pSERG Transition from benzodiazepines to non-benzodiazepine anti-seizure medications

---

Load needed packages

This step loads packages with functions needed for analysis and that are not present in base R.

```
# install.packages("gmodels")
library(gmodels)

# install.packages("gdata")
library(gdata)

## gdata: read.xls support for 'XLS' (Excel 97-2004) files ENABLED.

##

## gdata: Unable to load perl libaries needed by read.xls()
## gdata: to support 'XLSX' (Excel 2007+) files.

##

## gdata: Run the function 'installXLSXsupport()'
## gdata: to automatically download and install the perl
## gdata: libaries needed to support Excel XLS and XLSX formats.

##
## Attaching package: 'gdata'

## The following object is masked from 'package:stats':
##
##     nobs

## The following object is masked from 'package:utils':
##
##     object.size

## The following object is masked from 'package:base':
##
##     startsWith

# install.packages("tableone")
library(tableone)

## Warning: package 'tableone' was built under R version 3.5.2

# install.packages("dplyr")
library(dplyr)
```

```
## Warning: package 'dplyr' was built under R version 3.5.2
```

```
##
## Attaching package: 'dplyr'
```

```
## The following objects are masked from 'package:gdata':
##
##     combine, first, last
```

```
## The following objects are masked from 'package:stats':
##
##     filter, lag
```

```
## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
# install.packages("survival")
library(survival)

# devtools::install_github('hadley/ggplot2')
library(ggplot2)

#install.packages("MASS")
library(MASS)
```

```
##
## Attaching package: 'MASS'
```

```
## The following object is masked from 'package:dplyr':
##
##     select
```

Load the database

Load the pSERG database into R.

```
# Load pSERG database
pSERG <- read.csv("pserg_2020.csv")
```

Clean the database

Keep only the population of interest and transform variables for analysis.

```
# Keep only patients who have refractory status epilepticus
dim(pSERG)
```

```
## [1]  760 1582
```

```
pSERG <- pSERG[which(pSERG$SE_GROUP == "refractory_case"), ]
dim(pSERG)
```

```
## [1]  502 1582

# Transform date of status epilepticus onset into date format
pSERG$DATESEIZURE <- as.Date(pSERG$DATESEIZURE, format = "%m/%d/%Y")

# Order by patient and then by date of status epilepticus
pSERG <- pSERG[order(pSERG$PATIENT_LABEL, pSERG$DATESEIZURE), ]

# Delete duplicate episodes from the same patient
pSERG <- pSERG[!duplicated(pSERG$PATIENT_LABEL), ]
dim(pSERG)

## [1]  443 1582

# Transform age into numeric
pSERG$G_T_STTS_PLPTCUS_EPISODE_YEARS <-
as.numeric(as.character(pSERG$G_T_STTS_PLPTCUS_EPISODE_YEARS))

## Warning: NAs introduced by coercion

pSERG$G_T_STTS_PLPTCS_EPISODE_MONTHS <-
as.numeric(as.character(pSERG$G_T_STTS_PLPTCS_EPISODE_MONTHS))

## Warning: NAs introduced by coercion

# Transform age into a single variable with age in years
pSERG$ageyears <- pSERG$G_T_STTS_PLPTCUS_EPISODE_YEARS +
(pSERG$G_T_STTS_PLPTCS_EPISODE_MONTHS / 12)

# Delete patients with unknown age
pSERG <- pSERG[complete.cases(pSERG[ , "ageyears"]), ]
dim(pSERG)

## [1]  435 1583

# Delete patients with unknown sex
pSERG <- pSERG[which(pSERG$SEX == "male" | pSERG$SEX == "female"), ]
pSERG$SEX <- droplevels(pSERG$SEX)
dim(pSERG)

## [1]  434 1583

# Delete patients with unknown hospital onset
pSERG <- pSERG[which(pSERG$HOSPITALONSET == "yes" | pSERG$HOSPITALONSET ==
"no"), ]
pSERG$HOSPITALONSET <- droplevels(pSERG$HOSPITALONSET)
dim(pSERG)

## [1]  416 1583

# Create variable history of developmental delay
pSERG$delay[grepl("delay", pSERG$PAST)] <- 1
```

```r
pSERG$delay[!grepl("delay", pSERG$PAST)] <- 0

# Create variable history of cerebral palsy
pSERG$palsy[grepl("palsy", pSERG$PAST)] <- 1
pSERG$palsy[!grepl("palsy", pSERG$PAST)] <- 0

# Create variable febrile
pSERG$febrile[grepl("febrile", pSERG$PAST)] <- 1
pSERG$febrile[!grepl("febrile", pSERG$PAST)] <- 0

# Create variable history of epilepsy
pSERG$priorepilepsy[grepl("epi", pSERG$PAST)] <- 1
pSERG$priorepilepsy[!grepl("epi", pSERG$PAST)] <- 0

# Create variable history of status epilepticus
pSERG$priorSE[grepl("status", pSERG$PAST)] <- 1
pSERG$priorSE[!grepl("status", pSERG$PAST)] <- 0

# Create variable no prior neurological history
pSERG$none[grepl("none", pSERG$PAST)] <- 1
pSERG$none[!grepl("none", pSERG$PAST)] <- 0

# Transform convulsive duration into numeric
pSERG$CONVULSIVEDURATION <-
as.numeric(as.character(pSERG$CONVULSIVEDURATION))

## Warning: NAs introduced by coercion

# Create convulsive duration in minutes
pSERG$convulsivemin <- pSERG$CONVULSIVEDURATION
pSERG$convulsivehr <- pSERG$CONVULSIVEDURATION * 60
pSERG$convulsivedurationmin <- ifelse(pSERG$CONVULSIVEDURATIONUNITS == "min",
pSERG$convulsivemin, pSERG$convulsivehr)

# Delete patients with unknown convulsive duration
pSERG <- pSERG[complete.cases(pSERG[ , "convulsivedurationmin"]), ]
dim(pSERG)

## [1]  395 1592

# Delete patients with no data on non-benzodiazepine antiepileptic drugs and
continuous infusions
pSERG <- pSERG[!(pSERG$AEDMEDICATION.0 == "other" &
pSERG$AEDMEDICATIONOTHER.0 == "none" & pSERG$CONTMED.0 == "other" &
pSERG$CONTMEDALT.0 == "none"), ]
dim(pSERG)

## [1]  395 1592

# Transform time to first benzodiazepine to numeric
pSERG$BZDTIME.0 <- as.numeric(as.character(pSERG$BZDTIME.0))
```

```
## Warning: NAs introduced by coercion

# Delete patients with unknown time to first benzodiazepine
pSERG <- pSERG[complete.cases(pSERG[ , "BZDTIME.0"]), ]
dim(pSERG)

## [1]  366 1592

# Transform time to second benzodiazepine to numeric
pSERG$BZDTIME.1 <- as.numeric(as.character(pSERG$BZDTIME.1))

## Warning: NAs introduced by coercion

# Transform time to third benzodiazepine to numeric
pSERG$BZDTIME.2 <- as.numeric(as.character(pSERG$BZDTIME.2))

## Warning: NAs introduced by coercion

# Transform time to fourth benzodiazepine to numeric
pSERG$BZDTIME.3 <- as.numeric(as.character(pSERG$BZDTIME.3))

## Warning: NAs introduced by coercion

# Transform time to fifth benzodiazepine to numeric
pSERG$BZDTIME.4 <- as.numeric(as.character(pSERG$BZDTIME.4))

# Transform time to sixth benzodiazepine to numeric
pSERG$BZDTIME.5 <- as.numeric(as.character(pSERG$BZDTIME.5))

# Transform time to seventh benzodiazepine to numeric
pSERG$BZDTIME.6 <- as.numeric(as.character(pSERG$BZDTIME.6))

# Transform time to eighth benzodiazepine to numeric
pSERG$BZDTIME.7 <- as.numeric(as.character(pSERG$BZDTIME.7))

# Transform time to ninth benzodiazepine to numeric
pSERG$BZDTIME.8 <- as.numeric(as.character(pSERG$BZDTIME.8))

# Transform time to tenth benzodiazepine to numeric
pSERG$BZDTIME.9 <- as.numeric(as.character(pSERG$BZDTIME.9))

# Transform time to eleventh benzodiazepine to numeric
pSERG$BZDTIME.10 <- as.numeric(as.character(pSERG$BZDTIME.10))

# Transform time to twelfth benzodiazepine to numeric
pSERG$BZDTIME.11 <- as.numeric(as.character(pSERG$BZDTIME.11))

# Transform time to thirteenth benzodiazepine to numeric
pSERG$BZDTIME.12 <- as.numeric(as.character(pSERG$BZDTIME.12))

# Transform time to fourteenth benzodiazepine to numeric
```

```r
pSERG$BZDTIME.13 <- as.numeric(as.character(pSERG$BZDTIME.13))

# Transform time to fifteenth benzodiazepine to numeric
pSERG$BZDTIME.14 <- as.numeric(as.character(pSERG$BZDTIME.14))

# Transform time to sixteenth benzodiazepine to numeric
pSERG$BZDTIME.15 <- as.numeric(as.character(pSERG$BZDTIME.15))

# Transform time to seventeenth benzodiazepine to numeric
pSERG$BZDTIME.16 <- as.numeric(as.character(pSERG$BZDTIME.16))

# Transform time to first non-benzodiazepine ASM to numeric
pSERG$AEDTIME.0 <- as.numeric(as.character(pSERG$AEDTIME.0))

## Warning: NAs introduced by coercion

# Delete patients with unknown time to first non-benzodiazepine ASM
pSERG <- pSERG[complete.cases(pSERG[ , "AEDTIME.0"]), ]

# Transform time to first continuous infusion to numeric
#pSERG$CONTTIME.0
pSERG$CONTTIME.0 <- as.numeric(as.character(pSERG$CONTTIME.0))

## Warning: NAs introduced by coercion

summary(pSERG$CONTTIME.0)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.    NA's
##     0.0    98.5   170.0   526.8   532.5  7200.0     189

# Identify patients who received a continuous infusion
pSERG$CI <- ifelse(pSERG$CONTTIME.0 > 0, 1, 0)

# Eliminate patients who received first continuous infusion before or at the
same time than first benzodiazepine
pSERG[which(pSERG$CI == 1 & (pSERG$BZDTIME.0 >= pSERG$CONTTIME.0)),
c("BZDTIME.0", "BZDMED.0", "BZDMEDOTHER.0", "AEDTIME.0", "AEDMEDICATION.0",
"AEDMEDICATIONOTHER.0", "CONTTIME.0", "CONTMED.0", "CONTMEDALT.0")]

##     BZDTIME.0  BZDMED.0 BZDMEDOTHER.0 AEDTIME.0 AEDMEDICATION.0
## 449      1264     other    Clonazepam      1264   levetiracetam
## 512        60 lorazepam                    795   levetiracetam
## 556         5 midazolam                     10   levetiracetam
## 645        50 midazolam                     43   levetiracetam
##     AEDMEDICATIONOTHER.0 CONTTIME.0 CONTMED.0 CONTMEDALT.0
## 449                           330 midazolam
## 512                            20     other       versed
## 556                             5 midazolam
## 645                            49  propofol
```

```r
pSERG$CIbeforeBZD <- 0
pSERG$CIbeforeBZD[pSERG$CI == 1 & (pSERG$BZDTIME.0 >= pSERG$CONTTIME.0)] <- 1
pSERG <- pSERG[!(pSERG$CIbeforeBZD == 1), ]

# Eliminate patients who received first continuous infusion before or at the
same time than first non-benzodiazepine ASM
pSERG[which(pSERG$CI == 1 & (pSERG$AEDTIME.0 >= pSERG$CONTTIME.0)),
c("BZDTIME.0", "BZDMED.0", "BZDMEDOTHER.0", "AEDTIME.0", "AEDMEDICATION.0",
"AEDMEDICATIONOTHER.0", "CONTTIME.0", "CONTMED.0", "CONTMEDALT.0")]
```

```
##     BZDTIME.0  BZDMED.0 BZDMEDOTHER.0 AEDTIME.0 AEDMEDICATION.0
## 46          4 lorazepam                    1419    fosphenytoin
## 178        10 midazolam                     169    fosphenytoin
## 186        55 lorazepam                     220   phenobarbital
## 194        31 lorazepam                     170   phenobarbital
## 195       145  diazepam                    1440    fosphenytoin
## 228        55 lorazepam                     150   levetiracetam
## 279        27 lorazepam                      88   levetiracetam
## 362        30 midazolam                      45    fosphenytoin
## 422        70 lorazepam                     190   levetiracetam
## 481        90 lorazepam                     270        valproic
## 489        40 lorazepam                     480   levetiracetam
## 492         1 lorazepam                      20   levetiracetam
## 519        20 midazolam                     291      lacosamide
## 526      1132 midazolam                    1276    fosphenytoin
## 527        20  diazepam                     637   levetiracetam
## 573        15 midazolam                     118           other
## 633         3  diazepam                      38   levetiracetam
## 676        30 lorazepam                      75   levetiracetam
##     AEDMEDICATIONOTHER.0 CONTTIME.0 CONTMED.0 CONTMEDALT.0
## 46                           1175 midazolam
## 178                           165 midazolam
## 186                           168 midazolam
## 194                           100     other    Lorazepam
## 195                           992 midazolam
## 228                           143     other       Profol
## 279                            65  propofol
## 362                            45 midazolam
## 422                           180 midazolam
## 481                           210 midazolam
## 489                            70 midazolam
## 492                             5 midazolam
## 519                           215 midazolam
## 526                          1242 midazolam
## 527                            59 midazolam
## 573            fentanyl        88 midazolam
## 633                            29  propofol
## 676                            61  propofol
```

```r
pSERG$CIbeforeAED <- 0
pSERG$CIbeforeAED[pSERG$CI == 1 & (pSERG$AEDTIME.0 >= pSERG$CONTTIME.0)] <- 1
pSERG <- pSERG[!(pSERG$CIbeforeAED == 1), ]

# Eliminate patients who received first non-benzodiazepine ASM before or at
the same time than first benzodiazepine
pSERG[which(pSERG$BZDTIME.0 >= pSERG$AEDTIME.0), c("BZDTIME.0", "BZDMED.0",
"BZDMEDOTHER.0", "AEDTIME.0", "AEDMEDICATION.0", "AEDMEDICATIONOTHER.0",
"CONTTIME.0", "CONTMED.0", "CONTMEDALT.0")]
```

```
##     BZDTIME.0  BZDMED.0 BZDMEDOTHER.0 AEDTIME.0 AEDMEDICATION.0
## 12         72 midazolam                     70   levetiracetam
## 23         20 midazolam                      5   levetiracetam
## 44         38 lorazepam                     22    fosphenytoin
## 49        205 lorazepam                    150      lacosamide
## 59         23 lorazepam                     23   levetiracetam
## 100        10 lorazepam                      5   levetiracetam
## 142        91     other      Clobazam       91    fosphenytoin
## 177         5 lorazepam                      5    fosphenytoin
## 179       102 lorazepam                     28   levetiracetam
## 275        94 lorazepam                     20   levetiracetam
## 343        60     other      Clobazam       60   levetiracetam
## 350        55 midazolam                     10   levetiracetam
## 446        15 midazolam                      0    fosphenytoin
## 502      1853 lorazepam                   1320   levetiracetam
## 547        10 lorazepam                     10   levetiracetam
## 576       173 lorazepam                     10   levetiracetam
## 598       625 midazolam                    116    fosphenytoin
## 613       315 lorazepam                     15   phenobarbital
## 614      1440 lorazepam                    540   levetiracetam
## 634       460 lorazepam                    120    fosphenytoin
## 670       517 midazolam                    487    fosphenytoin
## 684       538 lorazepam                    538    fosphenytoin
## 723       180 lorazepam                     74   levetiracetam
##     AEDMEDICATIONOTHER.0 CONTTIME.0     CONTMED.0 CONTMEDALT.0
## 12                            645 pentobarbital
## 23                             NA         other         none
## 44                             NA
## 49                             NA
## 59                             NA
## 100                            NA
## 142                            NA
## 177                            NA
## 179                          1102 pentobarbital
## 275                           180     midazolam
## 343                            NA
## 350                            NA
## 446                            NA
## 502                            NA
## 547                            NA
```

```
## 576                                NA
## 598                                NA
## 613                               420     midazolam
## 614                                NA
## 634                               760     midazolam
## 670                                NA
## 684                               626     midazolam
## 723                               300     midazolam
```

```
pSERG$AEDbeforeBZD <- 0
pSERG$AEDbeforeBZD[pSERG$BZDTIME.0 >= pSERG$AEDTIME.0] <- 1
pSERG <- pSERG[!(pSERG$AEDbeforeBZD == 1), ]
```

