dyspnea
## Data Frame: data
##
##
## -----
##           dyspnea           no           yes           Total
##   CVD
##   no           1574.0 (45.6%)   1876.2 (54.4%)   3450.2 (100.0%)
##   yes           1196.9 (33.9%)   2337.6 (66.1%)   3534.4 (100.0%)
##   Total          2770.8 (39.7%)   4213.8 (60.3%)   6984.6 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##    100.3512      1      0
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.64      1.49      1.80
## -----
```

```
with(data, ctable(CVD, resp_dist, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Respiratory distress

```
## Cross-Tabulation, Row Proportions
## CVD * resp_dist
## Data Frame: data
##
##
## -----
##          resp_dist          no          yes          Total
##    CVD
##    no          1789.1 (52.1%)    1645.7 (47.9%)    3434.8 (100.0%)
##    yes          1578.1 (45.4%)    1900.2 (54.6%)    3478.3 (100.0%)
##    Total        3367.2 (48.7%)    3545.9 (51.3%)    6913.1 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      30.9549      1      0
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.31        1.19        1.44
## -----
```

```
with(data, ctable(CVD, saturation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Saturation

```
## Cross-Tabulation, Row Proportions
## CVD * saturation
## Data Frame: data
##
##
## -----
##          saturation          no          yes          Total
##    CVD
##    no          2164.0 (63.5%)    1241.8 (36.5%)    3405.8 (100.0%)
##    yes          1810.9 (52.3%)    1654.5 (47.7%)    3465.4 (100.0%)
##    Total        3974.9 (57.8%)    2896.3 (42.2%)    6871.2 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      89.2193      1      0
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
```

```
##      1.59      1.45      1.75
## -----
```

```
with(data, ctable(CVD, diarrhea, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Diarrhea

```
## Cross-Tabulation, Row Proportions
## CVD * diarrhea
## Data Frame: data
##
## -----
##      diarrhea      no      yes      Total
## CVD
## no      3021.0 (88.6%)  389.7 (11.4%)  3410.7 (100.0%)
## yes      3002.5 (89.0%)  371.5 (11.0%)  3374.1 (100.0%)
## Total      6023.5 (88.8%)  761.2 (11.2%)  6784.7 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      0.2517      1      0.6159
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      0.96      0.82      1.12
## -----
```

```
with(data, ctable(CVD, vomit, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Vomit

```
## Cross-Tabulation, Row Proportions
## CVD * vomit
## Data Frame: data
##
## -----
##      vomit      no      yes      Total
## CVD
## no      3062.7 (90.1%)  337.3 ( 9.9%)  3400.1 (100.0%)
## yes      2998.6 (89.3%)  359.5 (10.7%)  3358.1 (100.0%)
## Total      6061.3 (89.7%)  696.8 (10.3%)  6758.1 (100.0%)
```



```
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##     1.0397      1   0.3079
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##     1.09       0.93     1.27
## -----
```

```
with(data, ctable(CVD, fatigue, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Fatigue

```
## Cross-Tabulation, Row Proportions
## CVD * fatigue
## Data Frame: data
##
## -----
##           fatigue           no           yes           Total
##   CVD
##   no           1892.0 (76.5%)   579.8 (23.5%)   2471.8 (100.0%)
##   yes           1733.2 (74.8%)   583.8 (25.2%)   2317.0 (100.0%)
##   Total         3625.2 (75.7%)  1163.6 (24.3%)  4788.8 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##     1.871      1   0.1714
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##     1.10       0.96     1.25
## -----
```

```
with(data, ctable(CVD, loss_smell, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Loss of smell

```
## Cross-Tabulation, Row Proportions
## CVD * loss_smell
## Data Frame: data
##
##
## -----
##           loss_smell           no           yes           Total
##   CVD
##   no           2002.3 (81.1%)   467.5 (18.9%)   2469.8 (100.0%)
##   yes           1787.6 (77.5%)   520.4 (22.5%)   2308.0 (100.0%)
##   Total          3789.9 (79.3%)   987.9 (20.7%)   4777.7 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##      9.2983      1   0.0023
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.25      1.08      1.43
## -----
```

