Documentation of the article 'COVID-19 vaccines confer protection in hospitalized pregnant and postpartum women with severe COVID-19'

Codes and outputs

Feb 10, 2022

Sumário

Description

This file presents the documentation of the analysis of article "COVID-19 vaccines confer protection in hospitalized pregnant and postpartum women with severe COVID-19".

About the database and R packages used

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.

```r
#load packages
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(
    "readr",
    "readxl",
    "janitor",
    "dplyr",
    "forcats",
    "stringr",
    "lubridate",
    "summarytools",
    "magrittr",
    "questionr",
    "knitr",
    "data.table",
    "modelsummary",
    "kableExtra",
    "DescTools",
    "effectsize",
    "WeightIt",
    "MatchIt",
    "ggplot2",
    "ggpubr",
    "naniar",
    "mice",
    "miceafter",
    "VIM",
    "miceadds"
  )

lapply(packages, loadlibrary)
```

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

```r
#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))
```

This is a retrospective cohort study using the data from the Influenza Epidemiological Surveillance Information System, SIVEP-Gripe (Sistema de Informação de Vigilância Epidemiológica da Gripe) database.

The SIVEP-Gripe is a nationwide surveillance database created to monitor severe acute respiratory infections and data on virus circulation and respiratory infections in Brazil.

The period analyzed comprises epidemiological data from 2021, with a database obtained on December 2, 2021 on the website https://opendatasus.saude.gov.br. The dataset can be obtained at https://www.kaggle.com/agatharodrigues/covid19-vaccine-maternal-population. It is loaded below:

```r
#loading the datasets
#2021
dados <- read_delim(
  "INFLUD21-29-11-2021.csv",
  ";",
  escape_double = FALSE,
  locale = locale(encoding = "ISO-8859-2"),
  trim_ws = TRUE
)

#Create case year variable
dados <-  dados %>%
  dplyr::mutate(
    dt_sint = as.Date(DT_SIN_PRI, format = "%d/%m/%Y"), #date of first symptoms
    dt_nasc = as.Date(DT_NASC, format = "%d/%m/%Y"), #date of birth
    dt_vac_gripe = as.Date(DT_UT_DOSE, format = "%d/%m/%Y"), #date of Influenza vaccine
    ano = lubridate::year(dt_sint), #year of the case
  )
```

There are 1625471 observations in the database. To see the dictionary of variables, access (in Portuguese): https://opendatasus.saude.gov.br/dataset/ae90fa8f-3e94-467e-a33f-94adbb66edf8/resource/8f571374-c555-4ec0-8e44-00b1e8b11c25/download/dicionario-de-dados-srag-hospitalizado-27.07.2020-final.pdf

Case selection and data treatment

The first filter is to select cases from May 02, 2021 (18th epidemiological week of symptoms of 2021) to November 27, 2021 (epidemiological week 47 of 2021).

```
#selection of cases from 18th epidemiological week of symptoms (May 2, 2021)
#to November 27, 2021 (week 43 of 2021).
sem1 <- 18
sem2 <- 47

dados1 <- dados %>%
  filter(SEM_PRI >= sem1 &  SEM_PRI <= sem2)
```

There are 756681 observations in the database after selection of valid years.

The next selection is female:

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

There are 338892 observations in the database.

Selection of women of childbearing age (10 to 55 years):

```
#creating the age variable as the difference between dt_sint and dt_nasc.
#In cases without dt_nasc, we consider
#the NU_AGE_N field
dados2 <- dados2 %>%
  mutate(
        idade = as.period(interval(start = dt_nasc, end = dt_sint))$year,
        age = ifelse(is.na(idade), NU_IDADE_N, idade)
  )

#Filtering of cases aged 55 and under
dados3 <- dados2 %>%
  filter(age > 9 & age <= 55)
```

There are 141540 observations in the database.

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
##neither pregnant nor postpartum
dados3 <- dados3 %>%
  mutate(
    classi_gesta_puerp = case_when(
      CS_GESTANT == 1  ~ "1tri",
      CS_GESTANT == 2  ~ "2tri",
      CS_GESTANT == 3  ~ "3tri",
      CS_GESTANT == 4  ~ "IG_ig",
      CS_GESTANT == 5 &
        PUERPERA == 1 ~ "puerp",
      CS_GESTANT == 9 & PUERPERA == 1 ~ "puerp",
```

```
      TRUE ~ "no"
    )
  )

freq(dados3$classi_gesta_puerp)
```

```
##              n    %  val%
## 1tri       800  0.6   0.6
## 2tri      2110  1.5   1.5
## 3tri      4958  3.5   3.5
## IG_ig      368  0.3   0.3
## no      131497 92.9  92.9
## puerp     1807  1.3   1.3
```

```
#filtering only pregnant and postpartum women
dados4 <- dados3 %>%
  filter(classi_gesta_puerp != "no")
```

There are 10043 observations in the database.

We selected only confirmed cases of COVID-19.

```
dados4 <- dados4 %>%
  mutate(
    classi_fin = case_when(
      CLASSI_FIN == 5 ~ "covid",
      TRUE ~ "no"
    )
  )


#filtering only covid cases
dados5 <- dados4 %>%
    filter(CLASSI_FIN == 5)
```

There are 5806 observations in the database.

Now let's select the cases of COVID by PCR or antigen, but which are also not positive for Influenza.

```
#COVID case diagnosed by PCR
dados5 <- dados5 %>%
  mutate(pcr_covid_SN = case_when(
    (PCR_SARS2 == 1) |
      (
        str_detect(DS_PCR_OUT, "SARS|COVID|COV|CORONA|CIVID")
      ) ~ "yes",
    TRUE ~ "no"
  ))

#Influenza case diagnosed by PCR
dados5 <- dados5 %>%
  mutate(pcr_influenza_SN = case_when(
    (POS_PCRFLU == 1) |
```

```
    (
      str_detect(DS_PCR_OUT, "INFLU|INFLUENZA")
    ) ~ "yes",
    TRUE ~ "no"
  ))

with(dados5, table(pcr_influenza_SN, pcr_covid_SN))
```

```
##                 pcr_covid_SN
## pcr_influenza_SN   no  yes
##              no  2806 2999
##              yes    1    0
```

There is no case that is positive for COVID and for Influenza by PCR.

```
#Case of COVID diagnosed by antigen
dados5 <- dados5 %>%
  mutate(antigenio_covid_SN = case_when(
    (AN_SARS2 == 1) |
      (
        str_detect(DS_AN_OUT, "SARS|COVID|COV|CORONA|CIVID")
      ) ~ "yes",
    TRUE ~ "no"
  ))


#Influenza case diagnosed by antigen
dados5 <- dados5 %>%
  mutate(antigenio_influenza_SN = case_when(
    (POS_AN_FLU == 1) |
      (
        str_detect(DS_AN_OUT, "INFLU|INFLUENZA")
      ) ~ "yes",
    TRUE ~ "no"
  ))

with(dados5, table(antigenio_influenza_SN, antigenio_covid_SN))
```

```
##                       antigenio_covid_SN
## antigenio_influenza_SN   no  yes
##                    no  4306 1499
##                    yes    0    1
```

There is one positive case for COVID and for Influenza by antigen.

We will now select the cases of COVID confirmed by PCR or antigen.

```
with(dados5, table(pcr_covid_SN, antigenio_covid_SN))
```

```
##             antigenio_covid_SN
## pcr_covid_SN   no  yes
##          no  1518 1289
##          yes 2788  211
```

```
#filtering only covid cases by PCR or antigen
dados6 <- dados5 %>%
    filter(pcr_covid_SN == "yes" | antigenio_covid_SN == "yes")
```

There are 4288 observations in the database.

Now it's time to remove cases that are also positive for Influenza.

```
with(dados6, table(pcr_influenza_SN, antigenio_influenza_SN))
```

```
##                 antigenio_influenza_SN
## pcr_influenza_SN   no  yes
##              no  4287    0
##              yes    0    1
```

```
#filtering only negative cases of Influenza by PCR or antigen
dados7 <- dados6 %>%
    filter(pcr_influenza_SN != "yes" & antigenio_influenza_SN != "yes")
```

There are 4287 observations in the database.

We will only select the finalized cases (death or cure). The variable that indicates the outcome is EVOLUCAO, with the categories: 1-Cure; 2-Death; 3- Death from other causes; 9-Ignored.

```
with(dados7, freq(EVOLUCAO))
```

```
##        n    % val%
## 1   3351 78.2 84.9
## 2    487 11.4 12.3
## 3      8  0.2  0.2
## 9    100  2.3  2.5
## NA   341  8.0   NA
```

Let's select only the finalized cases:

```
#filtering only completed cases
dados8 <- dados7 %>%
  filter((EVOLUCAO == 1 | EVOLUCAO == 2 | EVOLUCAO == 3) & !is.na(EVOLUCAO))
```

```
#creating the evolution variable
dados8 <- dados8 %>%
  mutate(death = case_when(
    EVOLUCAO == 1 ~ "cure",
    EVOLUCAO == 2 ~ "death",
    EVOLUCAO == 3 ~ "death"
  ))

with(dados8, freq(death))
```

```
##          n    % val%
## cure   3351 87.1 87.1
## death   495 12.9 12.9
```

There are 3846 observations in the database.

The variable that indicates whether the person received a vaccine against COVID-19 is `VACINA_COV`, with categories: 1-yes; 2-no; 9-ignored.

```
#Frequency table for VACINA_COV
with(dados8, freq(VACINA_COV))
```

```
##        n    % val%
## 1    650 16.9 18.7
## 2   2084 54.2 60.0
## 9    738 19.2 21.3
## NA   374  9.7   NA
```

Let's now group "NA" and "9" in the same category (NA - missing data) and label the valid categories.

```
#recoding the vaccine_cov variable
dados8 <- dados8 %>%
  mutate(vaccine_cov = case_when(
    VACINA_COV == 1 ~ "yes",
    VACINA_COV == 2 ~ "no",
    TRUE ~ NA_character_
  ))
#frequency table for vaccine_cov
with(dados8, freq(vaccine_cov))
```

```
##        n    % val%
## no  2084 54.2 76.2
## yes  650 16.9 23.8
## NA  1112 28.9   NA
```

The next step is filtering cases that we have information about COVID-19 vaccination. These data are analyzed in the following.

```
#Filtering cases with information about vaccination
data_final <- dados8 %>%
  filter(!is.na(vaccine_cov))
```

```
with(data_final, freq(vaccine_cov))
```

```
##        n    % val%
## no  2084 76.2 76.2
## yes  650 23.8 23.8
```

The variable `vaccine_cov` only indicates if the pregnant or postpartum women took the vaccine, regardless of the dose. There is no information on whether the person only took the first dose or the second. The closest we come to this is to consider the column `DOSE_2_COV`, which indicates the date of the second dose.

```
#Create second dose date variable
data_final <-  data_final %>%
  dplyr::mutate(
```

```
    dt_dose2_cov = as.Date(DOSE_2_COV, format = "%d/%m/%Y")
  )

#Create variable that indicates that it has the date of the second dose
data_final <-  data_final%>%
  dplyr::mutate(
    indic_dt_dose2_cov = ifelse(is.na(dt_dose2_cov) & !is.na(vaccine_cov), 0, ifelse(is.na(vaccine_cov)
  )

# first dose date frequency table
with(data_final, freq(indic_dt_dose2_cov, total =  TRUE))
```

```
##           n      %  val%
## 0      2534  92.7  92.7
## 1       200   7.3   7.3
## Total 2734 100.0 100.0
```

There is only information on the date of the second dose for 200 cases of 650 cases indicated as "yes" for COVID-19 vaccine.

Now we will analyze the not vaccinated group versus two dose vaccinated group.