Variable first BZD dosing

```
table(pSERG$BZDMED.0)
```

```
##
##            diazepam lorazepam midazolam     other
##         0        89       166        43         5
```

```
CrossTable(pSERG[which(pSERG$BZDMED.0=="other"), ]$BZDMEDOTHER.0)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  5
##
##
##              |  clonazepam |  Clonazepam | clonazepam  |
##              |-------------|-------------|-------------|
##              |           1 |           3 |           1 |
##              |       0.200 |       0.600 |       0.200 |
##              |-------------|-------------|-------------|
##
##
##
##
```

```
# All others are clonazepam

# Delete patients with unknown route of administration
pSERG <- pSERG[!(pSERG$BZDROUTE.0== "other" & pSERG$BZDROUTEOTHER.0 == "Not
Documented"), ]
pSERG <- pSERG[!(pSERG$BZDROUTE.0== "other" & pSERG$BZDROUTEOTHER.0 ==
```

```
"Unknown"), ]
pSERG <- pSERG[!(pSERG$BZDROUTE.0== "other" & pSERG$BZDROUTEOTHER.0 ==
"N/A"), ]

#Transform BZD doses into numeric variable
class(pSERG$BZDDOSE.0)

## [1] "factor"

pSERG$BZDDOSE.0 <- as.numeric(as.character(pSERG$BZDDOSE.0))

## Warning: NAs introduced by coercion

#Delete patients with first BZD dose incomplete
pSERG <- pSERG[complete.cases(pSERG[ ,"BZDDOSE.0"]), ]



#Transform BZD time into numeric variable
pSERG$BZDTIME.0 <- as.numeric(as.character(pSERG$BZDTIME.0))

#Transform BZD time into numeric variable
pSERG$BZDDOSE.0 <- as.numeric(as.character(pSERG$BZDDOSE.0))

#Transform BZD time into numeric variable
class(pSERG$WEIGHT)

## [1] "factor"

pSERG$WEIGHT <- as.character(as.factor(pSERG$WEIGHT))
pSERG$WEIGHT <- as.numeric(as.character(pSERG$WEIGHT))

#Create variable BZD dose/Kg
table(pSERG$WEIGHTUNITS)

##
##      kg lbs
##   0 292   1

# pending to adapt 1 case in ibs
pSERG$BZDDOSE.0KG <- pSERG$BZDDOSE.0 / pSERG$WEIGHT



#Create variable for delayed treatment
pSERG$delayedtreatmentinitiation<-ifelse(pSERG$BZDTIME.0>10,1,0)



# Dimensions database after cleaning
dim(pSERG)

## [1]  293 1598
```

BZD dosing

Initial BZD

Identify the initial type of BZD

```
#Create variables for the type of BZD received
#Identify number of patients who received lorazepam as first single BZD
pSERG$FIRSTLZP<-ifelse(pSERG$BZDMED.0 == "lorazepam",1,0)

#Identify number of patients who received diazepam as first single BZD
pSERG$FIRSTDZP<-ifelse(pSERG$BZDMED.0 == "diazepam",1,0)

#Identify number of patients who received midazolam as first single BZD
pSERG$FIRSTMDZ<-ifelse(pSERG$BZDMED.0 == "midazolam",1,0)

#Identify number of patients who received clonazepam as first single BZD
pSERG$FIRSTCLZ<-ifelse(pSERG$BZDMED.0 == "other",1,0)
```

Identify the dose administered as initial BZD dose

LORAZEPAM

```
##Initial single dose of lorazepam
nobs(pSERG[which(pSERG$FIRSTLZP==1 & pSERG$WEIGHT < 40), ]$BZDDOSE.0KG)

## [1] 145

summary(pSERG[which(pSERG$FIRSTLZP==1 & pSERG$WEIGHT < 40), ]$BZDDOSE.0KG)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.02174 0.05666 0.09381 0.08840 0.10204 0.28169

nobs(pSERG[which(pSERG$FIRSTLZP==1 & pSERG$WEIGHT >= 40), ]$BZDDOSE.0)

## [1] 18

summary(pSERG[which(pSERG$FIRSTLZP==1 & pSERG$WEIGHT >= 40), ]$BZDDOSE.0)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   0.500   2.000   2.000   2.194   2.000   6.000
```