```
with(data, ctable(CVD, loss_taste, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Loss of taste

```
## Cross-Tabulation, Row Proportions
## CVD * loss_taste
## Data Frame: data
##
##
## -----
##           loss_taste           no           yes           Total
##   CVD
##   no           2008.7 (81.5%)   455.8 (18.5%)   2464.6 (100.0%)
##   yes           1792.7 (77.6%)   518.6 (22.4%)   2311.3 (100.0%)
##   Total          3801.4 (79.6%)   974.4 (20.4%)   4775.9 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##     11.1723      1   8e-04
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
```

```
##      1.27      1.11      1.47
## -----
```

```
with(data, ctable(CVD, abd_pain, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Abdominal pain

```
## Cross-Tabulation, Row Proportions
## CVD * abd_pain
## Data Frame: data
##
## -----
##      abd_pain      no      yes      Total
## CVD
## no      2243.3 (91.3%)  214.6 (8.7%)  2457.9 (100.0%)
## yes      2102.5 (92.1%)  180.7 (7.9%)  2283.2 (100.0%)
## Total    4345.8 (91.7%)  395.3 (8.3%)  4741.2 (100.0%)
## -----
##
## -----
##      Chi.squared  df  p.value
## -----
##      0.9274      1  0.3355
## -----
##
## -----
##      Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      0.90      0.73      1.10
## -----
```

Any respiratory symptom Now we are going to create the variable `resp_symp` indicating the presence of at least one respiratory symptom (Dyspnea, Fatigue, Saturation, Respiratory distress). Empty cells are considered missing data (<NA>). The variable `qt_resp_symp` indicates the number of respiratory symptoms of each case.

```
with(data, ctable(CVD, resp_symp, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * resp_symp
## Data Frame: data
##
## -----
##      resp_symp      no      yes      Total
## CVD
## no      1056.4 (30.5%)  2408.6 (69.5%)  3465.1 (100.0%)
## yes      738.7 (20.7%)  2834.6 (79.3%)  3573.4 (100.0%)
```

```
## Total 1795.2 (25.5%) 5243.3 (74.5%) 7038.5 (100.0%)
## -----
##
## -----
## Chi.squared df p.value
## -----
## 88.6786 1 0
## -----
##
## -----
## Odds Ratio Lo - 95% Hi - 95%
## -----
## 1.68 1.51 1.88
## -----
```

```
with(data, ctable(CVD, qt_resp_symp, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * qt_resp_symp
## Data Frame: data
##
##
```

```
## ----- qt_resp_symp 1 symptom 2 symptoms 3 symptoms 4 symptoms No respir
## CVD
## no 763.3 (22.0%) 616.1 (17.8%) 768.8 (22.2%) 260.4 (7.5%) 1
## yes 709.1 (19.8%) 892.6 (25.0%) 949.9 (26.6%) 283.0 (7.9%) 7
## Total 1472.4 (20.9%) 1508.7 (21.4%) 1718.8 (24.4%) 543.3 (7.7%) 1
## -----
##
## -----
## Chi.squared df p.value
## -----
## 127.2795 4 0
## -----
```

Any symptom Similar to the analysis of any respiratory symptom, we are going to create the variable `symp` indicating the presence of at least one symptom (Dyspnea, Fatigue, Saturation, Respiratory distress, Fever, Cough, Sore throat, Diarrhea, Vomit, Abdominal pain, Loss of smell, Loss of taste). Empty cells are considered missing data (<NA>).

```
with(data, ctable(CVD, symp, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * symp
## Data Frame: data
##
##
```

```
## ----- symp no yes Total
## CVD
## no 285.8 (8.2%) 3197.3 (91.8%) 3483.1 (100.0%)
```

```
##      yes      135.9 (3.8%)   3458.6 (96.2%)   3594.5 (100.0%)
##    Total      421.7 (6.0%)   6655.9 (94.0%)   7077.6 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##      61.0733     1       0
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      2.28       1.85       2.81
## -----
```

Outcome analysis after PSM:

ICU

```
with(data, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: data
##
## -----
##      icu      no      yes      Total
##    CVD
##    no      2421.5 (71.6%)   959.7 (28.4%)   3381.2 (100.0%)
##    yes      2318.3 (67.5%)   1117.4 (32.5%)   3435.7 (100.0%)
##    Total      4739.9 (69.5%)   2077.1 (30.5%)   6817.0 (100.0%)
## -----
##
## -----
##   Chi.squared   df   p.value
## -----
##      13.5876     1    2e-04
## -----
##
## -----
##   Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.22       1.10       1.35
## -----
```