```
#Create second dose date variable
data_final <- data_final %>%
  filter(vaccine_cov == "no" | (vaccine_cov == "yes" & indic_dt_dose2_cov == 1))

with(data_final, freq(vaccine_cov))
```

```
##         n     %  val%
## no   2084  91.2  91.2
## yes   200   8.8   8.8
```

#Analysis

Epidemiologic characteristics

```
# Ethnicity
data_final <-  data_final %>%
  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_
    ),
    white_color = case_when(
      ethnicity == "white" ~ "yes",
      is.na(ethnicity) ~ NA_character_,
```

```
      TRUE ~ "no"
    )
  )

# Education
data_final <-  data_final %>%
  mutate(
    education2 = case_when(
      CS_ESCOL_N <= 2 ~ "up to 9 years",
      CS_ESCOL_N == 3 ~ "from 9 to 12 years",
      CS_ESCOL_N == 4 ~ "over 12 years",
      TRUE ~ NA_character_
    )
  )
data_final$education2 <-
  factor(data_final$education2, levels = c("up to 9 years", "from 9 to 12 years", "over 12 years"))

# residence area
data_final <-  data_final %>%
  mutate(
    residence = case_when(
      CS_ZONA == 1 ~ "urban",
      CS_ZONA == 2 ~ "rural",
      CS_ZONA == 3 ~ "periurban",
      TRUE ~ NA_character_
    )
  )
```

Ethnicity

```
with(data_final, ctable(ethnicity, vaccine_cov,  prop = "c", useNA = "no", chisq = FALSE, OR = TRUE))
```

```
## Cross-Tabulation, Column Proportions
## ethnicity * vaccine_cov
## Data Frame: data_final
##
## ------------ -------------- ---------------- -------------- ----------------
##          vaccine_cov              no              yes            Total
##    ethnicity
##        black              96 (  5.1%)     6 (  3.3%)    102 (  4.9%)
##        brown             753 ( 39.9%)    61 ( 33.3%)    814 ( 39.3%)
##    indigenous              5 (  0.3%)     4 (  2.2%)      9 (  0.4%)
##        white            1022 ( 54.1%)   111 ( 60.7%)   1133 ( 54.7%)
##       yellow              12 (  0.6%)     1 (  0.5%)     13 (  0.6%)
##        Total            1888 (100.0%)   183 (100.0%)   2071 (100.0%)
## ------------ -------------- ---------------- -------------- ----------------
```

```
fisher.test(data_final$ethnicity, data_final$vaccine_cov)
```

```
##
```

```
##  Fisher's Exact Test for Count Data
##
## data:  data_final$ethnicity and data_final$vaccine_cov
## p-value = 0.007548
## alternative hypothesis: two.sided
```

White color

```
with(data_final, ctable(white_color, vaccine_cov,  prop = "c", useNA = "no", chisq = TRUE, OR = TRUE))
```

```
## Cross-Tabulation, Column Proportions
## white_color * vaccine_cov
## Data Frame: data_final
##
##
## ------------- ------------- --------------- ------------- ---------------
##             vaccine_cov               no             yes           Total
##    white_color
##            no               866 ( 45.9%)    72 ( 39.3%)    938 ( 45.3%)
##           yes              1022 ( 54.1%)   111 ( 60.7%)   1133 ( 54.7%)
##         Total              1888 (100.0%)   183 (100.0%)   2071 (100.0%)
## ------------- ------------- --------------- ------------- ---------------
##
## ---------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     2.6088     1    0.1063
## ---------------------------
##
## ------------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     1.31        0.96       1.78
## ------------------------------------
```

Education (years)

```
with(data_final, ctable(education2, vaccine_cov, prop = "c", useNA = "no", chisq = TRUE, OR = TRUE))
```

```
## Cross-Tabulation, Column Proportions
## education2 * vaccine_cov
## Data Frame: data_final
##
##
## -------------------- ------------- --------------- ------------- ---------------
##                 vaccine_cov               no             yes           Total
##           education2
##       up to 9 years               279 ( 26.7%)    20 ( 19.8%)    299 ( 26.1%)
##    from 9 to 12 years             573 ( 54.9%)    55 ( 54.5%)    628 ( 54.8%)
```

```
##          over 12 years                   192 ( 18.4%)    26 ( 25.7%)    218 ( 19.0%)
##                  Total                  1044 (100.0%)   101 (100.0%)   1145 (100.0%)
## -------------------- ------------- --------------- -------------- ---------------
##
## ---------------------------
##  Chi.squared   df    p.value
## ------------ ---- ---------
##    4.3072      2    0.1161
## ---------------------------
```

Age

```
datasummary((vaccine_cov) ~ age*(n+media+DP+mediana+q25+q75+IQR),
            data = data_final, output = 'markdown')
```

	n	media	DP	mediana	q25	q75	IQR
no	2084.00	29.72	7.09	30.00	25.00	35.00	10.00
yes	200.00	31.44	7.72	31.00	25.00	37.00	12.00

```
#t-test
t.test(age ~ vaccine_cov, data = data_final)
```

```
##
##  Welch Two Sample t-test
##
## data:  age by vaccine_cov
## t = -3.0298, df = 232.39, p-value = 0.002724
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -2.8372657 -0.6012756
## sample estimates:
##  mean in group no mean in group yes
##          29.72073          31.44000
```

```
#effect size
c_cohen <- cohens_d(age ~ as.factor(vaccine_cov), data=data_final)
c_cohen
```

```
## Cohen's d |        95% CI
## -------------------------
## -0.24     | [-0.39, -0.10]
##
## - Estimated using pooled SD.
```

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

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

Residence area

```r
with(data_final, ctable(residence, vaccine_cov, prop = "c", useNA = "no", chisq = FALSE, OR = TRUE))
```

```
## Cross-Tabulation, Column Proportions
## residence * vaccine_cov
## Data Frame: data_final
##
## ----------- -------------- --------------- -------------- ---------------
##              vaccine_cov              no             yes            Total
##    residence
##    periurban                  6 (  0.3%)      0 (  0.0%)      6 (  0.3%)
##        rural                113 (  5.8%)      9 (  4.8%)    122 (  5.7%)
##        urban               1838 ( 93.9%)    179 ( 95.2%)   2017 ( 94.0%)
##        Total               1957 (100.0%)    188 (100.0%)   2145 (100.0%)
## ----------- -------------- --------------- -------------- ---------------
```

```r
fisher.test(data_final$residence, data_final$vaccine_cov)
```

```
##
##  Fisher's Exact Test for Count Data
##
## data:  data_final$residence and data_final$vaccine_cov
## p-value = 0.8508
## alternative hypothesis: two.sided
```

Comorbities

```r
#Cardiac
data_final <-  data_final %>%
  mutate(cardiac = case_when(CARDIOPATI == 1 ~ "yes",
                             CARDIOPATI == 2 ~ "no",
                             TRUE ~ NA_character_))

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

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

#Asthma
data_final <-  data_final %>%
  mutate(asthma = case_when(ASMA == 1 ~ "yes",
                            ASMA == 2 ~ "no",
```

```
                            TRUE ~ NA_character_))

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

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

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

#Imunossupression
data_final <-  data_final %>%
  mutate(imuno = case_when(IMUNODEPRE == 1 ~ "yes",
                           IMUNODEPRE == 2 ~ "no",
                           TRUE ~ NA_character_))

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

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

Cardiac

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * cardiac
## Data Frame: data_final
##
##
## ------------- --------- ------------- ------------- --------------
##             cardiac           no           yes          Total
##    vaccine_cov
##            no            738 (87.6%)   104 (12.4%)   842 (100.0%)
```

```
##          yes                71 (76.3%)    22 (23.7%)    93 (100.0%)
##          Total             809 (86.5%)   126 (13.5%)   935 (100.0%)
## ------------- --------- ------------- ------------- --------------
##
## ----------------------------
## Chi.squared   df    p.value
## ------------- ---- ---------
##    8.2348      1     0.0041
## ----------------------------
##
## ------------------------------------
## Odds Ratio   Lo - 95%   Hi - 95%
## ----------- ---------- ----------
##    2.20        1.31       3.70
## ------------------------------------
```

Hematologic

```r
with(data_final, ctable(vaccine_cov, hematologic, prop = "r", useNA = "no", chisq = FALSE, OR = TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * hematologic
## Data Frame: data_final
##
##
## ------------- ------------- ------------- ---------- --------------
##              hematologic            no         yes          Total
##    vaccine_cov
##            no                807 (99.1%)   7 (0.9%)   814 (100.0%)
##           yes                 87 (97.8%)   2 (2.2%)    89 (100.0%)
##         Total                894 (99.0%)   9 (1.0%)   903 (100.0%)
## ------------- ------------- ------------- ---------- --------------
##
## ------------------------------------
## Odds Ratio   Lo - 95%   Hi - 95%
## ----------- ---------- ----------
##    2.65        0.54      12.96
## ------------------------------------
```

```r
fisher.test(data_final$hematologic, data_final$vaccine_cov)
```

```
##
##  Fisher's Exact Test for Count Data
##
## data:  data_final$hematologic and data_final$vaccine_cov
## p-value = 0.2198
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##   0.2642886 14.1850125
## sample estimates:
## odds ratio
##   2.646116
```

Diabetes

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * diabetes
## Data Frame: data_final
##
##
## ------------- ---------- ------------- ------------- --------------
##            diabetes            no            yes           Total
##   vaccine_cov
##           no            708 (83.1%)   144 (16.9%)   852 (100.0%)
##          yes             73 (77.7%)    21 (22.3%)    94 (100.0%)
##        Total            781 (82.6%)   165 (17.4%)   946 (100.0%)
## ------------- ---------- ------------- ------------- --------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ----------
##     1.382      1     0.2398
## ----------------------------
##
## ------------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     1.41        0.84       2.37
## ------------------------------------
```

Obesity

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * obesity
## Data Frame: data_final
##
##
## ------------- --------- ------------- ------------- --------------
##            obesity            no            yes           Total
##   vaccine_cov
##           no            680 (78.1%)   191 (21.9%)   871 (100.0%)
##          yes             76 (84.4%)    14 (15.6%)    90 (100.0%)
##        Total            756 (78.7%)   205 (21.3%)   961 (100.0%)
## ------------- --------- ------------- ------------- --------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ----------
##     1.6129     1     0.2041
```

```
## -----------------------------
##
## -----------------------------------
##  Odds Ratio    Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.66         0.36        1.19
## -----------------------------------
```

Asthma

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * asthma
## Data Frame: data_final
##
##
## ------------- -------- ------------- ------------ --------------
##               asthma            no           yes          Total
##    vaccine_cov
##            no          767 (92.2%)   65 ( 7.8%)   832 (100.0%)
##           yes           81 (90.0%)    9 (10.0%)    90 (100.0%)
##         Total          848 (92.0%)   74 ( 8.0%)   922 (100.0%)
## ------------- -------- ------------- ------------ --------------
##
##
## -----------------------------
##  Chi.squared   df   p.value
## ------------ ---- ---------
##    0.2718      1    0.6021
## -----------------------------
##
##
## -----------------------------------
##  Odds Ratio    Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     1.31         0.63        2.73
## -----------------------------------
```

Hepatic

```r
ctable(data_final$vaccine_cov, data_final$hepatic, chisq=FALSE, prop="r",  useNA = "no", OR = TRUE)
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * hepatic
## Data Frame: data_final
##
##
## ------------- -------- -------------- ---------- --------------
##               hepatic            no         yes          Total
##    vaccine_cov
```

```
##               no              807 ( 99.6%)    3 (0.4%)    810 (100.0%)
##              yes               88 ( 98.9%)    1 (1.1%)     89 (100.0%)
##            Total              895 ( 99.6%)    4 (0.4%)    899 (100.0%)
## ------------- --------- -------------- ---------- --------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##      3.06        0.31       29.70
## -----------------------------------
```

fisher.test(data_final**$**vaccine_cov, data_final**$**hepatic)

```
##
##   Fisher's Exact Test for Count Data
##
## data:  data_final$vaccine_cov and data_final$hepatic
## p-value = 0.3415
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##    0.05758056 38.46642499
## sample estimates:
## odds ratio
##    3.050859
```

Neurologic

ctable(data_final**$**vaccine_cov, data_final**$**neurologic, chisq=FALSE, prop="r", useNA = "no", OR = TRUE)