DIAZEPAM

```
#Diazepam PR
#Initial dose of diazepam PR in patients <2 years
nobs(pSERG[which( pSERG$FIRSTDZP==1 & pSERG$ageyears<2 &
pSERG$BZDROUTE.0=="per_rectum"), ]$BZDDOSE.0)

## [1] 22
```

```r
summary(pSERG[which( pSERG$FIRSTDZP==1 & pSERG$ageyears<2 &
pSERG$BZDROUTE.0=="per_rectum"), ]$BZDDOSE.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   2.500   2.500   3.250   4.273   5.000  10.000
```

```r
#Initial dose of diazepam PR in patients 2-5 years
nobs(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=2 & pSERG$ageyears<6 &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT <40), ]$BZDDOSE.0KG)
```

```
## [1] 29
```

```r
summary(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=2 & pSERG$ageyears<6
&pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT <40), ]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.1071  0.3731  0.4808  0.4625  0.5587  0.9524
```

```r
#Initial dose of diazepam PR in patients 6-11 years
nobs(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=6 & pSERG$ageyears<12 &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT <66.6), ]$BZDDOSE.0KG)
```

```
## [1] 10
```

```r
summary(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=6 &
pSERG$ageyears<12 & pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT <66.6),
]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.2000  0.2518  0.3278  0.3443  0.3854  0.5618
```

```r
#Initial dose of diazepam PR in patients >=12 years
nobs(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >= 12  &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT < 100), ]$BZDDOSE.0KG)
```

```
## [1] 12
```

```r
summary(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >= 12  &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT < 100), ]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.2045  0.2669  0.3251  0.3449  0.3581  0.7527
```

```r
#Diazepam administered by other routes
#Create variable with other routes
pSERG$DZPOTHERROUTES<- ifelse(pSERG$BZDMED.0 =="diazepam" &
pSERG$BZDROUTE.0!="per_rectum",1,0)

pSERG[which(pSERG$BZDMED.0
=="diazepam"),c("BZDMED.0","BZDROUTE.0","BZDROUTEOTHER.0","DZPOTHERROUTES")]
```

```
##     BZDMED.0    BZDROUTE.0 BZDROUTEOTHER.0 DZPOTHERROUTES
## 9   diazepam    per_rectum                              0
```

```
## 18  diazepam    per_rectum                          0
## 21  diazepam    per_rectum                          0
## 22  diazepam    per_rectum                          0
## 31  diazepam    per_rectum                          0
## 36  diazepam           Ivb                          1
## 51  diazepam    per_rectum                          0
## 53  diazepam    per_rectum                          0
## 62  diazepam           Ivb                          1
## 67  diazepam    per_rectum                          0
## 69  diazepam    per_rectum                          0
## 71  diazepam    per_rectum                          0
## 72  diazepam           Ivb                          1
## 73  diazepam           Ivb                          1
## 74  diazepam    per_rectum                          0
## 78  diazepam    per_rectum                          0
## 107 diazepam    per_rectum                          0
## 112 diazepam    per_rectum                          0
## 119 diazepam    per_rectum                          0
## 122 diazepam    per_rectum                          0
## 147 diazepam    per_rectum                          0
## 148 diazepam    per_rectum                          0
## 149 diazepam    per_rectum                          0
## 153 diazepam    per_rectum                          0
## 158 diazepam    per_rectum                          0
## 162 diazepam         other           Gtube          1
## 176 diazepam    per_rectum                          0
## 180 diazepam    per_rectum                          0
## 188 diazepam            po                          1
## 191 diazepam           Ivb                          1
## 193 diazepam    per_rectum                          0
## 200 diazepam    per_rectum                          0
## 201 diazepam           Ivb                          1
## 206 diazepam    per_rectum                          0
## 207 diazepam    per_rectum                          0
## 209 diazepam    per_rectum                          0
## 211 diazepam    per_rectum                          0
## 215 diazepam    per_rectum                          0
## 217 diazepam    per_rectum                          0
## 234 diazepam    per_rectum                          0
## 239 diazepam    per_rectum                          0
## 245 diazepam    per_rectum                          0
## 257 diazepam    per_rectum                          0
## 267 diazepam    per_rectum                          0
## 280 diazepam    per_rectum                          0
## 286 diazepam    per_rectum                          0
## 289 diazepam    per_rectum                          0
## 294 diazepam           Ivb                          1
## 319 diazepam    per_rectum                          0
## 322 diazepam    per_rectum                          0
## 328 diazepam            po                          1
```

```
## 331 diazepam    per_rectum                          0
## 349 diazepam    per_rectum                          0
## 355 diazepam    per_rectum                          0
## 367 diazepam    per_rectum                          0
## 369 diazepam    per_rectum                          0
## 412 diazepam    per_rectum                          0
## 413 diazepam    per_rectum                          0
## 415 diazepam    per_rectum                          0
## 419 diazepam    per_rectum            none          0
## 420 diazepam           Ivb                          1
## 426 diazepam    per_rectum                          0
## 438 diazepam    per_rectum                          0
## 442 diazepam    per_rectum                          0
## 462 diazepam    per_rectum                          0
## 469 diazepam    per_rectum                          0
## 475 diazepam    per_rectum                          0
## 479 diazepam    per_rectum                          0
## 483 diazepam           Ivb                          1
## 497 diazepam    per_rectum                          0
## 504 diazepam    per_rectum                          0
## 511 diazepam    per_rectum                          0
## 522 diazepam    per_rectum                          0
## 553 diazepam        buccal                          1
## 554 diazepam    per_rectum                          0
## 558 diazepam    per_rectum                          0
## 562 diazepam    per_rectum                          0
## 571 diazepam    per_rectum                          0
## 629 diazepam    per_rectum                          0
## 647 diazepam    per_rectum                          0
## 672 diazepam    per_rectum                          0
## 678 diazepam intramuscular                          1
## 685 diazepam    per_rectum                          0
## 686 diazepam    per_rectum                          0
## 697 diazepam    per_rectum                          0
## 724 diazepam    per_rectum                          0
## 760 diazepam    per_rectum                          0
```

```
CrossTable(pSERG[which(pSERG$FIRSTDZP==1), ]$DZPOTHERROUTES)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  87
##
```

```
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        73 |        14 |
##           |     0.839 |     0.161 |
##           |-----------|-----------|
##
##
##
##
```

```
#Initial dose of diazepam IV/IO/PO in patients with weight< 66.66 Kg
nobs(pSERG[which(pSERG$WEIGHT < 66.66 & pSERG$FIRSTDZP==1 &
pSERG$DZPOTHERROUTES==1),]$BZDDOSE.0KG)
```

```
## [1] 13
```

```
summary(pSERG[which(pSERG$WEIGHT < 66.66 & pSERG$FIRSTDZP==1 &
pSERG$DZPOTHERROUTES==1), ]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.03546 0.14164 0.22472 0.23854 0.30000 0.59524
```

```
#Initial dose of diazepam IV/IO/PO in patients with weight>= 66.66 Kg
nobs(pSERG[which(pSERG$WEIGHT >= 66.66 & pSERG$FIRSTDZP==1 &
pSERG$DZPOTHERROUTES==1),]$BZDDOSE.0)
```

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

```
summary(pSERG[which(pSERG$WEIGHT >= 66.66 & pSERG$FIRSTDZP==1 &
pSERG$DZPOTHERROUTES==1), ]$BZDDOSE.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##       5       5       5       5       5       5
```

MIDAZOLAM

```
#Midazolam IV
#Create a variable for MDZ administered IV
pSERG$MZDIV<- ifelse(pSERG$BZDMED.0=="midazolam" &
(pSERG$BZDROUTE.0=="Ivf"|pSERG$BZDROUTE.0=="Ivb"),1,0)

#Initial dose of midazolam IV
nobs(pSERG[which(pSERG$FIRSTMDZ==1 & pSERG$MZDIV==1), ]$BZDDOSE.0KG)
```

```
## [1] 10
```

```
summary(pSERG[which(pSERG$FIRSTMDZ==1 & pSERG$MZDIV==1), ]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.02051 0.05278 0.08425 0.11596 0.09335 0.43269
```

```r
#Midazolam IN
#Create a variable for MDZ administered IN
pSERG$MZDIN<- ifelse(pSERG$BZDROUTE.0=="intranasal",1,0)

#Initial dose of midazolam IN
nobs(pSERG[which(pSERG$FIRSTMDZ==1 & pSERG$MZDIN==1), ]$BZDDOSE.0KG)
```

```
## [1] 22
```

```r
summary(pSERG[which(pSERG$FIRSTMDZ==1 & pSERG$MZDIN==1), ]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.0229  0.1090  0.1696  0.1655  0.2000  0.4167
```

```r
# Midazolam Buccal
nobs(pSERG[which(pSERG$FIRSTMDZ==1 & pSERG$BZDROUTE.0=="buccal"),
]$BZDDOSE.0KG)
```

```
## [1] 0
```

```r
summary(pSERG[which(pSERG$FIRSTMDZ==1 & pSERG$BZDROUTE.0==" buccal"),
]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##
```

```r
#Midazolam IM
#Initial dose of midazolam in patients with weight  <13 kg
nobs(pSERG[which(pSERG$WEIGHT < 13 & pSERG$FIRSTMDZ==1 &
pSERG$BZDROUTE.0=="intramuscular"), ]$BZDDOSE.0KG)
```

```
## [1] 4
```

```r
summary(pSERG[which( pSERG$WEIGHT < 13 & pSERG$FIRSTMDZ==1 &
pSERG$BZDROUTE.0=="intramuscular"), ]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.08696 0.14402 0.18356 0.16511 0.20465 0.20635
```

```r
## First single dose of midazolam in patients with weight 13-40kg
nobs(pSERG[which(pSERG$WEIGHT >=13 & pSERG$WEIGHT <= 40 & pSERG$FIRSTMDZ==1 &
pSERG$BZDROUTE.0=="intramuscular"), ]$BZDDOSE.0)
```

```
## [1] 2
```

```r
summary(pSERG[which(pSERG$WEIGHT >=13 & pSERG$WEIGHT <= 40 &
pSERG$FIRSTMDZ==1 & pSERG$BZDROUTE.0=="intramuscular"), ]$BZDDOSE.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.5000  0.8125  1.1250  1.1250  1.4375  1.7500
```

CLONAZEPAM

```
# Create variable for route of administration Clonazepam
table(pSERG[which(pSERG$FIRSTCLZ==1), ]$BZDROUTE.0)

##
##                      buccal intramuscular    intranasal            io
##           0               2             0             0             0
##         Ivb             Ivf         other    per_rectum            po
##           0               0             2             0             1

CrossTable(pSERG[which(pSERG$FIRSTCLZ==1), ]$BZDROUTEOTHER.0)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  5
##
##
##              |              |       GTube | per G tube  |
##              |--------------|-------------|-------------|
##              |            3 |           1 |           1 |
##              |        0.600 |       0.200 |       0.200 |
##              |--------------|-------------|-------------|
##
##
##
##

#Initial dose of clonazepam in patients <=30kg
nobs(pSERG[which(pSERG$FIRSTCLZ==1 & pSERG$WEIGHT<= 30), ]$BZDDOSE.0KG)

## [1] 3

summary(pSERG[which(pSERG$FIRSTCLZ==1 & pSERG$WEIGHT<= 30), ]$BZDDOSE.0KG)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
## 0.01667 0.01833 0.02000 0.02159 0.02404 0.02809

#Initial dose of clonazepam in patients > 30kg
nobs(pSERG[which(pSERG$FIRSTCLZ==1 & pSERG$WEIGHT> 30), ]$BZDDOSE.0)

## [1] 2

summary(pSERG[which(pSERG$FIRSTCLZ==1 & pSERG$WEIGHT> 30), ]$BZDDOSE.0)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##  0.1250  0.2188  0.3125  0.3125  0.4062  0.5000
```

Identify low initial BZD dose

LORAZEPAM

```
#Lorazepam
#Number of patients with inadequate First single dose of lorazepam
pSERG$LZPinadequateSINGLEDOSELESS40 <- ifelse(pSERG$FIRSTLZP==1 &
pSERG$WEIGHT < 40 & pSERG$BZDDOSE.0KG< 0.1, 1, 0)
pSERG$LZPinadequateSINGLEDOSEMORE40 <- ifelse(pSERG$FIRSTLZP==1 &
pSERG$WEIGHT >=40 & pSERG$BZDDOSE.0 < 4,1,0)

# Total number of patients that received first single dose of lorazepam lower
than recommended
pSERG$LZPinadequateSINGLEDOSE <-
ifelse(pSERG$LZPinadequateSINGLEDOSELESS40==1|pSERG$LZPinadequateSINGLEDOSEMO
RE40==1,1,0)
CrossTable(pSERG[which(pSERG$FIRSTLZP==1), ]$LZPinadequateSINGLEDOSE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  163
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |        52 |       111 |
##            |     0.319 |     0.681 |
##            |-----------|-----------|
##
##
##
##
```