```
df43 <- data %>%
  filter(classi_gesta_puerp == "1tri")
```

```
with(df43, ctable(CVD, icu, prop="r", useNA = "no", OR=TRUE, chisq = TRUE, weights = weight))
```

1st trimester

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df43
##
## -----
##          icu          no          yes          Total
## CVD
## no      137.3 (76.8%)  41.4 (23.2%)  178.7 (100.0%)
## yes      83.2 (63.3%)  48.2 (36.7%)  131.4 (100.0%)
## Total   220.5 (71.1%)  89.6 (28.9%)  310.2 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      6.0614    1   0.0138
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.92      1.17    3.15
## -----
```

```
df43 <- data %>%
  filter(classi_gesta_puerp == "2tri")

with(df43, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

2nd trimester

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df43
##
## -----
##          icu          no          yes          Total
## CVD
## no      362.9 (68.1%)  169.9 (31.9%)  532.9 (100.0%)
## yes      377.5 (61.4%)  237.4 (38.6%)  614.9 (100.0%)
## Total   740.4 (64.5%)  407.4 (35.5%)  1147.8 (100.0%)
## -----
##
```

```
## -----
## Chi.squared  df  p.value
## -----
##      5.3395      1  0.0208
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.34      1.05      1.71
## -----
```

```
df43 <- data %>%
  filter(classi_gesta_puerp == "3tri")

with(df43, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

3rd trimester

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df43
##
##
## -----
##      icu          no          yes          Total
## CVD
## no      1058.1 (76.8%)  318.8 (23.2%)  1376.8 (100.0%)
## yes      1252.9 (74.1%)  437.2 (25.9%)  1690.1 (100.0%)
## Total      2311.0 (75.4%)  755.9 (24.6%)  3066.9 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      2.8646      1  0.0905
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.16      0.98      1.37
## -----
```

```
df43 <- data %>%
  filter(classi_gesta_puerp == "puerp")

with(df43, ctable(CVD, icu, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

Puerperium

```
## Cross-Tabulation, Row Proportions
## CVD * icu
## Data Frame: df43
##
## -----
##          icu          no          yes          Total
## CVD
## no      802.7 (66.3%)  407.6 (33.7%)  1210.3 (100.0%)
## yes     540.2 (60.3%)  355.7 (39.7%)   896.0 (100.0%)
## Total   1342.9 (63.8%)  763.4 (36.2%)  2106.3 (100.0%)
## -----
##
## -----
## Chi.squared  df    p.value
## -----
##    7.8264     1    0.0051
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##    1.30       1.08      1.55
## -----
```

Days of hospitalization in ICU

```
d_yes <- data %>%
  filter(CVD == "yes" & !is.na(icu_days))
d_no <- data %>%
  filter(CVD == "no" & !is.na(icu_days))

wtd.t.test(d_yes$icu_days, d_no$icu_days, weight = d_yes$weight, weighty = d_no$weight)

## $test
## [1] "Two Sample Weighted T-Test (Welch)"
##
## $coefficients
##      t.value      df      p.value
## 1.2896729 164.5233472  0.1989742
##
## $additional
## Difference    Mean.x    Mean.y    Std. Err
## 1.437357    11.941962    10.504606    1.114513
```

Ventilatory support


```
with(data, ctable(CVD, ven_support, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * ven_support
## Data Frame: data
##
## -----
##          ven_support          No    yes, invasive    yes, noninvasive          Total
## CVD
##   no          1693.0 (51.3%)    540.7 (16.4%)    1068.2 (32.4%)    3301.9 (100.0%)
##   yes          1611.5 (47.2%)    603.3 (17.7%)    1197.4 (35.1%)    3412.2 (100.0%)
## Total          3304.6 (49.2%)    1144.0 (17.0%)    2265.6 (33.7%)    6714.2 (100.0%)
## -----
##
## -----
## Chi.squared    df    p.value
## -----
##      10.9876      2    0.0041
## -----
```

Intubation