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * neurologic
## Data Frame: data_final
##
##
## ------------- ------------ ------------- ----------- --------------
##             neurologic            no          yes          Total
##    vaccine_cov
##            no              802 (98.9%)    9 (1.1%)    811 (100.0%)
##           yes               86 (97.7%)    2 (2.3%)     88 (100.0%)
##         Total              888 (98.8%)   11 (1.2%)    899 (100.0%)
## ------------- ------------ ------------- ----------- --------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##      2.07        0.44        9.75
## -----------------------------------
```

fisher.test(data_final**$**vaccine_cov, data_final**$**neurologic)

```
##
##  Fisher's Exact Test for Count Data
##
## data:  data_final$vaccine_cov and data_final$neurologic
## p-value = 0.2936
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##   0.2143274 10.2318114
## sample estimates:
## odds ratio
##   2.070139
```

Pneumologic

```r
ctable(data_final$vaccine_cov, data_final$pneumologic, chisq=FALSE, prop="r",  useNA = "no", OR = TRUE)
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * pneumologic
## Data Frame: data_final
##
##
## ------------- ------------- ------------- ----------- --------------
##              pneumologic              no           yes          Total
##    vaccine_cov
##            no                 805 (98.9%)     9 (1.1%)    814 (100.0%)
##           yes                  86 (96.6%)     3 (3.4%)     89 (100.0%)
##         Total                 891 (98.7%)    12 (1.3%)    903 (100.0%)
## ------------- ------------- ------------- ----------- --------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     3.12        0.83       11.74
## -----------------------------------
```

```r
fisher.test(data_final$vaccine_cov, data_final$pneumologic)
```

```
##
##  Fisher's Exact Test for Count Data
##
## data:  data_final$vaccine_cov and data_final$pneumologic
## p-value = 0.1059
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##   0.5323484 12.7897697
## sample estimates:
## odds ratio
##   3.114462
```

Imunossupression

```r
ctable(data_final$vaccine_cov, data_final$imuno, chisq=TRUE, prop="r", useNA = "no", OR = TRUE)
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * imuno
## Data Frame: data_final
##
##
## ------------- ------- ------------- ----------- --------------
##               imuno             no          yes          Total
##    vaccine_cov
##            no       801 (98.6%)    11 (1.4%)   812 (100.0%)
##           yes        84 (94.4%)     5 (5.6%)    89 (100.0%)
##         Total       885 (98.2%)    16 (1.8%)   901 (100.0%)
## ------------- ------- ------------- ----------- --------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     6.0925      1    0.0136
## ----------------------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     4.33        1.47       12.77
## -----------------------------------
```

Renal

```r
ctable(data_final$vaccine_cov, data_final$renal, chisq=FALSE, prop="r",  useNA = "no", OR = TRUE)
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * renal
## Data Frame: data_final
##
##
## ------------- ------- ------------- ----------- --------------
##               renal             no          yes          Total
##    vaccine_cov
##            no       797 (98.9%)     9 (1.1%)   806 (100.0%)
##           yes        87 (97.8%)     2 (2.2%)    89 (100.0%)
##         Total       884 (98.8%)    11 (1.2%)   895 (100.0%)
## ------------- ------- ------------- ----------- --------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     2.04        0.43       9.57
## -----------------------------------
```

```
fisher.test(data_final$renal, data_final$vaccine_cov)
```

```
##
##  Fisher's Exact Test for Count Data
##
## data:  data_final$renal and data_final$vaccine_cov
## p-value = 0.3002
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
##   0.21058 10.04877
## sample estimates:
## odds ratio
##   2.033657
```

Symptoms

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

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

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

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

# Respiratory discomfort
data_final <-  data_final %>%
  mutate(resp_disc = case_when(DESC_RESP == 1 ~ "yes",
                               DESC_RESP == 2 ~ "no",
                               TRUE ~ NA_character_))

# Desaturation
data_final <-  data_final %>%
  mutate(desaturation = case_when(SATURACAO == 1 ~ "yes",
                                  SATURACAO == 2 ~ "no",
                                  TRUE ~ NA_character_))
```

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


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


# Abdominal pain
data_final <-  data_final %>%
  mutate(abd_pain = case_when(DOR_ABD == 1 ~ "yes",
                              DOR_ABD == 2 ~ "no",
                              TRUE ~ NA_character_))


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


# Olfactory loss
data_final <-  data_final %>%
  mutate(olfac_loss = case_when(PERD_OLFT == 1 ~ "yes",
                                PERD_OLFT == 2 ~ "no",
                                TRUE ~ NA_character_))


# Loss of taste
data_final <-  data_final %>%
  mutate(loss_taste = case_when(PERD_PALA == 1 ~ "yes",
                                PERD_PALA == 2 ~ "no",
                                TRUE ~ NA_character_))


# Any respiratory symptom
df <- data_final %>%
  select(dyspnea,fatigue,desaturation,resp_disc)

soma <- function(x){
  if (sum(is.na(x))==4)
    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
data_final$qt_sintomas_resp_aux <- apply(df,1,soma)

data_final <-  data_final %>%
  mutate(resp_symp = case_when(qt_sintomas_resp_aux >=1 ~ "yes",
                               qt_sintomas_resp_aux ==0 ~ "no",
                               TRUE ~ NA_character_))
# Any symptom
```

```
df <- data_final %>%
  select(dyspnea,fatigue,desaturation,resp_disc,
         fever,cough,sore_throat,diarrhea,vomit,abd_pain,olfac_loss,loss_taste)
soma <- function(x){
  if (sum(is.na(x))==12)
    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
data_final$qt_sintomas_aux <- apply(df,1,soma)

data_final <-  data_final %>%
  mutate(symptom = case_when(qt_sintomas_aux >= 1 ~ "yes",
                             qt_sintomas_aux == 0 ~ "no",
                             TRUE ~ NA_character_))
```

Fever

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * fever
## Data Frame: data_final
##
##
## ------------- ------- ------------- -------------- ---------------
##           fever            no             yes            Total
##   vaccine_cov
##            no       783 (42.1%)    1077 (57.9%)   1860 (100.0%)
##           yes        94 (53.4%)      82 (46.6%)    176 (100.0%)
##         Total       877 (43.1%)    1159 (56.9%)   2036 (100.0%)
## ------------- ------- ------------- -------------- ---------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     7.9362     1    0.0048
## ----------------------------
##
## ---------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.63        0.47       0.86
## ---------------------------------
```

Cough

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * cough
## Data Frame: data_final
##
##
## ------------- ------- ------------- -------------- ---------------
##                cough            no           yes            Total
##     vaccine_cov
##             no       406 (20.9%)   1532 (79.1%)   1938 (100.0%)
##            yes        45 (24.7%)    137 (75.3%)    182 (100.0%)
##          Total       451 (21.3%)   1669 (78.7%)   2120 (100.0%)
## ------------- ------- ------------- -------------- ---------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     1.1998      1    0.2734
## ----------------------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.81        0.57       1.15
## -----------------------------------
```

Sore throat

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * sore_throat
## Data Frame: data_final
##
##
## ------------- ------------- -------------- ------------- ---------------
##          sore_throat              no           yes            Total
##     vaccine_cov
##             no        1263 (73.9%)   447 (26.1%)   1710 (100.0%)
##            yes         126 (79.2%)    33 (20.8%)    159 (100.0%)
##          Total        1389 (74.3%)   480 (25.7%)   1869 (100.0%)
## ------------- ------------- -------------- ------------- ---------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     1.9375      1    0.1639
## ----------------------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.74        0.50       1.10
```

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

Dyspnea

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * dyspnea
## Data Frame: data_final
##
##
## ------------- --------- ------------- -------------- ---------------
##               dyspnea            no            yes           Total
##    vaccine_cov
##            no         565 (29.5%)    1349 (70.5%)    1914 (100.0%)
##           yes          76 (43.9%)      97 (56.1%)     173 (100.0%)
##         Total         641 (30.7%)    1446 (69.3%)    2087 (100.0%)
## ------------- --------- ------------- -------------- ---------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     14.8145    1      1e-04
## ----------------------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.53         0.39       0.73
## -----------------------------------
```

Respiratory discomfort

```
with(data_final, ctable(vaccine_cov, resp_disc, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * resp_disc
## Data Frame: data_final
##
##
## ------------- ----------- ------------- -------------- ---------------
##               resp_disc           no            yes           Total
##    vaccine_cov
##            no         792 (43.5%)    1028 (56.5%)    1820 (100.0%)
##           yes          95 (55.2%)      77 (44.8%)     172 (100.0%)
##         Total         887 (44.5%)    1105 (55.5%)    1992 (100.0%)
## ------------- ----------- ------------- -------------- ---------------
##
## ----------------------------
```

```
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    8.2652       1     0.004
## --------------------------

##
## ----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.62        0.46       0.86
## ----------------------------------
```

Desaturation

```r
with(data_final, ctable(vaccine_cov, desaturation, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * desaturation
## Data Frame: data_final
##
##
## ------------- -------------- ------------- -------------- ---------------
##               desaturation            no            yes           Total
##    vaccine_cov
##            no                815 (44.3%)   1025 (55.7%)   1840 (100.0%)
##           yes                103 (59.9%)     69 (40.1%)    172 (100.0%)
##         Total                918 (45.6%)   1094 (54.4%)   2012 (100.0%)
## ------------- -------------- ------------- -------------- ---------------
##
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    14.7886      1     1e-04
## --------------------------

##
## ----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.53        0.39       0.73
## ----------------------------------
```

Diarrhea

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * diarrhea
## Data Frame: data_final
##
##
```

```
## ------------- ---------- -------------- ------------- ---------------
##               diarrhea             no           yes           Total
##    vaccine_cov
##           no               1488 (88.7%)   189 (11.3%)   1677 (100.0%)
##          yes                143 (89.9%)    16 (10.1%)    159 (100.0%)
##        Total               1631 (88.8%)   205 (11.2%)   1836 (100.0%)
## ------------- ---------- -------------- ------------- ---------------
##
##
## ---------------------------
## Chi.squared   df   p.value
## ------------- ---- ---------
##     0.109     1     0.7412
## ---------------------------
##
##
## ------------------------------------
## Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.88        0.51        1.51
## ------------------------------------
```

Vomit

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * vomit
## Data Frame: data_final
##
##
## ------------- ------- -------------- ------------- ---------------
##               vomit              no           yes           Total
##    vaccine_cov
##           no               1480 (88.0%)   202 (12.0%)   1682 (100.0%)
##          yes                143 (89.9%)    16 (10.1%)    159 (100.0%)
##        Total               1623 (88.2%)   218 (11.8%)   1841 (100.0%)
## ------------- ------- -------------- ------------- ---------------
##
##
## ---------------------------
## Chi.squared   df   p.value
## ------------- ---- ---------
##    0.3573     1      0.55
## ---------------------------
##
##
## ------------------------------------
## Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.82        0.48        1.40
## ------------------------------------
```

Abdominal pain

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * abd_pain
## Data Frame: data_final
##
##
## ------------- ---------- -------------- ------------- ---------------
##               abd_pain              no            yes           Total
##   vaccine_cov
##            no           1494 (90.1%)    164 ( 9.9%)    1658 (100.0%)
##           yes            138 (88.5%)     18 (11.5%)     156 (100.0%)
##         Total           1632 (90.0%)    182 (10.0%)    1814 (100.0%)
## ------------- ---------- -------------- ------------- ---------------
##
## ---------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     0.2655     1    0.6064
## ---------------------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     1.19        0.71       1.99
## -----------------------------------
```

Fatigue

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * fatigue
## Data Frame: data_final
##
##
## ------------- --------- -------------- ------------- ---------------
##               fatigue              no            yes           Total
##   vaccine_cov
##            no           1147 (66.0%)    590 (34.0%)    1737 (100.0%)
##           yes            110 (67.5%)     53 (32.5%)     163 (100.0%)
##         Total           1257 (66.2%)    643 (33.8%)    1900 (100.0%)
## ------------- --------- -------------- ------------- ---------------
##
## ---------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     0.0829     1    0.7735
```

28

```
## ----------------------------
##
## ----------------------------------
##   Odds Ratio    Lo - 95%    Hi - 95%
## ------------ ---------- ----------
##      0.94         0.67        1.32
## ----------------------------------
```

Olfactory loss