DIAZEPAM

```
#Diazepam PR

#Number of patients (< 2 years) with inadequate first single dose of diazepam
PR (minimum recommended absolute dose is 2.5mg/dose)
pSERG$DZPinadequateSINGLEDOSE_LESS2PR<-ifelse(pSERG$FIRSTDZP==1 &
pSERG$ageyears<2 & pSERG$BZDROUTE.0=="per_rectum" & pSERG$BZDDOSE.0 <
2.5,1,0)
nobs(pSERG$DZPinadequateSINGLEDOSE_LESS2PR==1)
```

```
## [1] 293

#Number of patients (2-5 years) with inadequate initial dose of diazepam PR
(minimum recommended recommended dose 0.5 mg/kg)
pSERG$DZPinadequateSINGLEDOSE_25<-ifelse(pSERG$FIRSTDZP==1 & pSERG$ageyears
>=2 & pSERG$ageyears<6 & pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT <40 &
pSERG$BZDDOSE.0KG < 0.5,1,0)
CrossTable(pSERG[which(pSERG$FIRSTDZP==1), ]$DZPinadequateSINGLEDOSE_25)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  87
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        71 |        16 |
##           |     0.816 |     0.184 |
##           |-----------|-----------|
##
##
##
##

#Accounting for maximum dose of 20mg in patients with 2-5 years
nobs(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=2 & pSERG$ageyears<6
&pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT >=40), ]$BZDDOSE.0)

## [1] 0

summary(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=2 & pSERG$ageyears<6
&pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT >=40), ]$BZDDOSE.0)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##

## Number of patients ( 6-11 years) with Inadequate initial dose of diazepam
PR (minimum recommended absolute dose is 0.30 mg/kg)
pSERG$DZPinadequateSINGLEDOSE_611pr<-ifelse(pSERG$FIRSTDZP==1 &
pSERG$ageyears >=6 & pSERG$ageyears<12 & pSERG$BZDROUTE.0=="per_rectum" &
pSERG$WEIGHT <66.6 & pSERG$BZDDOSE.0KG <0.3,1,0)
CrossTable(pSERG[which(pSERG$FIRSTDZP==1), ]$DZPinadequateSINGLEDOSE_611pr)

##
##
```

```
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  87
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        82 |         5 |
##           |     0.943 |     0.057 |
##           |-----------|-----------|
##
##
##
##
```

```
#Accounting for maximum dose of 20mg
nobs(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=6 & pSERG$ageyears<12 &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT >= 66.6), ]$BZDDOSE.0KG)
```

```
## [1] 0
```

```
summary(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >=6 &
pSERG$ageyears<12 & pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT >= 66.6),
]$BZDDOSE.0KG)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##
```

```
#Number of patients  (>= 12 years) with inadequate initial dose of diazepam
PR (minimum recommended absolute dose is 0.20 mg/kg)
pSERG$DZPinadequateSINGLEDOSE_12pr<-ifelse(pSERG$FIRSTDZP==1 & pSERG$ageyears
>= 12  & pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT < 100 &
pSERG$BZDDOSE.0KG <0.2,1,0)
nobs(pSERG$DZPinadequateSINGLEDOSE_12pr==1)
```

```
## [1] 293
```

```
#Accounting for maximum dose of 20mg
nobs(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >= 12  &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT >= 100), ]$BZDDOSE.0)
```

```
## [1] 0
```

```
summary(pSERG[which(pSERG$FIRSTDZP==1 & pSERG$ageyears >= 12  &
pSERG$BZDROUTE.0=="per_rectum" & pSERG$WEIGHT >= 100), ]$BZDDOSE.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##

#Number of patients (weight <66.66 Kg) with inadequate first single dose of
diazepam IV/IO/PO
pSERG$DZPinadequateSINGLEDOSE_otherroutes_less66<-ifelse(pSERG$WEIGHT < 66.66
& pSERG$FIRSTDZP==1 & pSERG$DZPOTHERROUTES==1 & pSERG$BZDDOSE.0KG <0.15,1,0)
CrossTable(pSERG$DZPinadequateSINGLEDOSE_otherroutes_less66)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |       289 |         4 |
##            |     0.986 |     0.014 |
##            |-----------|-----------|
##
##
##
##

CrossTable(pSERG[which(pSERG$FIRSTDZP==1),
]$DZPinadequateSINGLEDOSE_otherroutes_less66)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  87
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |        83 |         4 |
##            |     0.954 |     0.046 |
##            |-----------|-----------|
```

```
##
##
##
##

pSERG$DZPinadequateSINGLEDOSE_otherroutes_more66<-ifelse(pSERG$WEIGHT >=
66.66 & pSERG$FIRSTDZP==1 & pSERG$DZPOTHERROUTES==1 & pSERG$BZDDOSE.0 <
10,1,0)
CrossTable(pSERG$DZPinadequateSINGLEDOSE_otherroutes_more66)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |       292 |         1 |
##            |     0.997 |     0.003 |
##            |-----------|-----------|
##
##
##
##

CrossTable(pSERG[which(pSERG$FIRSTDZP==1),
]$DZPinadequateSINGLEDOSE_otherroutes_more66)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  87
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |        86 |         1 |
##            |     0.989 |     0.011 |
```

```
##           |-----------|-----------|
##
##
##
##
```

```
# Total number of patients who received initial DZP dose lower than
recommended regardless of the administration route
pSERG$TOTALDZPINADEQUATESINGLEDOSE<-
ifelse(pSERG$DZPinadequateSINGLEDOSE_otherroutes_less66==1|pSERG$DZPinadequat
eSINGLEDOSE_otherroutes_more66==1|pSERG$DZPinadequateSINGLEDOSE_611pr==1|pSER
G$DZPinadequateSINGLEDOSE_25==1|pSERG$DZPinadequateSINGLEDOSE_LESS2PR==1,1,0)
CrossTable(pSERG[which(pSERG$FIRSTDZP==1), ]$TOTALDZPINADEQUATESINGLEDOSE)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  87
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        61 |        26 |
##           |     0.701 |     0.299 |
##           |-----------|-----------|
##
##
##
##
```

MIDAZOLAM

```
#Midazolam IV
#Number of patients with inadquate first single dose of midazolam IV (minimum
recommended of 0.2 mg/kg)
pSERG$MDZinadequateSINGLEDOSE_IV<-ifelse(pSERG$FIRSTMDZ==1 & pSERG$MZDIV==1 &
pSERG$BZDDOSE.0KG <0.2,1,0)
CrossTable(pSERG[which(pSERG$FIRSTMDZ==1), ]$MDZinadequateSINGLEDOSE_IV)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
```

```
## |-------------------------|
##
##
## Total Observations in Table:  38
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        29 |         9 |
##           |     0.763 |     0.237 |
##           |-----------|-----------|
##
##
##
##
```

```
#Number of patients with inadequate initial dose of midazolam IN (minimum
recommended of 0.2 mg/kg)
pSERG$MDZinadequateSINGLEDOSE_IN<-ifelse(pSERG$FIRSTMDZ==1 & pSERG$MZDIN==1 &
pSERG$BZDDOSE.0KG <0.2,1,0)
CrossTable(pSERG[which(pSERG$FIRSTMDZ==1), ]$MDZinadequateSINGLEDOSE_IN)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  38
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        23 |        15 |
##           |     0.605 |     0.395 |
##           |-----------|-----------|
##
##
##
##
```

```
#Number of patients (weight  <13 kg) with inadequate initial dose of
midazolam (minimum recommended doses  0.2mg/kg)
pSERG$MDZinadequateSINGLEDOSE_IMLESS13<-ifelse(pSERG$WEIGHT < 13 &
pSERG$FIRSTMDZ==1 & pSERG$BZDROUTE.0=="intramuscular" & pSERG$BZDDOSE.0KG
<0.2,1,0)
```

```
CrossTable(pSERG[which(pSERG$FIRSTMDZ==1),
]$MDZinadequateSINGLEDOSE_IMLESS13)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  38
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        36 |         2 |
##           |     0.947 |     0.053 |
##           |-----------|-----------|
##
##
##
##

#Number of patients (weight 13-40kg)  with inadequate initial dose of
midazolam - minimum recommended doses absolute 5mg/dose
pSERG$MDZinadequateSINGLEDOSE_IM13_40<-ifelse(pSERG$WEIGHT >=13 &
pSERG$WEIGHT <= 40 & pSERG$FIRSTMDZ==1 & pSERG$BZDROUTE.0=="intramuscular" &
pSERG$BZDDOSE.0<5,1,0)
CrossTable(pSERG[which(pSERG$FIRSTMDZ==1), ]$MDZinadequateSINGLEDOSE_IM13_40)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  38
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        36 |         2 |
##           |     0.947 |     0.053 |
##           |-----------|-----------|
##
```

```
##
##
##

#Total inadequate initial dose of  MZD regardless of the route of
administration
pSERG$TOTALMDZINADEQUATESINGLEDOSE<-
ifelse(pSERG$MDZinadequateSINGLEDOSE_IV==1|pSERG$MDZinadequateSINGLEDOSE_IN==
1|pSERG$MDZinadequateSINGLEDOSE_IMLESS13==1|pSERG$MDZinadequateSINGLEDOSE_IM1
3_40==1,1,0)
CrossTable(pSERG[which(pSERG$FIRSTMDZ==1), ]$TOTALMDZINADEQUATESINGLEDOSE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  38
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        10 |        28 |
##           |     0.263 |     0.737 |
##           |-----------|-----------|
##
##
##
##
```

CLONAZEPAM

```
#Clonazepam
#Number of patients <=30kg  with inadequate dose  (minimum recommended dose
0.01 mg/kg)
pSERG$CLZinadequateSINGLEDOSE_less30<-ifelse(pSERG$FIRSTCLZ==1 &
pSERG$WEIGHT<= 30 & pSERG$BZDDOSE.0KG < 0.01,1,0)
nobs(pSERG$CLZinadequateSINGLEDOSE_less30==1)

## [1] 293

#Number of patients > 30kg  with inadequate dose (minimum recommended dose
0.5 mg/dose)
pSERG$CLZinadequateSINGLEDOSE_more30<-ifelse(pSERG$FIRSTCLZ==1 &
pSERG$WEIGHT> 30 & pSERG$BZDDOSE.0 < 0.5,1,0)
CrossTable(pSERG[which(pSERG$FIRSTCLZ==1), ]$CLZinadequateSINGLEDOSE_more30)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  5
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |         4 |         1 |
##            |     0.800 |     0.200 |
##            |-----------|-----------|
##
##
##
##
```

```
#Total inadequate initial dose of  clonazepam
pSERG$TOTALCLZINADEQUATESINGLEDOSE<-
ifelse(pSERG$CLZinadequateSINGLEDOSE_less30==1|
pSERG$CLZinadequateSINGLEDOSE_more30,1,0)
CrossTable(pSERG[which(pSERG$FIRSTCLZ==1), ]$TOTALCLZINADEQUATESINGLEDOSE)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  5
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |         4 |         1 |
##            |     0.800 |     0.200 |
##            |-----------|-----------|
##
##
##
##
```