```
with(data, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: data
##
## -----
##          intubation          no          yes          Total
## CVD
##   no          2761.2 (83.6%)    540.7 (16.4%)    3301.9 (100.0%)
##   yes          2809.0 (82.3%)    603.3 (17.7%)    3412.2 (100.0%)
## Total          5570.2 (83.0%)    1144.0 (17.0%)    6714.2 (100.0%)
## -----
##
## -----
## Chi.squared    df    p.value
## -----
##      1.9271      1    0.1651
## -----
##
## -----
## Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.10      0.97      1.25
## -----
```

1st trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "1tri")

with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))

## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
##
## -----
##           intubation           no           yes           Total
## CVD
## no           153.4 (88.7%)    19.6 (11.3%)    173.0 (100.0%)
## yes           97.1 (80.6%)    23.4 (19.4%)    120.5 (100.0%)
## Total        250.5 (85.3%)    43.0 (14.7%)    293.5 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##      3.1142      1   0.0776
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.89      0.98      3.62
## -----
```

2nd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "2tri")

with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))

## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
##
## -----
##           intubation           no           yes           Total
## CVD
## no           429.5 (84.4%)    79.6 (15.6%)    509.2 (100.0%)
## yes           493.7 (81.6%)   111.4 (18.4%)    605.1 (100.0%)
## Total        923.2 (82.9%)   191.1 (17.1%)   1114.3 (100.0%)
```

```
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      1.31      1  0.2524
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.22      0.89    1.67
## -----
```

3rd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "3tri")

with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
## -----
##          intubation          no          yes          Total
## CVD
## no          1205.3 (89.1%)    147.2 (10.9%)    1352.5 (100.0%)
## yes          1479.2 (86.3%)    234.6 (13.7%)    1713.7 (100.0%)
## Total        2684.5 (87.5%)    381.8 (12.5%)    3066.3 (100.0%)
## -----
##
## -----
## Chi.squared  df  p.value
## -----
##      5.1945      1  0.0227
## -----
##
## -----
## Odds Ratio  Lo - 95%  Hi - 95%
## -----
##      1.30      1.04    1.62
## -----
```

Puerperium

```
df4 <- data %>%
  filter(classi_gesta_puerp == "puerp")
```

```
with(df4, ctable(CVD, intubation, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * intubation
## Data Frame: df4
##
##
## -----
##          intubation          no          yes          Total
##    CVD
##    no          903.0 (76.3%)    280.6 (23.7%)    1183.6 (100.0%)
##    yes          654.0 (75.2%)    215.5 (24.8%)    869.5 (100.0%)
##    Total        1557.0 (75.8%)    496.2 (24.2%)    2053.1 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      0.2619        1    0.6088
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.06         0.86       1.30
## -----
##
```

Outcome - cure x death

```
with(data, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))
```

```
## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: data
##
##
## -----
##          evolution          cure          death          Total
##    CVD
##    no          3020.3 (86.0%)    491.3 (14.0%)    3511.6 (100.0%)
##    yes          2974.7 (82.4%)    636.8 (17.6%)    3611.5 (100.0%)
##    Total        5995.0 (84.2%)    1128.1 (15.8%)    7123.1 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##     17.433        1     0
## -----
##
```

```
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.32      1.16      1.50
## -----
```

1st trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "1tri")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))

## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##      evolution      cure      death      Total
##      CVD
##      no      165.5 (90.4%)   17.5 ( 9.6%)   183.1 (100.0%)
##      yes      121.1 (88.1%)   16.4 (11.9%)   137.4 (100.0%)
##      Total      286.6 (89.4%)   33.9 (10.6%)   320.5 (100.0%)
## -----
##
## -----
##      Chi.squared   df   p.value
## -----
##      0.2366        1   0.6267
## -----
##
## -----
##      Odds Ratio   Lo - 95%   Hi - 95%
## -----
##      1.28      0.62      2.60
## -----
```

2nd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "2tri")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))

## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
```

```
##
## -----
##           evolution           cure           death           Total
##    CVD
##    no           471.8 (86.2%)       75.7 (13.8%)       547.5 (100.0%)
##    yes           484.2 (76.2%)       151.0 (23.8%)       635.3 (100.0%)
##    Total         956.0 (80.8%)       226.7 (19.2%)       1182.7 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      18.1283      1      0
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.94        1.43        2.63
## -----
```