```
with(data_final, ctable(vaccine_cov, olfac_loss, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * olfac_loss
## Data Frame: data_final
##
##
## ------------- ------------ -------------- ------------- ---------------
##                 olfac_loss             no           yes           Total
##    vaccine_cov
##            no            1372 (81.6%)    310 (18.4%)    1682 (100.0%)
##           yes             127 (79.4%)     33 (20.6%)     160 (100.0%)
##         Total            1499 (81.4%)    343 (18.6%)    1842 (100.0%)
## ------------- ------------ -------------- ------------- ---------------
##
## ----------------------------
##   Chi.squared    df    p.value
## ------------ ---- ---------
##      0.3308      1     0.5652
## ----------------------------
##
## ----------------------------------
##   Odds Ratio    Lo - 95%    Hi - 95%
## ------------ ---------- ----------
##      1.15         0.77        1.72
## ----------------------------------
```

Loss of taste

```
with(data_final, ctable(vaccine_cov, loss_taste, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * loss_taste
## Data Frame: data_final
##
##
## ------------- ------------ -------------- ------------- ---------------
##                 loss_taste             no           yes           Total
##    vaccine_cov
```

29

```
##            no         1403 (83.2%)    284 (16.8%)    1687 (100.0%)
##           yes          129 (81.1%)     30 (18.9%)     159 (100.0%)
##         Total         1532 (83.0%)    314 (17.0%)    1846 (100.0%)
## ------------- ----------- -------------- ------------ ---------------
##
## ---------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     0.2937     1    0.5879
## ---------------------------
##
## -------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     1.15        0.76       1.74
## -------------------------------
```

Any respiratory symptom

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * resp_symp
## Data Frame: data_final
##
##
## ------------- ----------- -------------- -------------- ---------------
##              resp_symp           no            yes           Total
##    vaccine_cov
##            no          361 (18.2%)   1618 (81.8%)   1979 (100.0%)
##           yes           56 (30.6%)    127 (69.4%)    183 (100.0%)
##         Total          417 (19.3%)   1745 (80.7%)   2162 (100.0%)
## ------------- ----------- -------------- -------------- ---------------
##
## ---------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    15.6528     1    1e-04
## ---------------------------
##
## -------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.51        0.36       0.71
## -------------------------------
```

Any symptom

```
with(data_final, ctable(vaccine_cov, symptom, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * symptom
## Data Frame: data_final
##
##
## ------------- --------- ----------- -------------- ---------------
##              symptom          no            yes           Total
## vaccine_cov
##          no           78 (3.8%)   1980 (96.2%)   2058 (100.0%)
##         yes           16 (8.2%)    178 (91.8%)    194 (100.0%)
##       Total           94 (4.2%)   2158 (95.8%)   2252 (100.0%)
## ------------- --------- ----------- -------------- ---------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------ ---- ---------
##     7.727      1     0.0054
## ----------------------------
##
## ------------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.44        0.25        0.77
## ------------------------------------
```

Outcome

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


# Length time in ICU
data_final<-  data_final%>%
  mutate(dt_enticu  = as.Date(DT_ENTUTI,  format = "%d/%m/%Y"),
         dt_exicu = as.Date(DT_SAIDUTI, format = "%d/%m/%Y"),
         time_icu = as.numeric(dt_exicu - dt_enticu)
  )

# ventilatory support
data_final <- data_final %>%
  mutate(ventilatory_support = case_when(SUPORT_VEN == 1 ~ "invasive",
                                         SUPORT_VEN == 2 ~ "non-invasive",
                                         SUPORT_VEN == 3 ~ "no",
                                         TRUE ~ NA_character_))

# Intubation
data_final <- data_final %>%
  mutate(intubation = case_when(SUPORT_VEN == 1 ~ "yes",
                                SUPORT_VEN == 2 | SUPORT_VEN == 3 ~ "no",
```

```
                      TRUE ~ NA_character_))
```

ICU

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * icu
## Data Frame: data_final
##
##
## ------------- ----- -------------- ------------- ---------------
##            icu             no            yes           Total
##   vaccine_cov
##            no      1239 (62.6%)   740 (37.4%)   1979 (100.0%)
##           yes       143 (76.5%)    44 (23.5%)    187 (100.0%)
##         Total      1382 (63.8%)   784 (36.2%)   2166 (100.0%)
## ------------- ----- -------------- ------------- ---------------
##
##
## ---------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     13.6244    1     2e-04
## ---------------------------
##
##
## ---------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.52        0.36       0.73
## ---------------------------------
```

Length time in ICU

```
data_final_aux <- data_final %>%
  filter (icu == "yes")
```

```
datasummary((vaccine_cov) ~ time_icu*(n+media+DP+mediana+q25+q75+IQR),
            data = data_final_aux, output = 'markdown')
```

	n	media	DP	mediana	q25	q75	IQR
no	548.00	13.09	12.22	10.00	5.00	18.00	13.00
yes	21.00	9.38	9.30	5.00	3.00	13.00	10.00

```
#t-test
t.test(time_icu ~ vaccine_cov, data = data_final_aux)
```

```
##
##  Welch Two Sample t-test
##
## data:  time_icu by vaccine_cov
## t = 1.7692, df = 22.727, p-value = 0.09028
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -0.6305326  8.0474599
## sample estimates:
##  mean in group no mean in group yes
##          13.089416          9.380952
```

Ventilatory support

```r
with(data_final, ctable(vaccine_cov, ventilatory_support, prop = "r", useNA = "no", chisq = TRUE, OR=TR
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * ventilatory_support
## Data Frame: data_final
##
##
## ------------- --------------------- ------------- ------------- -------------- ---------------
##              ventilatory_support      invasive             no   non-invasive            Total
##    vaccine_cov
##            no                     368 (18.8%)   711 (36.3%)    880 (44.9%)   1959 (100.0%)
##           yes                       9 ( 4.8%)    99 (52.4%)     81 (42.9%)    189 (100.0%)
##         Total                     377 (17.6%)   810 (37.7%)    961 (44.7%)   2148 (100.0%)
## ------------- --------------------- ------------- ------------- -------------- ---------------
##
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##     31.3063    2       0
## ----------------------------
```

Intubation

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * intubation
## Data Frame: data_final
##
##
## ------------- ------------- -------------- ------------- ---------------
##              intubation              no            yes            Total
##    vaccine_cov
##            no                  1591 (81.2%)   368 (18.8%)   1959 (100.0%)
##           yes                   180 (95.2%)     9 ( 4.8%)    189 (100.0%)
```

```
##        Total                    1771 (82.4%)   377 (17.6%)   2148 (100.0%)
## ------------- ------------ -------------- ------------- ---------------
##
## ---------------------------
## Chi.squared   df   p.value
## ------------- ---- ---------
##    22.4651     1       0
## ---------------------------
##
## ------------------------------------
## Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.22        0.11       0.43
## ------------------------------------
```

Death

```r
with(data_final, ctable(vaccine_cov, death, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * death
## Data Frame: data_final
##
##
## ------------- ------- -------------- ------------- ---------------
##               death          cure          death          Total
##    vaccine_cov
##            no         1790 (85.9%)   294 (14.1%)   2084 (100.0%)
##           yes          194 (97.0%)     6 ( 3.0%)    200 (100.0%)
##        Total         1984 (86.9%)   300 (13.1%)   2284 (100.0%)
## ------------- ------- -------------- ------------- ---------------
##
## ---------------------------
## Chi.squared   df   p.value
## ------------- ---- ---------
##    18.7715     1       0
## ---------------------------
##
## ------------------------------------
## Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##    0.188       0.083      0.428
## ------------------------------------
```

Propensity Scoring Method (PSM) - information about date of second dose

```r
data_final <- data_final %>%
  mutate(vaccine1 = ifelse(vaccine_cov == "yes", 1, 0),
```

```r
        id = 1:dim(data_final)[1])

data_final1 <- data_final %>%
  select(id, vaccine1, age, cardiac)

data_final1 <- data_final1 %>%
  mutate(
    cardiac1 = ifelse(is.na(cardiac) == TRUE, "na", cardiac)
  )

#PSM
psm1 <- matchit(vaccine1 ~ age + cardiac1, data = data_final1, method = "nearest", ratio =1)

summary(psm1)
```

```
##
## Call:
## matchit(formula = vaccine1 ~ age + cardiac1, data = data_final1,
##     method = "nearest", ratio = 1)
##
## Summary of Balance for All Data:
##            Means Treated Means Control Std. Mean Diff. Var. Ratio eCDF Mean
## distance          0.0965        0.0867          0.2648     1.9872    0.0595
## age              31.4400       29.7207          0.2227     1.1850    0.0409
## cardiac1na        0.5350        0.5960         -0.1222          .    0.0610
## cardiac1no        0.3550        0.3541          0.0018          .    0.0009
## cardiac1yes       0.1100        0.0499          0.1921          .    0.0601
##            eCDF Max
## distance     0.1179
## age          0.1056
## cardiac1na   0.0610
## cardiac1no   0.0009
## cardiac1yes  0.0601
##
##
## Summary of Balance for Matched Data:
##            Means Treated Means Control Std. Mean Diff. Var. Ratio eCDF Mean
## distance          0.0965        0.0965          0.0010     1.0023    0.0002
## age              31.4400       31.2950          0.0188     1.0431    0.0035
## cardiac1na        0.5350        0.5300          0.0100          .    0.0050
## cardiac1no        0.3550        0.3550          0.0000          .    0.0000
## cardiac1yes       0.1100        0.1150         -0.0160          .    0.0050
##            eCDF Max Std. Pair Dist.
## distance      0.010         0.0042
## age           0.015         0.0214
## cardiac1na    0.005         0.0100
## cardiac1no    0.000         0.0000
## cardiac1yes   0.005         0.0160
##
## Percent Balance Improvement:
##            Std. Mean Diff. Var. Ratio eCDF Mean eCDF Max
## distance              99.6       99.7      99.6     91.5
## age                   91.6       75.2      91.6     85.8
```

```
## cardiac1na              91.8          .      91.8     91.8
## cardiac1no             100.0          .     100.0    100.0
## cardiac1yes             91.7          .      91.7     91.7
##
## Sample Sizes:
##           Control Treated
## All          2084     200
## Matched       200     200
## Unmatched    1884       0
## Discarded       0       0
```