Demographics

Demographic features of our study population.

```
# Age
nobs(pSERG$ageyears)

## [1] 293

summary(pSERG$ageyears)

##     Min.  1st Qu.   Median     Mean  3rd Qu.     Max.
##  0.08333  1.27222  3.75000  5.69220  9.25000 20.74167

sd(pSERG$ageyears, na.rm = TRUE)

## [1] 5.173674

# Age by subgroups
nobs(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$ageyears)

## [1] 201

summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$ageyears)

##     Min.  1st Qu.   Median     Mean  3rd Qu.     Max.
##  0.08333  1.16667  3.16667  5.36813  8.91667 19.33333

sd(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$ageyears, na.rm = TRUE)

## [1] 5.217706

nobs(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$ageyears)

## [1] 92

summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$ageyears)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   0.125   2.000   4.792   6.400  10.229  20.742

sd(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$ageyears, na.rm = TRUE)

## [1] 5.031566

# Sex
CrossTable(pSERG$SEX)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
```

```
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |    female |      male |
##            |-----------|-----------|
##            |       131 |       162 |
##            |     0.447 |     0.553 |
##            |-----------|-----------|
##
##
##
##
```

```
# Sex by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$SEX)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##            |    female |      male |
##            |-----------|-----------|
##            |        81 |       120 |
##            |     0.403 |     0.597 |
##            |-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$SEX)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
```

```
##
## Total Observations in Table:  92
##
##
##            |    female |      male |
##            |-----------|-----------|
##            |        50 |        42 |
##            |     0.543 |     0.457 |
##            |-----------|-----------|
##
##
##
##

# Race
CrossTable(pSERG$RACE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##                                      |       american_indian_alaska_native
|                              arabic |                                 asian |
black_or_african_american | native_hawaiian_or_pacific_islander |
##                                      |-------------------------------------
|-------------------------------------|-------------------------------------
|-------------------------------------|-------------------------------------|
##                                      |                                   1
|                                   8 |                                  10 |
57 |                                   2 |
##                                      |                               0.003
|                               0.027 |                               0.034 |
0.195 |                               0.007 |
##                                      |-------------------------------------
|-------------------------------------|-------------------------------------
|-------------------------------------|-------------------------------------|
##
##
##                                      |                        not_reported
|                             unknown |                               white |
##                                      |-------------------------------------
|-------------------------------------|-------------------------------------|
```

```
##                                       |                                     9
|                                    19 |                                   187 |
##                                       |                                 0.031
|                                 0.065 |                                 0.638 |
##                                       |-----------------------------------
|---------------------------------------|-----------------------------------|
##
##
##
##

# Race by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$RACE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##                                       |                                arabic
|                                 asian |           black_or_african_american |
native_hawaiian_or_pacific_islander |                         not_reported |
##                                       |-----------------------------------
|---------------------------------------|-----------------------------------
|---------------------------------------|-----------------------------------|
##                                       |                                     5
|                                    5 |                                    42 |
2 |                                    6 |
##                                       |                                 0.025
|                                 0.025 |                                 0.209 |
0.010 |                               0.030 |
##                                       |-----------------------------------
|---------------------------------------|-----------------------------------
|---------------------------------------|-----------------------------------|
##
##
##                                       |                               unknown
|                                 white |
##                                       |-----------------------------------
|---------------------------------------|
##                                       |                                    15
|                                   126 |
##                                       |                                 0.075
```

```
|                                0.627 |
##                                      |-----------------------------------
|-----------------------------------|
##
##
##
##

CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$RACE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##                               | american_indian_alaska_native |
arabic |                         asian |     black_or_african_american |
not_reported |
##                               |-------------------------------|-----------
--------------------|-------------------------------|-----------------------
-------|-------------------------------|
##                               |                             1 |
3 |                             5 |                            15 |
3 |
##                               |                         0.011 |
0.033 |                         0.054 |                         0.163 |
0.033 |
##                               |-------------------------------|-----------
--------------------|-------------------------------|-----------------------
-------|-------------------------------|
##
##
##                               |                       unknown |
white |
##                               |-------------------------------|-----------
--------------------|
##                               |                             4 |
61 |
##                               |                         0.043 |
0.663 |
##                               |-------------------------------|-----------
--------------------|
##
```

```
##
##
##

# Ethnicity
CrossTable(pSERG$ETHNICITY)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##                          |     hispanic_or_latino | not_hispanic_or_latino |
not_reported |                unknown |
##                          |------------------------|------------------------
|------------------------|------------------------|
##                          |                     43 |                    225 |
15 |                     10 |
##                          |                  0.147 |                  0.768 |
0.051 |                  0.034 |
##                          |------------------------|------------------------
|------------------------|------------------------|
##
##
##
##

# Ethnicity by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$ETHNICITY)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##                          |     hispanic_or_latino | not_hispanic_or_latino |
not_reported |                unknown |
```

```
##                          |-------------------------|-------------------------
|-------------------------|-------------------------|
##                          |                      32 |                     150 |
11 |                       8 |
##                          |                   0.159 |                   0.746 |
0.055 |                   0.040 |
##                          |-------------------------|-------------------------
|-------------------------|-------------------------|
##
##
##
##

CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$ETHNICITY)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##                          |     hispanic_or_latino | not_hispanic_or_latino |
not_reported |               unknown |
##                          |-------------------------|-------------------------
|-------------------------|-------------------------|
##                          |                      11 |                     75 |
4 |                       2 |
##                          |                   0.120 |                   0.815 |
0.043 |                   0.022 |
##                          |-------------------------|-------------------------
|-------------------------|-------------------------|
##
##
##
##

# History of developmental delay
CrossTable(pSERG$delay)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
```

```
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       139 |       154 |
##           |     0.474 |     0.526 |
##           |-----------|-----------|
##
##
##
##
```

```
# History of developmental delay by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$delay)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        93 |       108 |
##           |     0.463 |     0.537 |
##           |-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$delay)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
```

```
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        46 |        46 |
##           |     0.500 |     0.500 |
##           |-----------|-----------|
##
##
##
##
```

```
# History of cerebral palsy
CrossTable(pSERG$palsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       262 |        31 |
##           |     0.894 |     0.106 |
##           |-----------|-----------|
##
##
##
##
```

```
# History of cerebral palsy by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$palsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
```

```
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       182 |        19 |
##           |     0.905 |     0.095 |
##           |-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$palsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        80 |        12 |
##           |     0.870 |     0.130 |
##           |-----------|-----------|
##
##
##
##
```

```
# Febrile
CrossTable(pSERG$febrile)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
```

```
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |       259 |        34 |
##            |     0.884 |     0.116 |
##            |-----------|-----------|
##
##
##
##
```

```
# Febrile by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$febrile)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |       178 |        23 |
##            |     0.886 |     0.114 |
##            |-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$febrile)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##            |         0 |         1 |
```

```
##           |-----------|-----------|
##           |        81 |        11 |
##           |     0.880 |     0.120 |
##           |-----------|-----------|
##
##
##
##
```

```
# History of prior epilepsy
CrossTable(pSERG$priorepilepsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       147 |       146 |
##           |     0.502 |     0.498 |
##           |-----------|-----------|
##
##
##
##
```

```
# History of prior epilepsy by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$priorepilepsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
```

```
##           |        99 |       102 |
##           |     0.493 |     0.507 |
##           |-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$priorepilepsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        48 |        44 |
##           |     0.522 |     0.478 |
##           |-----------|-----------|
##
##
##
##
```

```
# History of prior status epilepticus
CrossTable(pSERG$priorSE)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       230 |        63 |
##           |     0.785 |     0.215 |
```

```
##           |-----------|-----------|
##
##
##
##

# History of prior status epilepticus by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$priorSE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       161 |        40 |
##           |     0.801 |     0.199 |
##           |-----------|-----------|
##
##
##
##

CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$priorSE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        69 |        23 |
##           |     0.750 |     0.250 |
##           |-----------|-----------|
##
```

```
##
##
##

# No prior neurological history
CrossTable(pSERG$none)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       197 |        96 |
##           |     0.672 |     0.328 |
##           |-----------|-----------|
##
##
##
##

# No prior neurological history by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$none)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       141 |        60 |
##           |     0.701 |     0.299 |
##           |-----------|-----------|
##
##
```

```
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$none)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |        56 |        36 |
##            |     0.609 |     0.391 |
##            |-----------|-----------|
##
##
##
##
```

```
# Duration of convulsive status epilepticus
nobs(pSERG$convulsivedurationmin)
```

```
## [1] 293
```

```
summary(pSERG$convulsivedurationmin)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##       0      60     127    2402     286  172800
```

```
# Duration of convulsive status epilepticus by subgroups
nobs(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$convulsivedurationmin)
```

```
## [1] 201
```

```
summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$convulsivedurationmin)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##       0      75     140    2486     300  172800
```

```
nobs(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$convulsivedurationmin)
```

```
## [1] 92
```

```
summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$convulsivedurationmin)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##     0.0    47.5   107.5  2219.2   182.0 90720.0
```

```
# Type of status epilepticus
CrossTable(pSERG$TYPESTATUS)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##              |   continuous | intermittent |
##              |--------------|--------------|
##              |          102 |          191 |
##              |        0.348 |        0.652 |
##              |--------------|--------------|
##
##
##
##
```

```
# Type of status epilepticus by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$TYPESTATUS)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##              |   continuous | intermittent |
##              |--------------|--------------|
##              |           75 |          126 |
##              |        0.373 |        0.627 |
##              |--------------|--------------|
##
##
```

```
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$TYPESTATUS)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##              |   continuous | intermittent |
##              |--------------|--------------|
##              |           27 |           65 |
##              |        0.293 |        0.707 |
##              |--------------|--------------|
##
##
##
##
```

```
# Etiology of SE
CrossTable(pSERG$ETIOLOGY)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |            |    genetic |  metabolic |      other |
structural |
##            |------------|------------|------------|------------|----------
--|
##            |          1 |         57 |         15 |         47 |
70 |
##            |      0.003 |      0.195 |      0.051 |      0.160 |
0.239 |
##            |------------|------------|------------|------------|----------
```

```
--|
##
##
##            |    unknown |
##            |------------|
##            |        103 |
##            |      0.352 |
##            |------------|
##
##
##
##
```

```
# Etiology of SE by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$ETIOLOGY)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##            |            |    genetic |  metabolic |      other |
structural |
##            |------------|------------|------------|------------|----------
--|
##            |          1 |         44 |          9 |         33 |
44 |
##            |      0.005 |      0.219 |      0.045 |      0.164 |
0.219 |
##            |------------|------------|------------|------------|----------
--|
##
##
##            |    unknown |
##            |------------|
##            |         70 |
##            |      0.348 |
##            |------------|
##
##
##
##
```

```r
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$ETIOLOGY)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##            |    genetic |  metabolic |      other | structural |
unknown |
##            |------------|------------|------------|------------|----------
--|
##            |         13 |          6 |         14 |         26 |
33 |
##            |      0.141 |      0.065 |      0.152 |      0.283 |
0.359 |
##            |------------|------------|------------|------------|----------
--|
##
##
##
##
```

```r
# Time to first benzodiazepine
nobs(pSERG$BZDTIME.0)
```

```
## [1] 293
```

```r
summary(pSERG$BZDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.00    5.00   15.00   45.04   37.00  720.00
```

```r
# Time to first benzodiazepine by subgroups
nobs(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$BZDTIME.0)
```

```
## [1] 201
```

```r
summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$BZDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.00    5.00   20.00   56.12   50.00  720.00
```

```r
nobs(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$BZDTIME.0)
```

```
## [1] 92
```

```r
summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$BZDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.00    4.00    8.00   20.82   20.00  360.00
```

```r
# Time to first non-benzodiazepine ASM
nobs(pSERG$AEDTIME.0)
```

```
## [1] 293
```

```r
summary(pSERG$AEDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##     3.0    35.0    63.0   143.5   126.0  4320.0
```

```r
# Time to first non-benzodiazepine ASM by subgroups
nobs(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$AEDTIME.0)
```

```
## [1] 201
```

```r
summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$AEDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    10.0    45.0    76.0   171.1   155.0  4320.0
```

```r
nobs(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$AEDTIME.0)
```

```
## [1] 92
```

```r
summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$AEDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    3.00   24.00   39.00   83.27   71.50 1488.00
```

```r
# Location of the initial benzodiazepine
pSERG$BZDLOCATION.0 <- drop.levels(pSERG$BZDLOCATION.0)
CrossTable(pSERG$BZDLOCATION.0)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |       EMS |      home |  outsideh |    studyh |
##            |-----------|-----------|-----------|-----------|
##            |        53 |        56 |        61 |       123 |
```

```
##            |     0.181 |     0.191 |     0.208 |     0.420 |
##            |-----------|-----------|-----------|-----------|
##
##
##
##
```

PRIMARY OUTCOME. Benzodiazepines administered before non-BZD ASMs

Description of benzodiazepine administration given before non-benzodiazepine ASMs.

```
### NUMBER OF BENZODIAZEPINES GIVEN BEFORE NON-BENZODIAZEPINE ANTI-SEIZURE
MEDICATIONS

## Number of benzodiazepines administered before non-benzodiazepine ASMs
# Generate the variable of benzodiazepine given before non-benzodiazepine
ASMs
for (i in 1 : dim(pSERG)[1]) {
  pSERG$preAEDBZDs[i] <- 0
  if (!is.na(pSERG$BZDTIME.0[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.0[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.1[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.1[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.2[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.2[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.3[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.3[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.4[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.4[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.5[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.5[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.6[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.6[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.7[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.7[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.8[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.8[i] <
pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.9[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.9[i] <
pSERG$AEDTIME.0[i])) {
```

```
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.10[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.10[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.11[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.11[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.12[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.12[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.13[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.13[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.14[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.14[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.15[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.15[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
  if (!is.na(pSERG$BZDTIME.16[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.16[i]
< pSERG$AEDTIME.0[i])) {
    pSERG$preAEDBZDs[i] <- pSERG$preAEDBZDs[i] + 1}
}

# Benzodiazepine doses before non-BZD ASMs
summary(pSERG$preAEDBZDs)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   1.000   1.000   2.000   2.369   3.000  10.000

CrossTable(pSERG$preAEDBZDs)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         1 |         2 |         3 |         4 |         5 |
##           |-----------|-----------|-----------|-----------|-----------|
##           |        76 |       111 |        61 |        28 |         8 |
##           |     0.259 |     0.379 |     0.208 |     0.096 |     0.027 |
##           |-----------|-----------|-----------|-----------|-----------|
##
```

```
##
##           |         6 |         7 |        10 |
##           |-----------|-----------|-----------|
##           |         5 |         3 |         1 |
##           |     0.017 |     0.010 |     0.003 |
##           |-----------|-----------|-----------|
##
##
##
##
```

```
pSERG$threeormorepreAEDBZDs <- ifelse(pSERG$preAEDBZDs >= 3, 1, 0)
CrossTable(pSERG$threeormorepreAEDBZDs)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       187 |       106 |
##           |     0.638 |     0.362 |
##           |-----------|-----------|
##
##
##
##
```

```
## HOSPITAL ONSET
# Division by hospital onset
summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$preAEDBZDs)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   1.000   1.000   2.000   2.458   3.000  10.000
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$threeormorepreAEDBZDs)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
```

```
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       123 |        78 |
##           |     0.612 |     0.388 |
##           |-----------|-----------|
##
##
##
##
```

```
summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$preAEDBZDs)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##   1.000   1.000   2.000   2.174   3.000   6.000
```