3rd trimester

```
df4 <- data %>%
  filter(classi_gesta_puerp == "3tri")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))

## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##           evolution           cure           death           Total
##    CVD
##    no           1279.2 (89.5%)       150.6 (10.5%)       1429.8 (100.0%)
##    yes           1565.4 (86.8%)       237.9 (13.2%)       1803.3 (100.0%)
##    Total         2844.6 (88.0%)       388.5 (12.0%)       3233.1 (100.0%)
## -----
##
## -----
##    Chi.squared    df    p.value
## -----
##      5.0783      1    0.0242
## -----
##
## -----
##    Odds Ratio    Lo - 95%    Hi - 95%
## -----
##      1.29        1.04        1.60
## -----
```

Puerperium

```
df4 <- data %>%
  filter(classi_gesta_puerp == "puerp")

with(df4, ctable(CVD, evolution, prop="r", OR=TRUE, useNA = "no", chisq = TRUE, weights = weight))

## Cross-Tabulation, Row Proportions
## CVD * evolution
## Data Frame: df4
##
## -----
##           evolution           cure           death           Total
## CVD
## no           1009.5 (81.0%)    237.0 (19.0%)    1246.5 (100.0%)
## yes           709.0 (77.1%)    210.6 (22.9%)    919.6 (100.0%)
## Total        1718.5 (79.3%)    447.5 (20.7%)    2166.1 (100.0%)
## -----
##
## -----
## Chi.squared   df   p.value
## -----
##    4.6463      1   0.0311
## -----
##
## -----
## Odds Ratio   Lo - 95%   Hi - 95%
## -----
##    1.27       1.03      1.56
## -----
```

Time elapsed between the start of symptoms and the outcome (days) after PSM

```
d_yes <- data %>%
  filter(CVD == "yes" & !is.na(days_symp_evol))
d_no <- data %>%
  filter(CVD == "no" & !is.na(days_symp_evol))

# Performing weighted Student's t-tests to compare the CVD and non-CVD groups with respect to the time
wtd.t.test(d_yes$days_symp_evol, d_no$days_symp_evol, weight = d_yes$weight, weighty = d_no$weight)

## $test
## [1] "Two Sample Weighted T-Test (Welch)"
##
## $coefficients
##      t.value      df      p.value
## 0.1099694 1063.6837670 0.9124544
##
## $additional
```

```
## Difference      Mean.x      Mean.y      Std. Err
## 0.06197107 16.09992551 16.03795444 0.56353002
```

Considering only death cases

```
df <- data[!is.na(data$days_symp_evol) & !is.na(data$CVD),]

df <- df %>%
  filter(evolution == "death")
```

```
d_yes <- df %>%
  filter(CVD == "yes" & !is.na(days_symp_evol))
d_no <- df %>%
  filter(CVD == "no" & !is.na(days_symp_evol))
```

Fixed the death cases, we perform a weighted Student's t-tests to compare the CVD and non-CVD groups

```
wtd.t.test(d_yes$days_symp_evol, d_no$days_symp_evol, weight = d_yes$weight, weighty = d_no$weight)
```

```
## $test
## [1] "Two Sample Weighted T-Test (Welch)"
##
## $coefficients
##      t.value      df      p.value
## -1.2611092 209.4593901 0.2086723
##
## $additional
## Difference      Mean.x      Mean.y      Std. Err
## -1.603168 18.525606 20.128775 1.271237
```

Considering only cure cases

```
df <- data[!is.na(data$days_symp_evol) & !is.na(data$CVD),]

df <- df %>%
  filter(evolution == "cure")
```

```
d_yes <- df %>%
  filter(CVD == "yes" & !is.na(days_symp_evol))
d_no <- df %>%
  filter(CVD == "no" & !is.na(days_symp_evol))
```

Fixed the cure cases, we perform a weighted Student's t-tests to compare the CVD and non-CVD groups

```
wtd.t.test(d_yes$days_symp_evol, d_no$days_symp_evol, weight = d_yes$weight, weighty = d_no$weight)
```

```
## $test
## [1] "Two Sample Weighted T-Test (Welch)"
##
## $coefficients
##      t.value      df      p.value
```



```
## 0.3550948 844.4701089 0.7226072
##
## $additional
## Difference      Mean.x      Mean.y    Std. Err
## 0.2215880 15.5695136 15.3479256 0.6240249
```