```
plot(psm1, type = "jitter", interactive = FALSE)
```
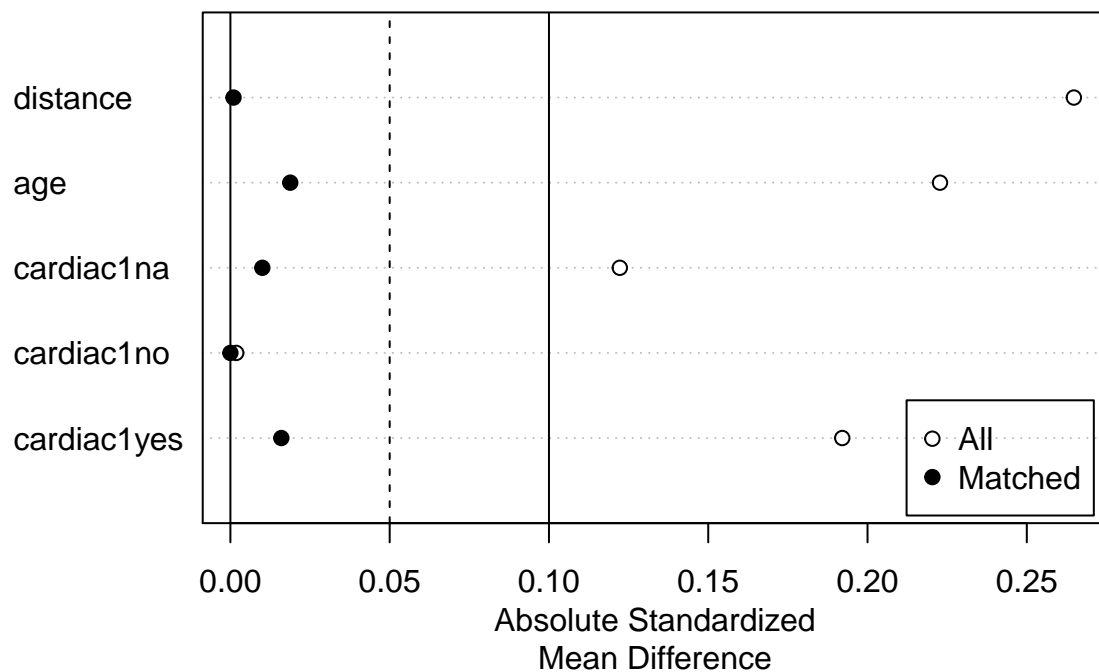
Distribution of Propensity Scores
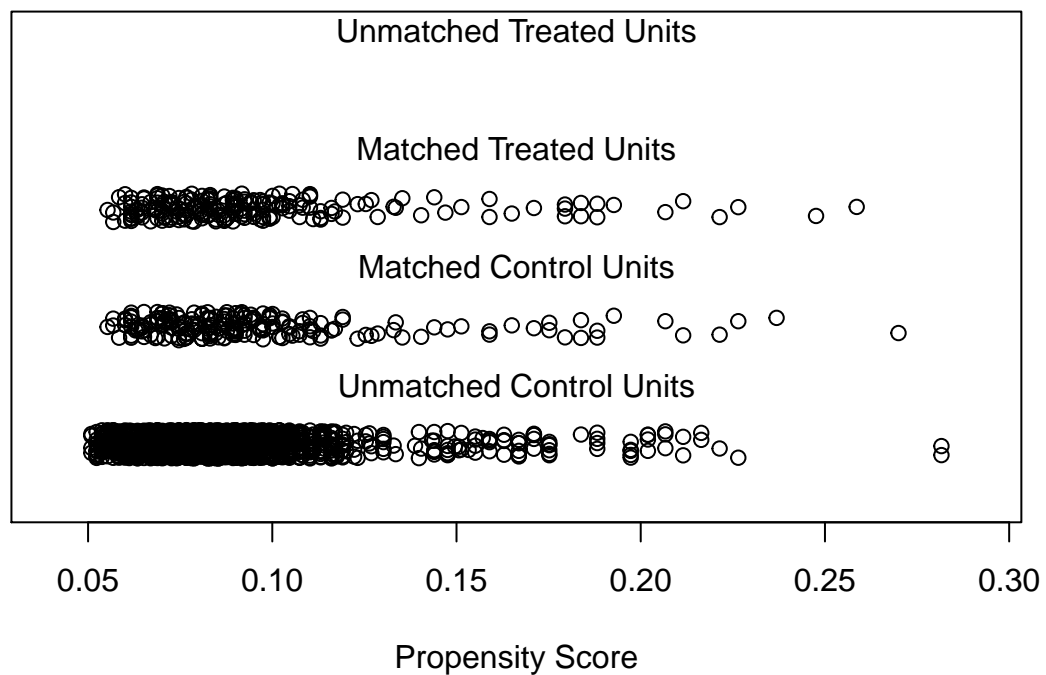

```
plot(psm1, type = "qq", interactive = FALSE,
     which.xs = c("age", "cardiac1"))
```

eQQ Plots

All   Matched

age

cardiac1na

cardiac1no

Treated Units

Control Units

eQQ Plots

cardiac1yes

All   Matched

Treated Units

Control Units
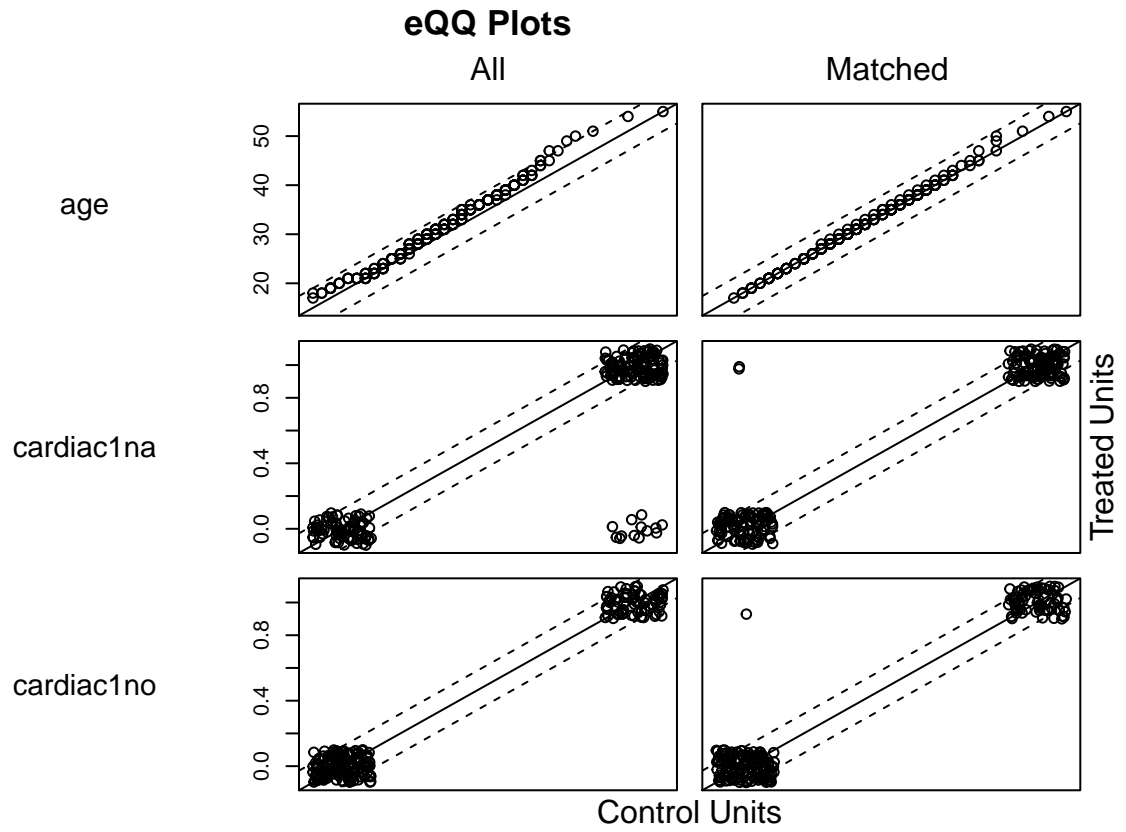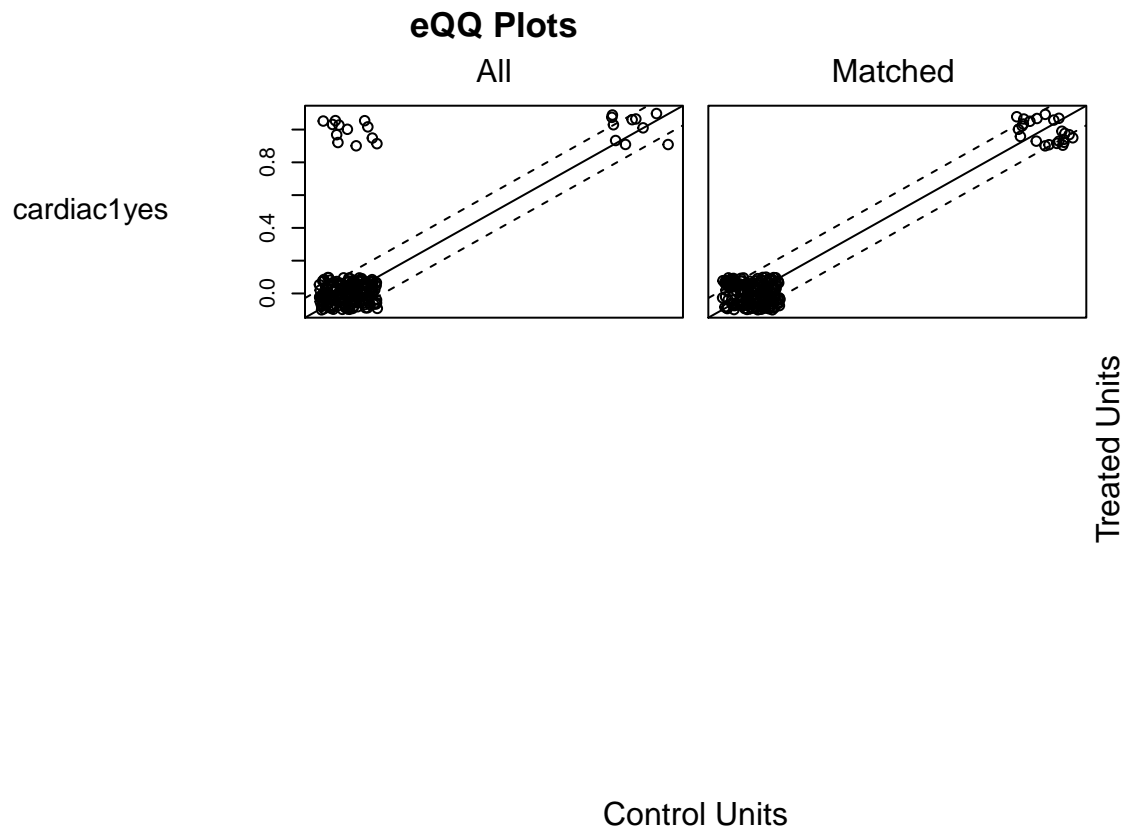
```r
plot(summary(psm1))
```

```
#Selecting only the selected observations
data_aux <- data_final1[psm1$weights==1, ]

#Now let's join data_aux with data_final

data_psm <- right_join(data_final, data_aux, by= c("id", "vaccine1", "age", "cardiac"))

freq(data_psm$vaccine_cov)
```

```
##        n  % val%
## no   200 50    50
## yes  200 50    50
```

For outcomes

ICU

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * icu
## Data Frame: data_psm
##
```

```
## 
## ------------- ----- ------------- ------------- --------------
##           icu            no           yes         Total
##    vaccine_cov
##          no      121 (63.7%)    69 (36.3%)   190 (100.0%)
##         yes      143 (76.5%)    44 (23.5%)   187 (100.0%)
##       Total      264 (70.0%)   113 (30.0%)   377 (100.0%)
## ------------- ----- ------------- ------------- --------------
## 
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    6.7444      1    0.0094
## ----------------------------
## 
## ----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##     0.54        0.34       0.85
## ----------------------------------
```

Length time in ICU

```r
data_psm_aux <- data_psm %>%
  filter (icu == "yes")
```

```r
datasummary((vaccine_cov) ~ time_icu*(n+media+DP+mediana+q25+q75+IQR),
            data = data_psm_aux, output = 'markdown')
```

	n	media	DP	mediana	q25	q75	IQR
no	57.00	14.09	11.67	12.00	5.00	18.00	13.00
yes	21.00	9.38	9.30	5.00	3.00	13.00	10.00

```r
#teste t
t.test(time_icu ~ vaccine_cov, data = data_psm_aux)
```

```
## 
##  Welch Two Sample t-test
## 
## data:  time_icu by vaccine_cov
## t = 1.8447, df = 44.556, p-value = 0.07173
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -0.4335558  9.8470897
## sample estimates:
##  mean in group no mean in group yes
##         14.087719          9.380952
```

Ventilatory support

```
with(data_psm, ctable(vaccine_cov, ventilatory_support, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE)
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * ventilatory_support
## Data Frame: data_psm
##
##
## ------------- ---------------------- ------------ ------------- -------------- --------------
##               ventilatory_support       invasive            no   non-invasive          Total
##    vaccine_cov
##            no                        39 (20.6%)    68 (36.0%)     82 (43.4%)    189 (100.0%)
##           yes                         9 ( 4.8%)    99 (52.4%)     81 (42.9%)    189 (100.0%)
##         Total                        48 (12.7%)   167 (44.2%)    163 (43.1%)    378 (100.0%)
## ------------- ---------------------- ------------ ------------- -------------- --------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    24.5106     2       0
## ----------------------------
```

Intubation

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

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * intubation
## Data Frame: data_psm
##
##
## ------------- ------------ ------------- ------------ --------------
##                 intubation            no          yes          Total
##    vaccine_cov
##            no                150 (79.4%)    39 (20.6%)    189 (100.0%)
##           yes                180 (95.2%)     9 ( 4.8%)    189 (100.0%)
##         Total                330 (87.3%)    48 (12.7%)    378 (100.0%)
## ------------- ------------ ------------- ------------ --------------
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    20.0693     1       0
## ----------------------------
##
## -----------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ----------- ---------- ----------
##     0.19        0.09       0.41
## -----------------------------------
```

Death

```
with(data_psm, ctable(vaccine_cov, death, prop = "r", useNA = "no", chisq = TRUE, OR=TRUE))
```

```
## Cross-Tabulation, Row Proportions
## vaccine_cov * death
## Data Frame: data_psm
##
##
## ------------- ------- ------------- ------------ --------------
##               death         cure         death          Total
##   vaccine_cov
##            no        174 (87.0%)   26 (13.0%)   200 (100.0%)
##           yes        194 (97.0%)    6 ( 3.0%)   200 (100.0%)
##         Total        368 (92.0%)   32 ( 8.0%)   400 (100.0%)
## ------------- ------- ------------- ------------ --------------
##
##
## ----------------------------
##  Chi.squared   df   p.value
## ------------- ---- ---------
##    12.2622     1     5e-04
## ----------------------------
##
##
## ---------------------------------
##  Odds Ratio   Lo - 95%   Hi - 95%
## ------------ ---------- ----------
##    0.207       0.083      0.515
## ---------------------------------
```

Multivariate Imputation by Chained Equations (MICE)

A total of 2284 patients were analyzed and divided into two groups, according to their COVID-19 vaccination status: unvaccinated (n = 2084; 91.2%) and vaccinated (n = 200; 8.8%) groups. With respect to this dataset, to deal with possible nonresponse bias, we explore the missing values and we conduct a multiple imputation.