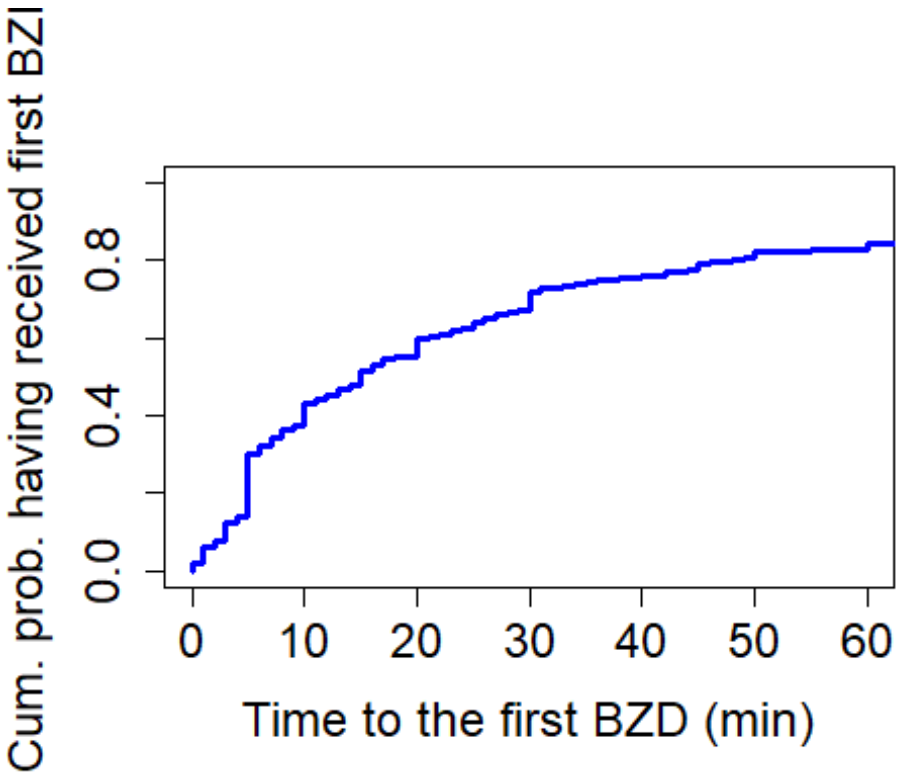
```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"),
]$threeormorepreAEDBZDs)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        64 |        28 |
##           |     0.696 |     0.304 |
##           |-----------|-----------|
##
##
##
##
```

TIME TO BENZODIAZEPINES GIVEN BEFORE NON-BENZODIAZEPINE ASMS

```
## Time to first benzodiazepine
# Time to first benzodiazepine
summary(pSERG$BZDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.00    5.00   15.00   45.04   37.00  720.00

sd(pSERG$BZDTIME.0)

## [1] 92.32378

survfit(Surv(pSERG$BZDTIME.0) ~ 1)

## Call: survfit(formula = Surv(pSERG$BZDTIME.0) ~ 1)
##
##       n  events  median 0.95LCL 0.95UCL
##     293     293      15      12      20

# Figure time to first BZD
plot(survfit(Surv(pSERG$BZDTIME.0) ~ 1), fun = "event",
     conf.int = FALSE, xlim = c(0, 60), col = "blue", lwd = 3,
     cex.axis = 1.5, cex.lab = 1.5,
     xlab="Time to the first BZD (min)", ylab="Cum. prob. having received
first BZD")
```




```
## Time to first benzodiazepine by hospital onset
# Time to first benzodiazepine by hospital onset group
summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$BZDTIME.0)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.00    5.00   20.00   56.12   50.00  720.00
```

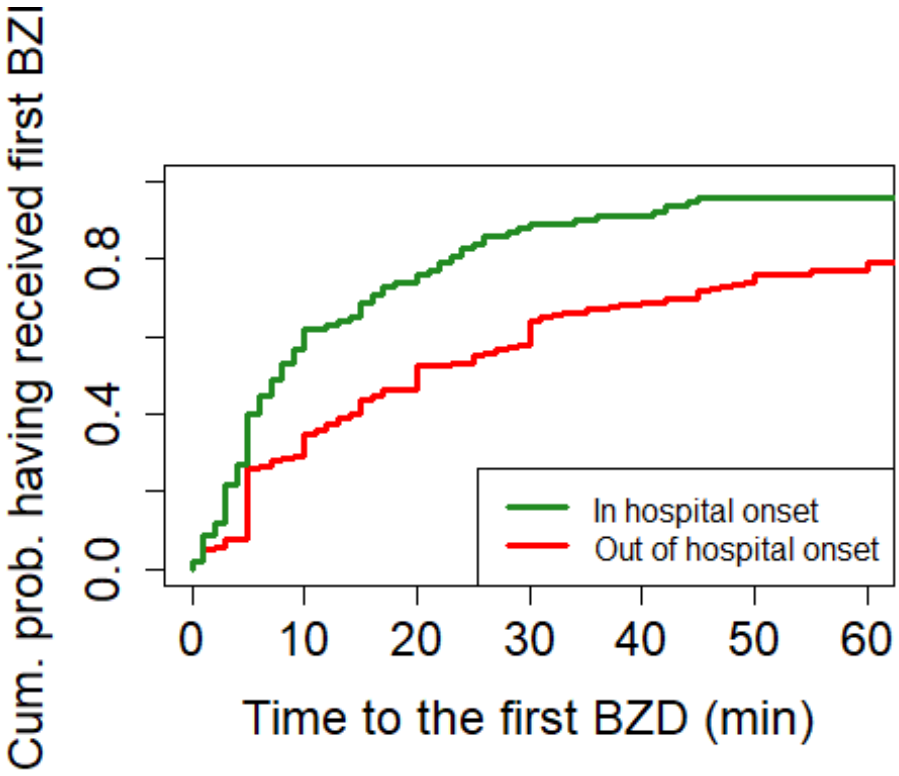
```r
summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$BZDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    0.00    4.00    8.00   20.82   20.00  360.00
```

```r
pSERG$hospitalonsetnumeric <- ifelse(pSERG$HOSPITALONSET == "yes", 1, 0)
survdiff(Surv(pSERG$BZDTIME.0) ~ pSERG$hospitalonsetnumeric, rho = 1)
```

```
## Call:
## survdiff(formula = Surv(pSERG$BZDTIME.0) ~ pSERG$hospitalonsetnumeric,
##     rho = 1)
##
##                                 N Observed Expected (O-E)^2/E (O-E)^2/V
## pSERG$hospitalonsetnumeric=0 201     93.8    117.0      4.61      29.1
## pSERG$hospitalonsetnumeric=1  92     59.5     36.3     14.82      29.1
##
##  Chisq= 29.1  on 1 degrees of freedom, p= 7e-08
```

```r
# Figure time to first BZD by hospital onset
plot(survfit(Surv(pSERG$BZDTIME.0) ~ pSERG$hospitalonsetnumeric), fun =
"event",
     conf.int = FALSE, xlim = c(0, 60), col = c("red", "forestgreen"), lwd =
3,
     cex.axis = 1.5, cex.lab = 1.5,
     xlab="Time to the first BZD (min)", ylab="Cum. prob. having received
first BZD")
legend(x = "bottomright", legend = c("In hospital onset", "Out of hospital
onset"), col = c("forestgreen", "red"), lty = 1, lwd = 3)
```




```
## Benzodiazepines before non-benzodiazepine ASMs given after 30 minutes of
seizure onset
# Create the variable benzodiazepines before non-benzodiazepine ASMs given
after 30 minutes of seizure onset
for (i in 1 : dim(pSERG)[1]) {
  pSERG$preAEDBZDsmorethan30[i] <- 0
  if (!is.na(pSERG$BZDTIME.0[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.0[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.0[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.1[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.1[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.1[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.2[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.2[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.2[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.3[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.3[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.3[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.4[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.4[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.4[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.5[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.5[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.5[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.6[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.6[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.6[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
```

```
  if (!is.na(pSERG$BZDTIME.7[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.7[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.7[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.8[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.8[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.8[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.9[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.9[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.9[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.10[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.10[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.10[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.11[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.11[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.11[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.12[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.12[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.12[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.13[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.13[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.13[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.14[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.14[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.14[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.15[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.15[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.15[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
  if (!is.na(pSERG$BZDTIME.16[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.16[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.16[i] > 30) {
    pSERG$preAEDBZDsmorethan30[i] <- pSERG$preAEDBZDsmorethan30[i] + 1}
}

# Benzodiazepines before non-benzodiazepine ASMs given after 30 minutes of
seizure onset
CrossTable(pSERG$preAEDBZDsmorethan30)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |         0 |         1 |         2 |         3 |         4 |
##            |-----------|-----------|-----------|-----------|-----------|
```

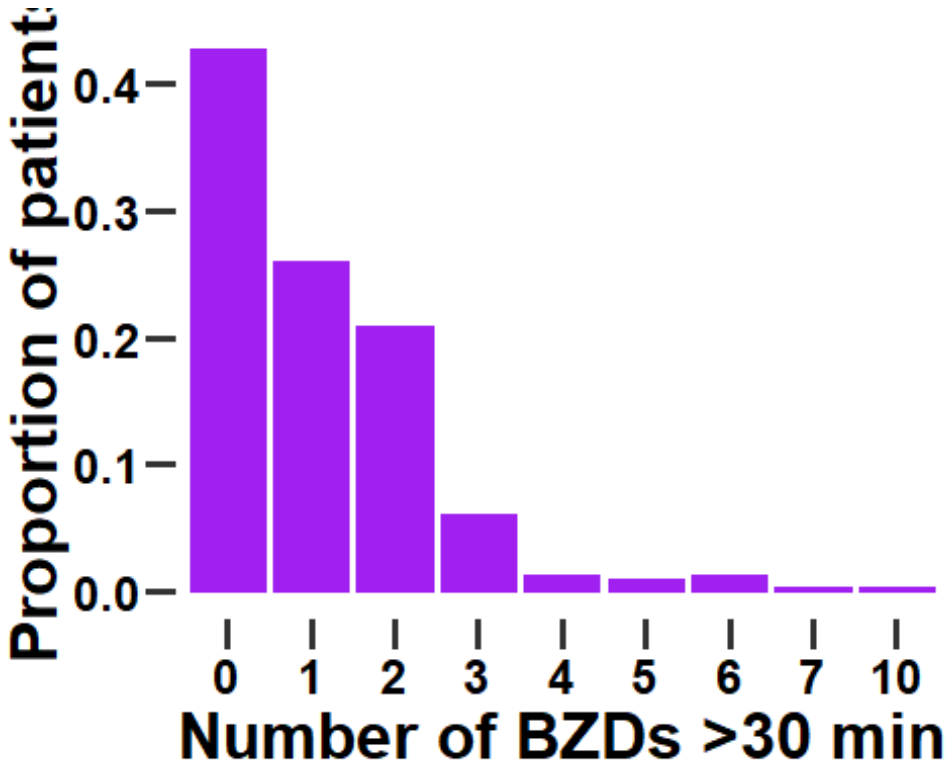
```
##           |       125 |        76 |        61 |        18 |         4 |
##           |     0.427 |     0.259 |     0.208 |     0.061 |     0.014 |
##           |-----------|-----------|-----------|-----------|-----------|
##
##
##           |         5 |         6 |         7 |        10 |
##           |-----------|-----------|-----------|-----------|
##           |         3 |         4 |         1 |         1 |
##           |     0.010 |     0.014 |     0.003 |     0.003 |
##           |-----------|-----------|-----------|-----------|
##
##
##
##
```

```
pSERG$preAEDBZDsmorethan30yesno <- ifelse(pSERG$preAEDBZDsmorethan30 == 0, 0,
1)
CrossTable(pSERG$preAEDBZDsmorethan30yesno)
```