```
data_na <- data_final %>%
  select(
    vaccine_cov,
    age,
    white_color,
    cardiac,
    diabetes,
    hematologic,
    obesity,
    asthma,
    hepatic,
    neurologic,
    pneumologic,
    imuno,
    renal,
    education2,
```

```
    residence,
    fever,
    cough,
    sore_throat,
    dyspnea,
    resp_disc,
    desaturation,
    diarrhea,
    vomit,
    abd_pain,
    fatigue,
    olfac_loss,
    loss_taste,
    icu,
    intubation,
    death
  )

data_na$vaccine_cov <- as.factor(data_na$vaccine_cov)
data_na$white_color <- as.factor(data_na$white_color)
data_na$cardiac <- as.factor(data_na$cardiac)
data_na$diabetes <- as.factor(data_na$diabetes)
data_na$hematologic <- as.factor(data_na$hematologic)
data_na$obesity <- as.factor(data_na$obesity)
data_na$asthma <- as.factor(data_na$asthma)
data_na$hepatic <- as.factor(data_na$hepatic)
data_na$neurologic <- as.factor(data_na$neurologic)
data_na$pneumologic <- as.factor(data_na$pneumologic)
data_na$imuno <- as.factor(data_na$imuno)
data_na$renal <- as.factor(data_na$renal)
data_na$residence <- as.factor(data_na$residence)
data_na$fever <- as.factor(data_na$fever)
data_na$cough <- as.factor(data_na$cough)
data_na$sore_throat <- as.factor(data_na$sore_throat)
data_na$dyspnea <- as.factor(data_na$dyspnea)
data_na$resp_disc <- as.factor(data_na$resp_disc)
data_na$desaturation <- as.factor(data_na$desaturation)
data_na$diarrhea <- as.factor(data_na$diarrhea)
data_na$vomit <- as.factor(data_na$vomit)
data_na$abd_pain <- as.factor(data_na$abd_pain)
data_na$fatigue <- as.factor(data_na$fatigue)
data_na$olfac_loss <- as.factor(data_na$olfac_loss)
data_na$loss_taste <- as.factor(data_na$loss_taste)
data_na$icu <- as.factor(data_na$icu)
data_na$intubation <- as.factor(data_na$intubation)
data_na$death <- as.factor(data_na$death)

print(dfSummary(data_na, varnumbers = FALSE), method = "render")
```

Note that all comorbities variables and the education variable have high proportions of missing data. The percentage of valid responses is, at least, of 79,4% for variables related to the symptoms.

Missing (28.7%) Present (71.3%)
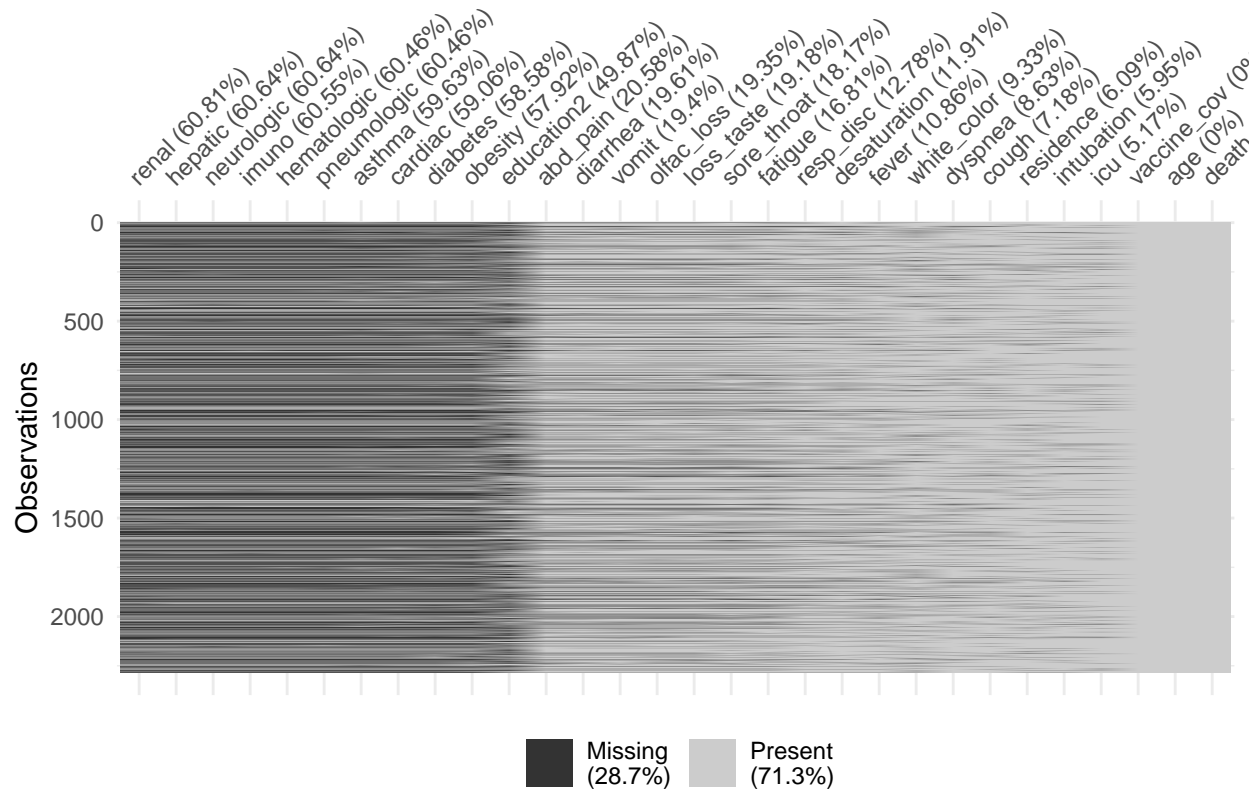
To deal with missing data, we consider a multiple imputation by fully conditional specification. The mice package implements this method, where each incomplete variable is imputed by a separate model. According to the previously analysis, the most of the variables with missing data are binary. We considered as a imputation method for this kind of variable the logistic regression (logreg), except when the percentage of missing values for the variable is greater than 50%. In this situation, we consider a bootstrapped logistic regression model (logreg.boot). For the residence variable, we considered a polytomous logistic regression (polyreg), and for the education, we considered a proportional odds model (polr). Following, because of high percentage of some variables, we present 60 imputed datasets e the trace plots to investigate the convergence of the method.

```
imputed_Data <-
  mice(
    data_na,
    m = 60,
    maxit = 70,
    method = c(
      "",
      "pmm",
      "logreg",
      rep("logreg.boot", 10),
      "polr",
      "polyreg",
      rep("logreg", 15)
    ),
    seed = 510,
    printFlag = FALSE
```