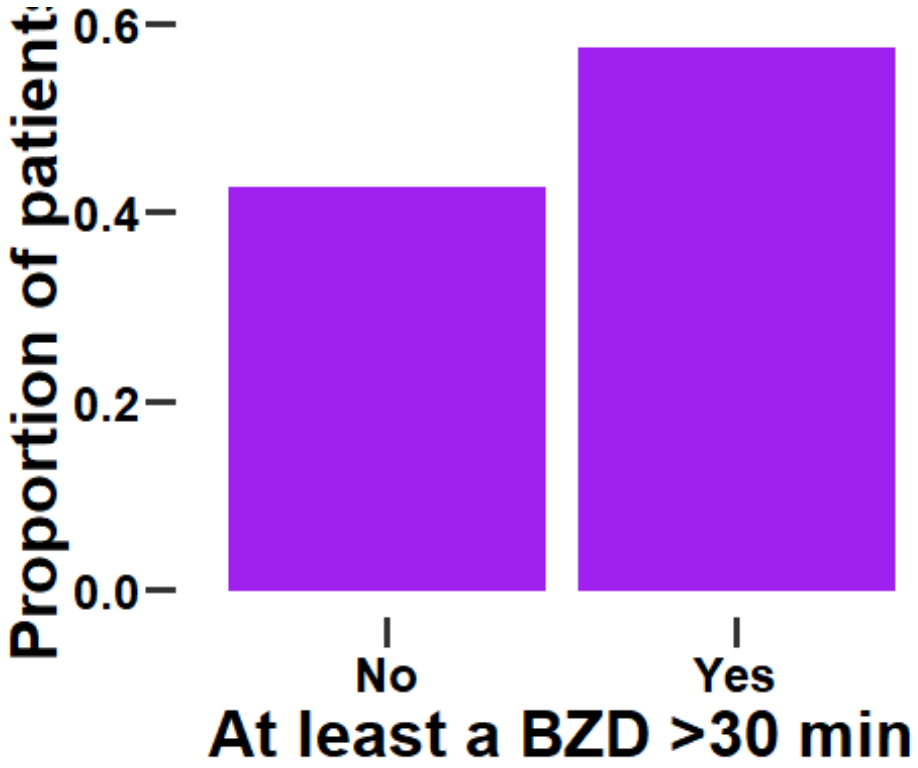
```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       125 |       168 |
##           |     0.427 |     0.573 |
##           |-----------|-----------|
##
##
##
##
```

```
# Figure number of benzodiazepines before non-benzodiazepine ASMs given after
30 minutes of seizure onset
figurenumbermorethan30 <- ggplot(pSERG, aes(x =
as.factor(preAEDBZDsmorethan30))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
```

```
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  xlab("Number of BZDs >30 min") +
  ylab("Proportion of patients")
figurenumbermorethan30
```




```
# Figure proportion patients with at least one benzodiazepine given after 30
minutes
figureproportionmorethan30yesno <- ggplot(pSERG, aes(x =
as.factor(preAEDBZDsmorethan30yesno))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  scale_x_discrete(labels = c("0" = "No", "1" = "Yes")) +
  xlab("At least a BZD >30 min") +
  ylab("Proportion of patients")
figureproportionmorethan30yesno
```




```
# Number of benzodiazepines received more than 30 minutes by subgroups of
hospital onset
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$preAEDBZDsmorethan30)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |         2 |         3 |         4 |
##           |-----------|-----------|-----------|-----------|-----------|
##           |        65 |        58 |        50 |        16 |         4 |
##           |     0.323 |     0.289 |     0.249 |     0.080 |     0.020 |
##           |-----------|-----------|-----------|-----------|-----------|
##
##
##           |         5 |         6 |         7 |        10 |
##           |-----------|-----------|-----------|-----------|
##           |         2 |         4 |         1 |         1 |
##           |     0.010 |     0.020 |     0.005 |     0.005 |
```

```
##           |-----------|-----------|-----------|-----------|
##
##
##
##
```

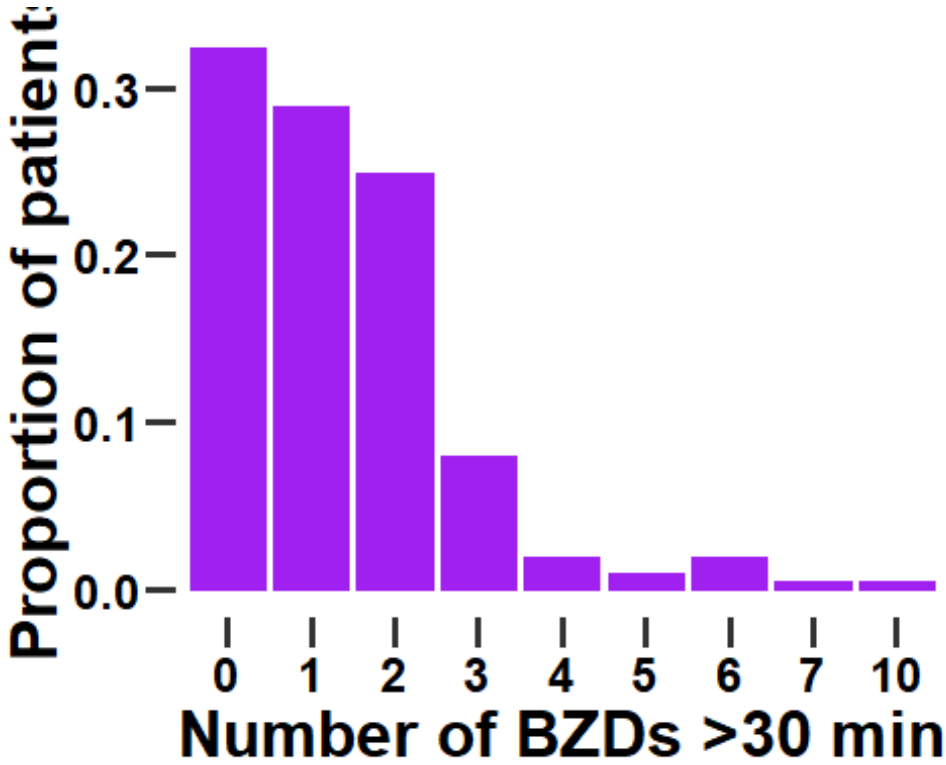
```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$preAEDBZDsmorethan30)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |         2 |         3 |         5 |
##           |-----------|-----------|-----------|-----------|-----------|
##           |        60 |        18 |        11 |         2 |         1 |
##           |     0.652 |     0.196 |     0.120 |     0.022 |     0.011 |
##           |-----------|-----------|-----------|-----------|-----------|
##
##
##
##
```

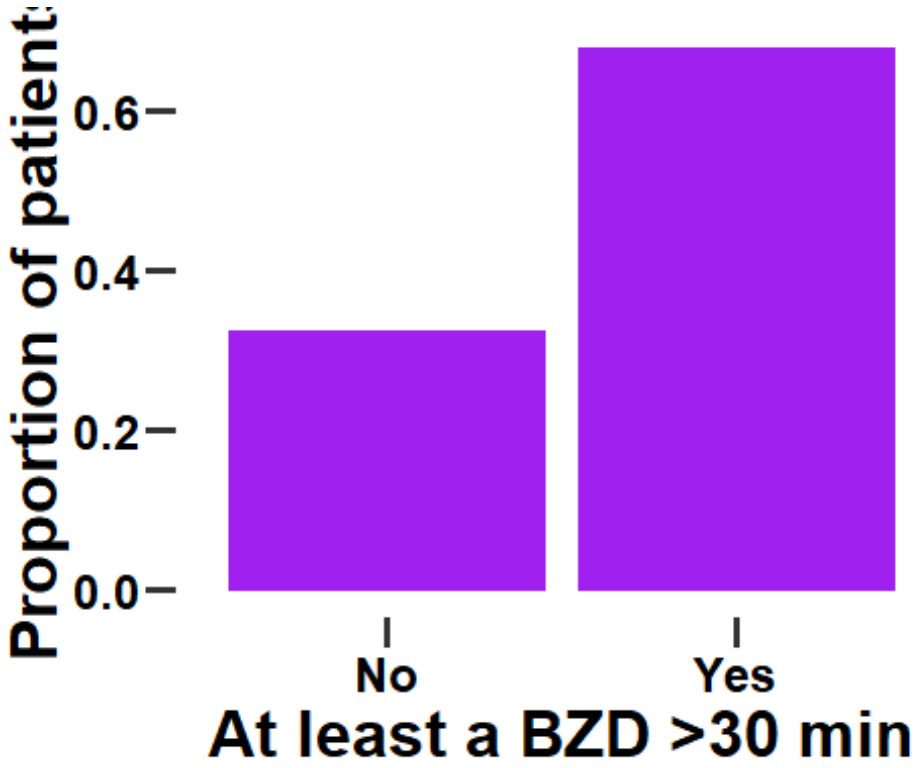
```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"),
]$preAEDBZDsmorethan30yesno)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        65 |       136 |
##           |     0.323 |     0.677 |
##           |-----------|-----------|
##
```

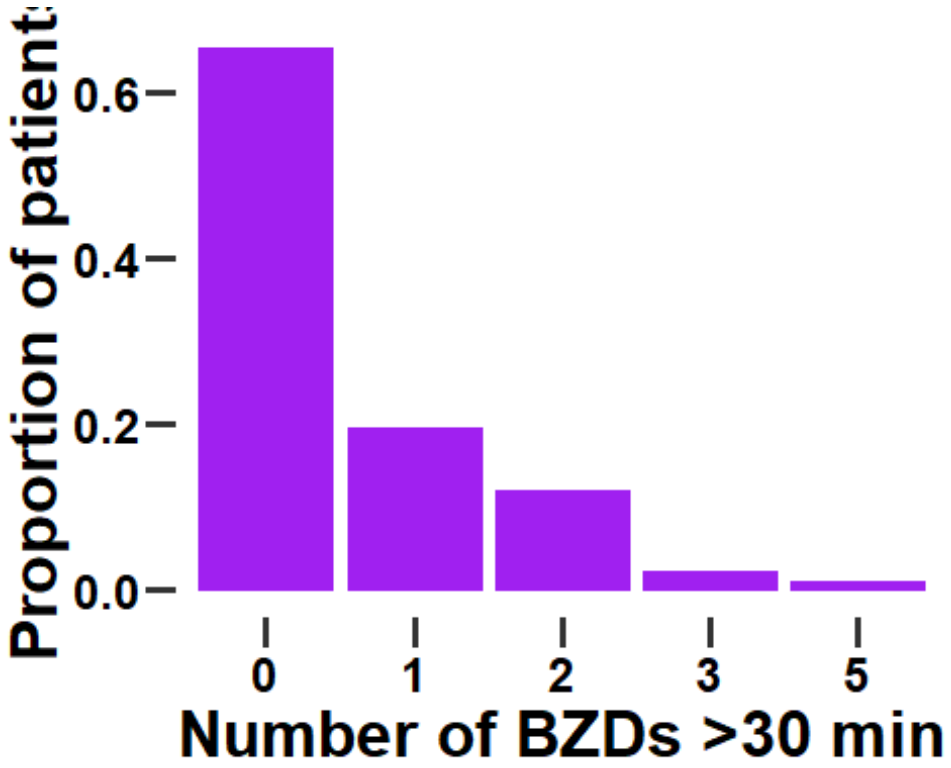
```
##
##
##

CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"),
]$preAEDBZDsmorethan30yesno)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |        60 |        32 |
##            |     0.652 |     0.348 |
##            |-----------|-----------|
##
##
##
##

table(pSERG$preAEDBZDsmorethan30yesno, pSERG$HOSPITALONSET)

##
##      no yes
##   0  65  60
##   1 136  32

# Figure number of benzodiazepines before non-benzodiazepine ASMs given after
30 minutes of seizure onset out of hospital onset
figurenumbermorethan30out <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "no"),
], aes(x = as.factor(preAEDBZDsmorethan30))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  xlab("Number of BZDs >30 min") +
  ylab("Proportion of patients")
figurenumbermorethan30out
```