```
  )
summary(imputed_Data)
```

```
## Class: mids
## Number of multiple imputations:  60
## Imputation methods:
##    vaccine_cov              age    white_color         cardiac         diabetes
##              ""               ""       "logreg"  "logreg.boot"  "logreg.boot"
##    hematologic          obesity         asthma        hepatic       neurologic
## "logreg.boot"  "logreg.boot"  "logreg.boot"  "logreg.boot"  "logreg.boot"
##    pneumologic            imuno          renal     education2        residence
## "logreg.boot"  "logreg.boot"  "logreg.boot"         "polr"       "polyreg"
##          fever            cough    sore_throat        dyspnea        resp_disc
##       "logreg"         "logreg"       "logreg"       "logreg"         "logreg"
##   desaturation         diarrhea          vomit        abd_pain          fatigue
##       "logreg"         "logreg"       "logreg"       "logreg"         "logreg"
##     olfac_loss       loss_taste            icu      intubation           death
##       "logreg"         "logreg"       "logreg"       "logreg"              ""
## PredictorMatrix:
##            vaccine_cov age white_color cardiac diabetes hematologic obesity
## vaccine_cov           0   1           1       1        1           1       1
## age                   1   0           1       1        1           1       1
## white_color           1   1           0       1        1           1       1
## cardiac               1   1           1       0        1           1       1
## diabetes              1   1           1       1        0           1       1
## hematologic           1   1           1       1        1           0       1
##            asthma hepatic neurologic pneumologic imuno renal education2
## vaccine_cov      1       1          1           1     1     1          1
## age              1       1          1           1     1     1          1
## white_color      1       1          1           1     1     1          1
## cardiac          1       1          1           1     1     1          1
## diabetes         1       1          1           1     1     1          1
## hematologic      1       1          1           1     1     1          1
##            residence fever cough sore_throat dyspnea resp_disc desaturation
## vaccine_cov         1     1     1           1       1         1            1
## age                 1     1     1           1       1         1            1
## white_color         1     1     1           1       1         1            1
## cardiac             1     1     1           1       1         1            1
## diabetes            1     1     1           1       1         1            1
## hematologic         1     1     1           1       1         1            1
##            diarrhea vomit abd_pain fatigue olfac_loss loss_taste icu
## vaccine_cov        1     1        1       1          1          1   1
## age                1     1        1       1          1          1   1
## white_color        1     1        1       1          1          1   1
## cardiac            1     1        1       1          1          1   1
## diabetes           1     1        1       1          1          1   1
## hematologic        1     1        1       1          1          1   1
##            intubation death
## vaccine_cov          1     1
## age                  1     1
## white_color          1     1
## cardiac              1     1
## diabetes             1     1
```
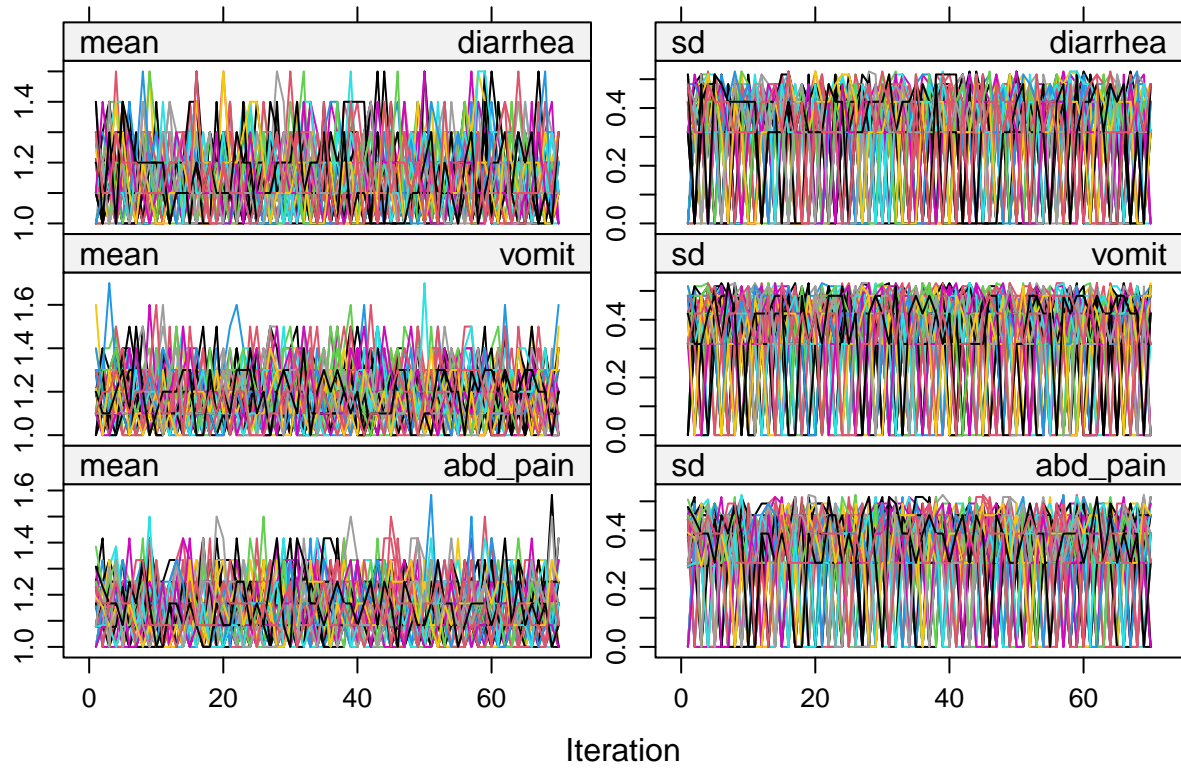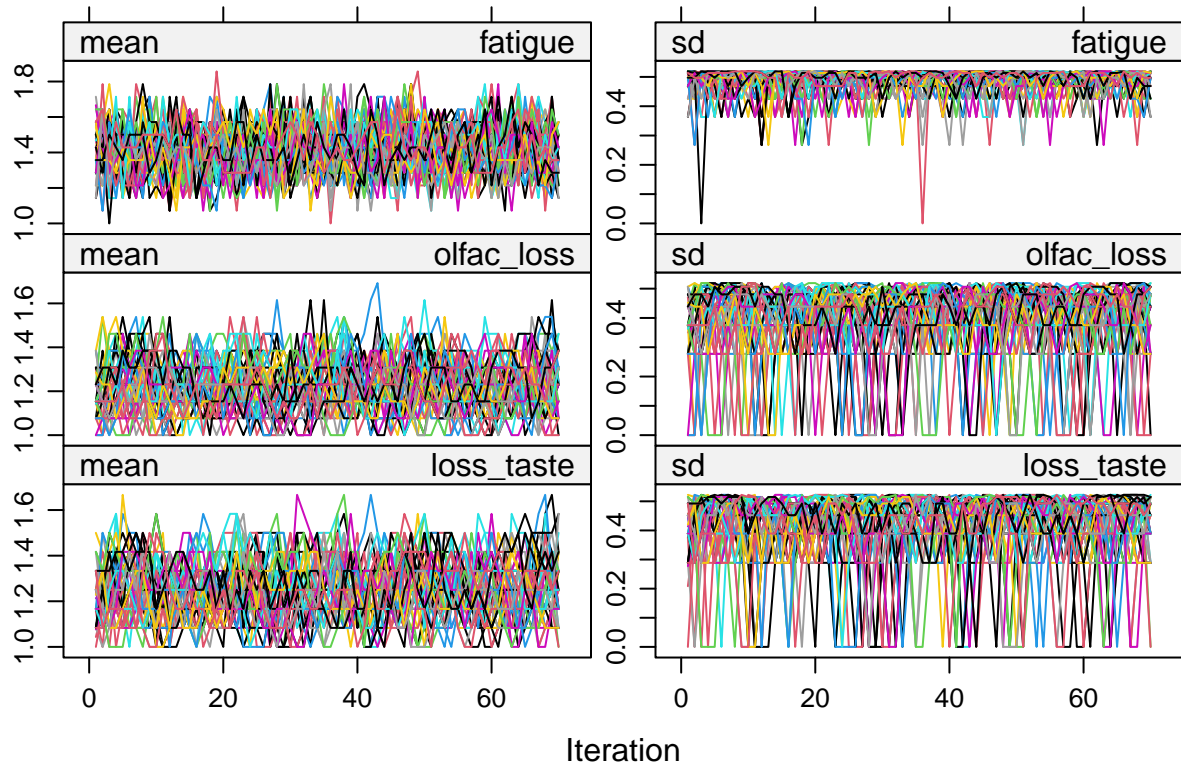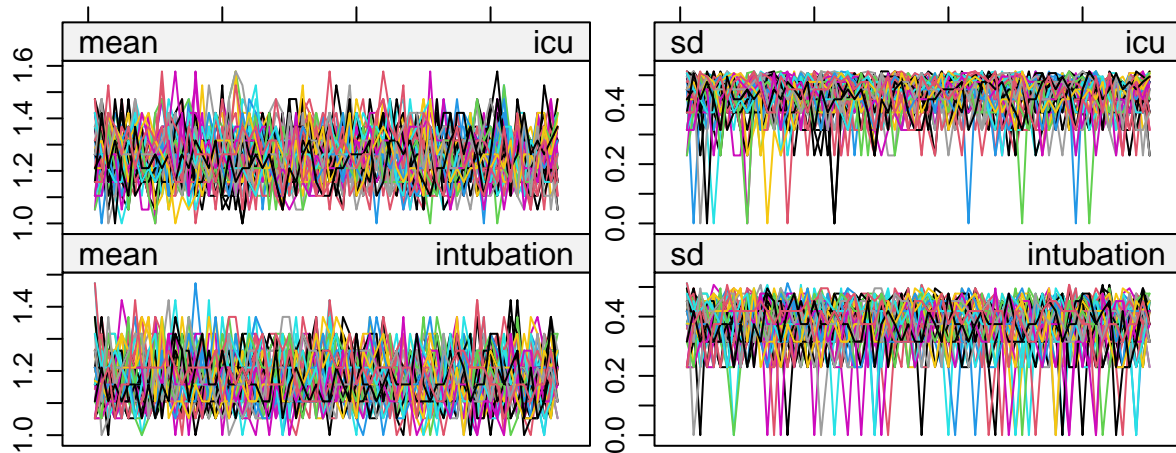
```
## hematologic              1       1
```

```
plot(imputed_Data)
```
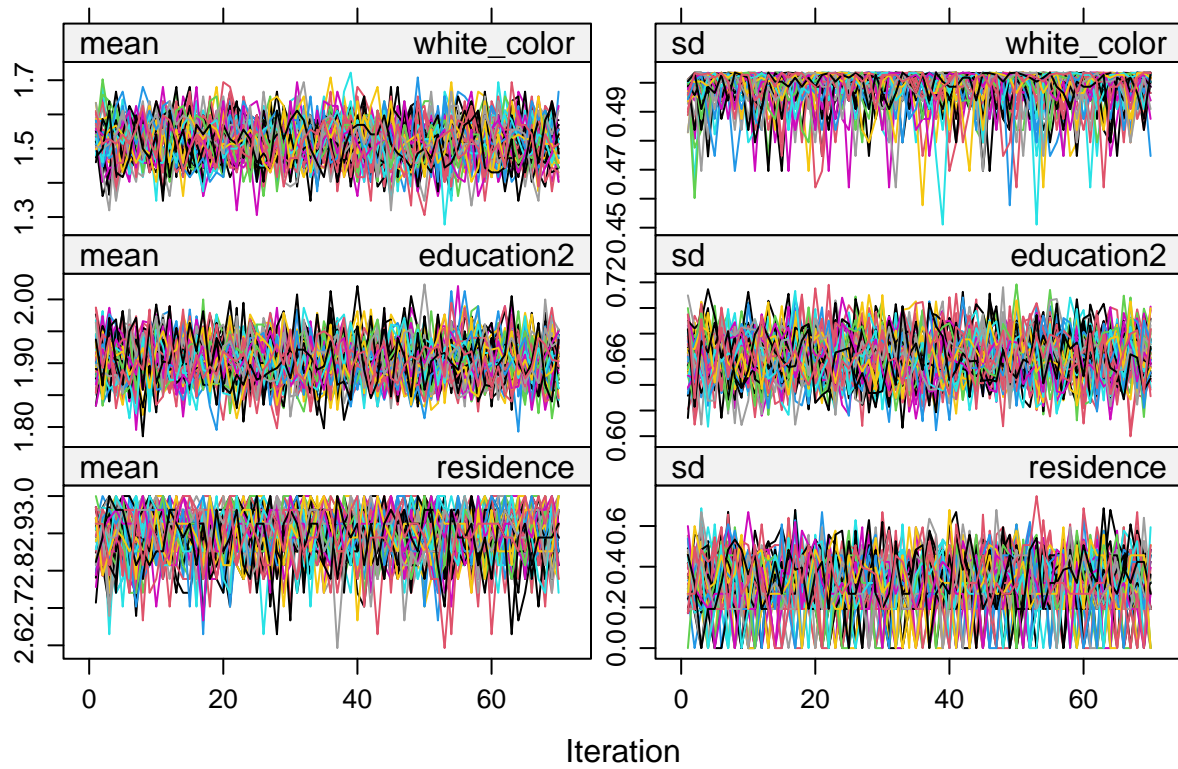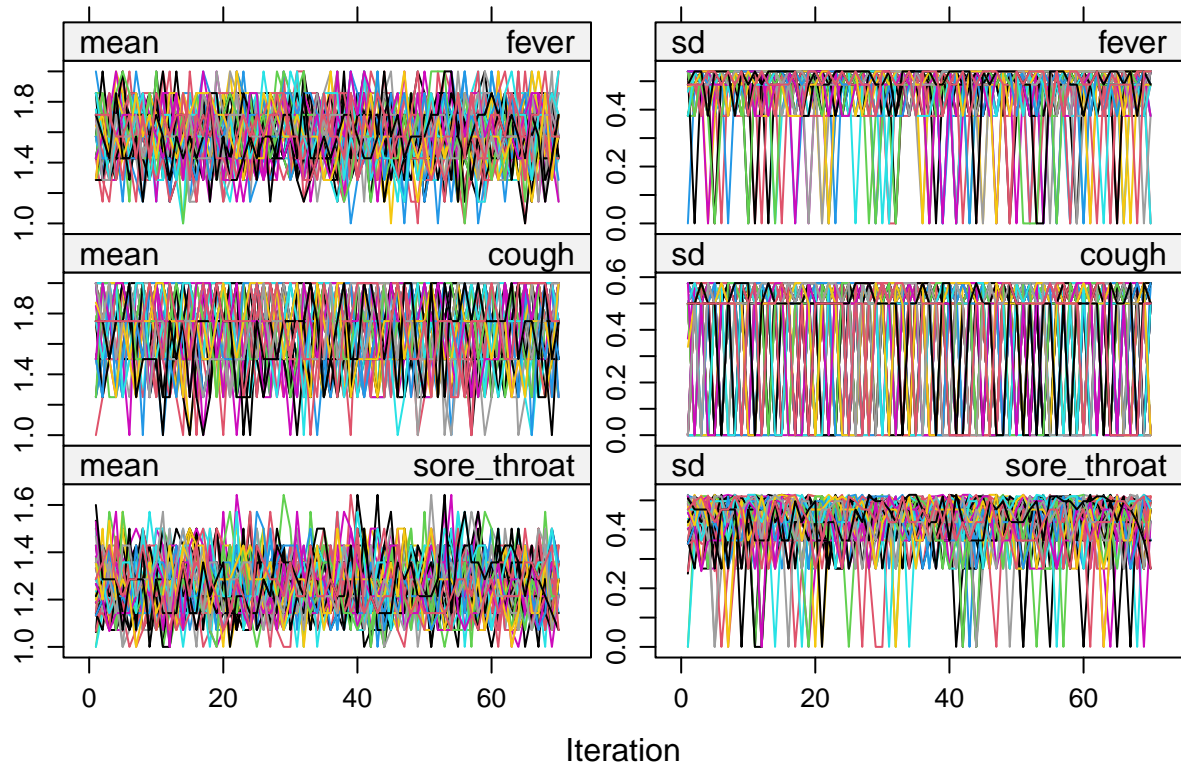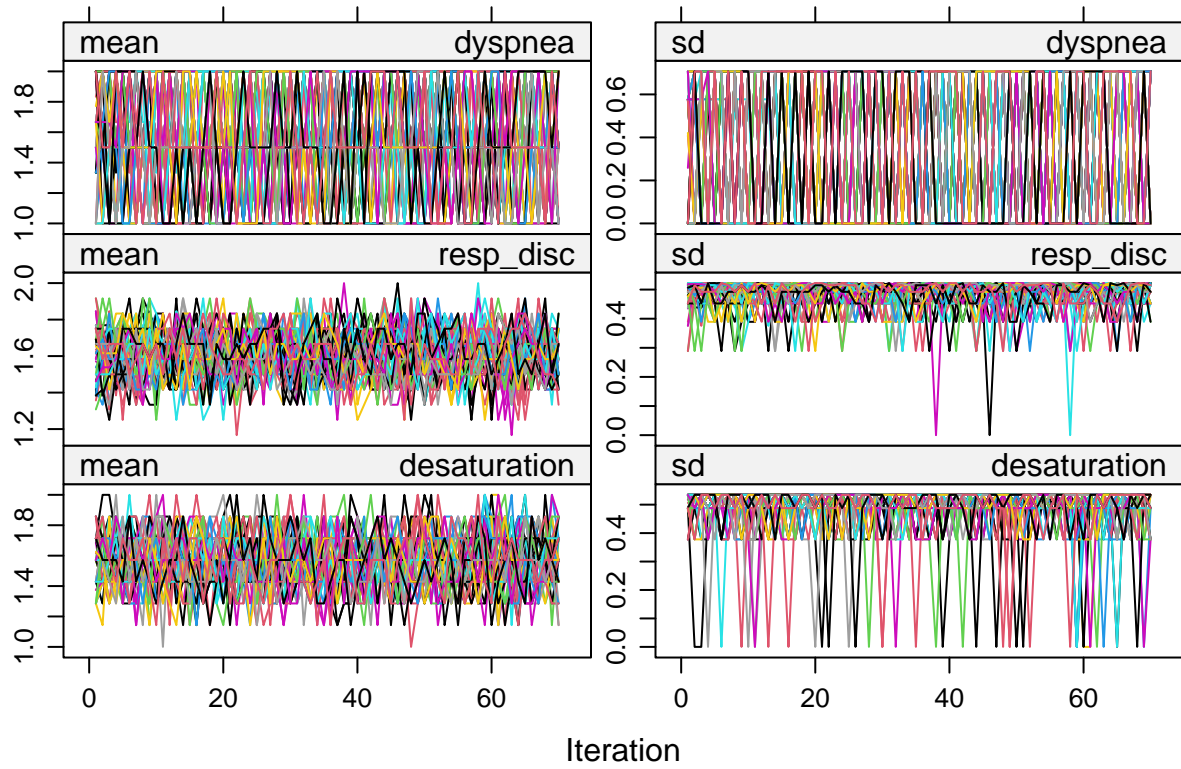
Iteration

```
dat_imp <- mids2milist(imputed_Data)
```

Each one of these 60 imputed datasets were analysed using the function `with()`, and including an expression for the statistical analysis approach. Procedures to pool Chi-square values are available in the miceadds package. To combine the 60 odds ratios, we use the miceafter package.

Baseline characteristics of the subjects according to vaccination status

White color

```
fit_w <- with(dat_imp, exp = chisq.test(vaccine_cov, white_color))
Stat_w <- numeric()
for (i in 1:imputed_Data$m) Stat_w[i] <- fit_w$statistics[[i]]$statistic
micombine.chisquare(Stat_w, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 180134.77)=2.974      p=0.08463
```

Cardiac

```
fit_c <- with(dat_imp, exp = chisq.test(vaccine_cov, cardiac))
Stat_c <- numeric()
for (i in 1:imputed_Data$m) Stat_c[i] <- fit_c$statistics[[i]]$statistic
micombine.chisquare(Stat_c, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 368059231.67)=8.195     p=0.0042
```

Diabetes

```
fit_d <- with(dat_imp, exp = chisq.test(vaccine_cov, diabetes))
Stat_d <- numeric()
for (i in 1:imputed_Data$m) Stat_d[i] <- fit_d$statistics[[i]]$statistic
micombine.chisquare(Stat_d, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 3287161934.41)=1.389     p=0.23857
```

Hematologic

```
fit_hem <- with(dat_imp, exp = chisq.test(vaccine_cov, hematologic))
Stat_hem<- numeric()
for (i in 1:imputed_Data$m) Stat_hem[i] <- fit_hem$statistics[[i]]$statistic
micombine.chisquare(Stat_hem, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 1.57426720882724e+34)=0.475     p=0.49088
```

Obesity

```
fit_o <- with(dat_imp, exp = chisq.test(vaccine_cov, obesity))
Stat_o <- numeric()
for (i in 1:imputed_Data$m) Stat_o[i] <- fit_o$statistics[[i]]$statistic
micombine.chisquare(Stat_o, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 1375360.94)=1.608     p=0.20479
```

Asthma

```
fit_a <- with(dat_imp, exp = chisq.test(vaccine_cov, asthma))
Stat_a <- numeric()
for (i in 1:imputed_Data$m) Stat_a[i] <- fit_a$statistics[[i]]$statistic
micombine.chisquare(Stat_a, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 7714332.78)=0.255     p=0.61342
```

Hepatic

```
fit_hep <- with(dat_imp, exp = chisq.test(vaccine_cov, hepatic))
Stat_hep <- numeric()
for (i in 1:imputed_Data$m) Stat_hep[i] <- fit_hep$statistics[[i]]$statistic
micombine.chisquare(Stat_hep, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 151466625527897)=0.031     p=0.8606
```

Neurologic

```
fit_n <- with(dat_imp, exp = chisq.test(vaccine_cov, neurologic))
Stat_n <- numeric()
for (i in 1:imputed_Data$m) Stat_n[i] <- fit_n$statistics[[i]]$statistic
micombine.chisquare(Stat_n, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 234097084096590)=0.187     p=0.66503
```

Pneumologic

```
fit_p <- with(dat_imp, exp = chisq.test(vaccine_cov, pneumologic))
Stat_p <- numeric()
for (i in 1:imputed_Data$m) Stat_p[i] <- fit_p$statistics[[i]]$statistic
micombine.chisquare(Stat_p, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 9.83917005517025e+32)=1.649     p=0.19903
```

Imunossupression

```
fit_i <- with(dat_imp, exp = chisq.test(vaccine_cov, imuno))
Stat_i <- numeric()
for (i in 1:imputed_Data$m) Stat_i[i] <- fit_i$statistics[[i]]$statistic
micombine.chisquare(Stat_i, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 376103329.56)=6.087     p=0.01362
```

Renal

```
fit_r <- with(dat_imp, exp = chisq.test(vaccine_cov, renal))
Stat_r <- numeric()
for (i in 1:imputed_Data$m) Stat_r[i] <- fit_r$statistics[[i]]$statistic
micombine.chisquare(Stat_r, 1, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(1, 6.29706883530895e+34)=0.17     p=0.68052
```

Education

```
fit_e <- with(dat_imp, exp = chisq.test(vaccine_cov, education2))
Stat_e <- numeric()
for (i in 1:imputed_Data$m) Stat_e[i] <- fit_e$statistics[[i]]$statistic
micombine.chisquare(Stat_e, 2, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(2, 1775.1)=1.299     p=0.27318
```

Residence

```
fit_res <- with(dat_imp, exp = chisq.test(vaccine_cov, residence))
Stat_res <- numeric()
for (i in 1:imputed_Data$m) Stat_res[i] <- fit_res$statistics[[i]]$statistic
micombine.chisquare(Stat_res, 2, display = TRUE, version=1)
```

```
## Combination of Chi Square Statistics for Multiply Imputed Data
## Using 60 Imputed Data Sets
## F(2, 3634852.58)=0.467     p=0.62712
```

Characteristics of COVID-19 symptoms by vaccination status

Fever

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ fever)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.6337778 0.4646731  0.8644235
## attr(,"class")
## [1] "mipool"
```

Cough

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ cough)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.8081693  0.567067   1.151782
## attr(,"class")
## [1] "mipool"
```

Sore throat

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ sore_throat)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.7471958 0.5022417   1.111619
## attr(,"class")
## [1] "mipool"
```

Dyspnea

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ dyspnea)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.5348665 0.3899044  0.7337241
## attr(,"class")
## [1] "mipool"
```

Respiratory discomfort

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ resp_disc)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.6265195 0.4573952  0.8581785
## attr(,"class")
## [1] "mipool"
```

Desaturation

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ desaturation)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.5324589 0.3871596  0.7322883
## attr(,"class")
## [1] "mipool"
```

Diarrhea

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ diarrhea)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.8778949 0.5121951   1.504699
## attr(,"class")
## [1] "mipool"
```

Vomit

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ vomit)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.8252639 0.4823693   1.411907
## attr(,"class")
## [1] "mipool"
```

Abdominal pain

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ abd_pain)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,]  1.196979 0.7141685   2.006191
## attr(,"class")
## [1] "mipool"
```

Fatigue

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ fatigue)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.9349494 0.6638525   1.316754
## attr(,"class")
## [1] "mipool"
```

Loss of smell

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ olfac_loss)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,]  1.170665 0.7841372   1.747724
## attr(,"class")
## [1] "mipool"
```

Loss of taste

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ loss_taste)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,]  1.156474 0.7625695   1.753851
## attr(,"class")
## [1] "mipool"
```

Any respiratory symptom

```
for (i in 1:imputed_Data$m){
df <- dat_imp[[i]] %>%
  select(dyspnea,fatigue,desaturation,resp_disc)

soma <- function(x){
  if (sum(is.na(x))==4)
    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
dat_imp[[i]]$qt_sintomas_resp_aux <- apply(df,1,soma)

dat_imp[[i]] <-  dat_imp[[i]] %>%
  mutate(resp_symp = case_when(qt_sintomas_resp_aux >=1 ~ "yes",
                               qt_sintomas_resp_aux ==0 ~ "no",
                               TRUE ~ NA_character_))
}

pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ resp_symp)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.5053652 0.3616196   0.7062504
## attr(,"class")
## [1] "mipool"
```

Any symptom

```
for (i in 1:imputed_Data$m){
df <- dat_imp[[i]] %>%
  select(dyspnea,fatigue,desaturation,resp_disc,
         fever,cough,sore_throat,diarrhea,vomit,abd_pain,olfac_loss,loss_taste)
soma <- function(x){
  if (sum(is.na(x))==12)
    return(NA_character_)
  else
    return(sum(!is.na(x) & x=="yes"))
}
dat_imp[[i]]$qt_sintomas_aux <- apply(df,1,soma)

dat_imp[[i]] <-  dat_imp[[i]] %>%
  mutate(symptom = case_when(qt_sintomas_aux >= 1 ~ "yes",
                             qt_sintomas_aux == 0 ~ "no",
                             TRUE ~ NA_character_))
}


pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ symptom)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.4431581 0.2521491   0.778861
## attr(,"class")
## [1] "mipool"
```

Characteristics of COVID-19 symptoms by vaccination status

ICU

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ icu)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.5155597 0.3632835   0.7316649
## attr(,"class")
## [1] "mipool"
```

Intubation

```
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ intubation)))
```

```
##      pooled OR 95 CI low 95 CI high
## [1,] 0.2148788 0.1089456   0.4238159
## attr(,"class")
## [1] "mipool"
```

Death

```r
pool_odds_ratio(with(dat_imp, expr=odds_ratio(vaccine_cov ~ death)))
```

```
##      pooled OR  95 CI low 95 CI high
## [1,] 0.1883021 0.08279405  0.4282638
## attr(,"class")
## [1] "mipool"
```