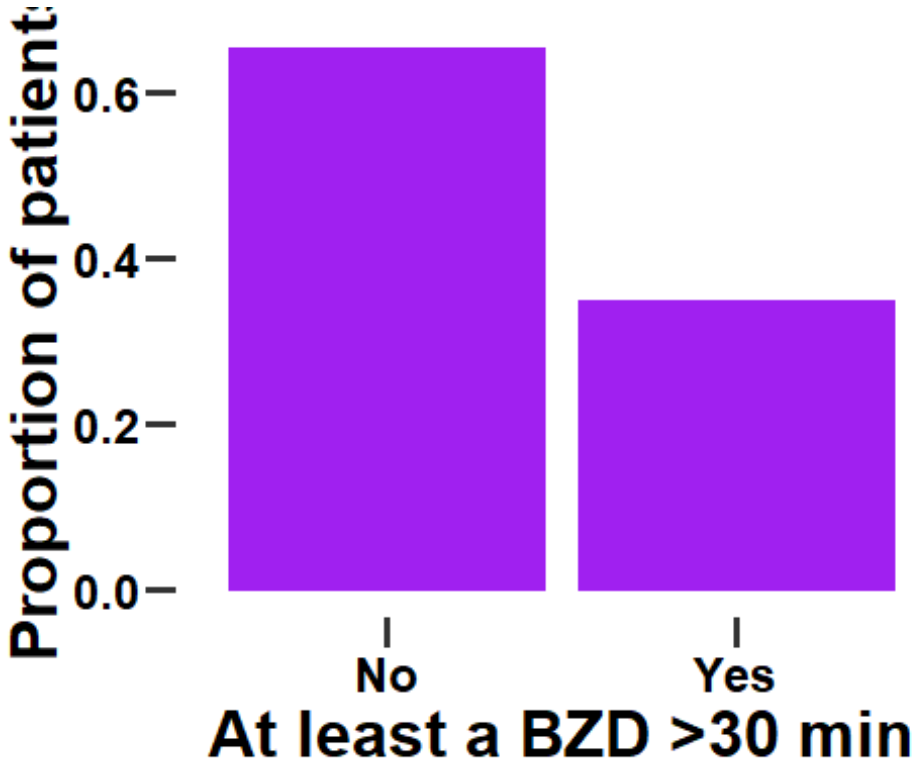

```
# Figure proportion patients with at least one benzodiazepine given after 30
minutes out of the hospital
figureproportionmorethan30yesnoout <- ggplot(pSERG[which(pSERG$HOSPITALONSET
== "no"), ], aes(x = as.factor(preAEDBZDsmorethan30yesno))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  scale_x_discrete(labels = c("0" = "No", "1" = "Yes")) +
  xlab("At least a BZD >30 min") +
  ylab("Proportion of patients")
figureproportionmorethan30yesnoout
```




```
# Figure number of benzodiazepines before non-benzodiazepine ASMs given after
30 minutes of seizure onset with onset in the hospital
figurenumbermorethan30in <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "yes"),
], aes(x = as.factor(preAEDBZDsmorethan30))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  xlab("Number of BZDs >30 min") +
  ylab("Proportion of patients")
figurenumbermorethan30in
```




```r
# Figure proportion patients with at least one benzodiazepine given after 30 minutes in the hospital
figureproportionmorethan30yesnoin <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "yes"), ], aes(x = as.factor(preAEDBZDsmorethan30yesno))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill = "purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size = 1.2)) +
  scale_x_discrete(labels = c("0" = "No", "1" = "Yes")) +
  xlab("At least a BZD >30 min") +
  ylab("Proportion of patients")
figureproportionmorethan30yesnoin
```




```
## Benzodiazepines before non-benzodiazepine ASMs given after 45 minutes of
seizure onset
# Create the variable benzodiazepines before non-benzodiazepine ASMs given
after 45 minutes of seizure onset
for (i in 1 : dim(pSERG)[1]) {
  pSERG$preAEDBZDsmorethan45[i] <- 0
  if (!is.na(pSERG$BZDTIME.0[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.0[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.0[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.1[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.1[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.1[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.2[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.2[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.2[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.3[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.3[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.3[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.4[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.4[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.4[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.5[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.5[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.5[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.6[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.6[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.6[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
```

```
  if (!is.na(pSERG$BZDTIME.7[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.7[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.7[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.8[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.8[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.8[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.9[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.9[i] <
pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.9[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.10[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.10[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.10[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.11[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.11[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.11[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.12[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.12[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.12[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.13[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.13[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.13[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.14[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.14[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.14[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.15[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.15[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.15[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
  if (!is.na(pSERG$BZDTIME.16[i] < pSERG$AEDTIME.0[i]) & (pSERG$BZDTIME.16[i]
< pSERG$AEDTIME.0[i]) & pSERG$BZDTIME.16[i] > 45) {
    pSERG$preAEDBZDsmorethan45[i] <- pSERG$preAEDBZDsmorethan45[i] + 1}
}

# Benzodiazepines before non-benzodiazepine ASMs given after 45 minutes of
seizure onset
CrossTable(pSERG$preAEDBZDsmorethan45)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##           |         0 |         1 |         2 |         3 |         4 |
##           |-----------|-----------|-----------|-----------|-----------|
```

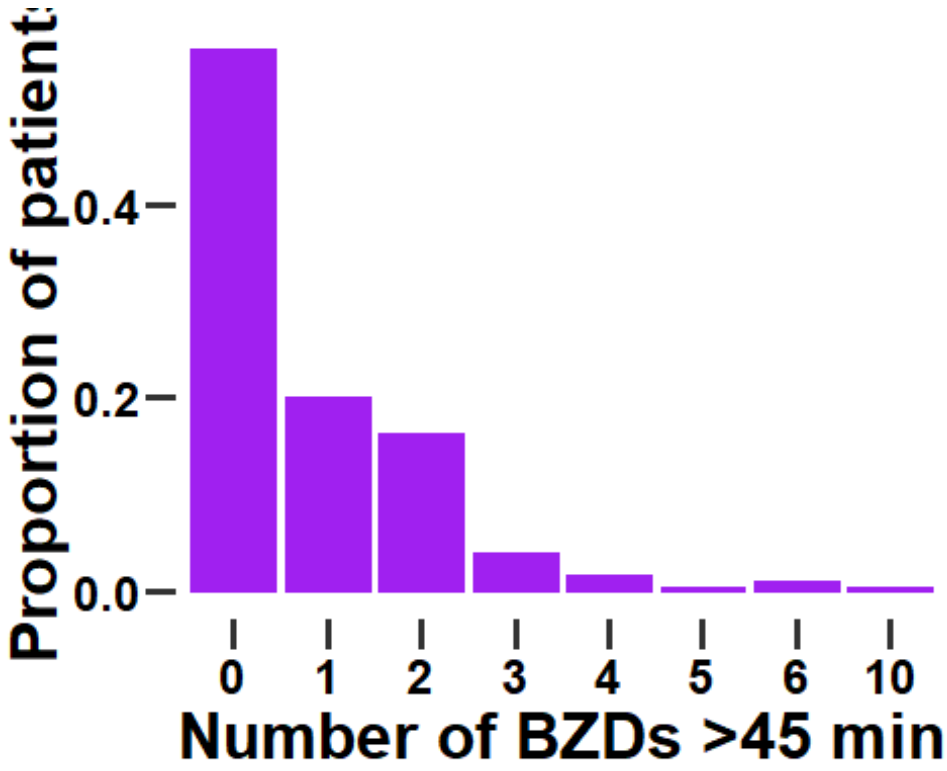
```
##            |       164 |        59 |        48 |        12 |         5 |
##            |     0.560 |     0.201 |     0.164 |     0.041 |     0.017 |
##            |-----------|-----------|-----------|-----------|-----------|
##
##
##            |         5 |         6 |        10 |
##            |-----------|-----------|-----------|
##            |         1 |         3 |         1 |
##            |     0.003 |     0.010 |     0.003 |
##            |-----------|-----------|-----------|
##
##
##
##
```

```
pSERG$preAEDBZDsmorethan45yesno <- ifelse(pSERG$preAEDBZDsmorethan45 == 0, 0,
1)
CrossTable(pSERG$preAEDBZDsmorethan45yesno)
```

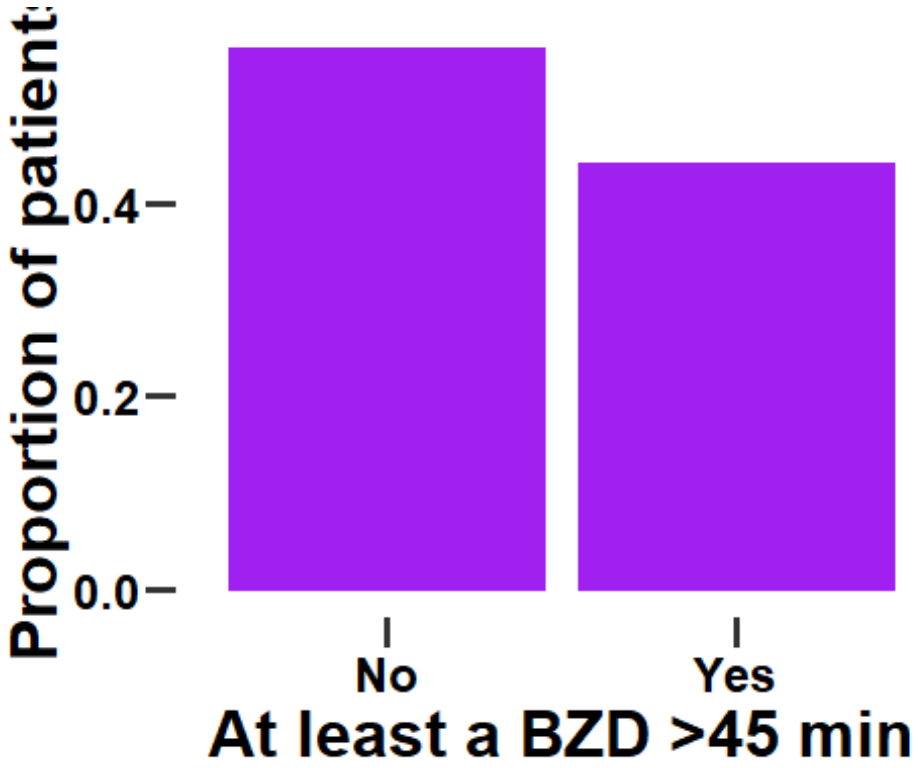
```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  293
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |       164 |       129 |
##            |     0.560 |     0.440 |
##            |-----------|-----------|
##
##
##
##
```

```
# Figure number of benzodiazepines before non-benzodiazepine ASMs given after
45 minutes of seizure onset
figurenumbermorethan45 <- ggplot(pSERG, aes(x =
as.factor(preAEDBZDsmorethan45))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
```

```
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  xlab("Number of BZDs >45 min") +
  ylab("Proportion of patients")
figurenumbermorethan45
```




```
# Figure proportion patients with at least one benzodiazepine given after 45
minutes
figureproportionmorethan45yesno <- ggplot(pSERG, aes(x =
as.factor(preAEDBZDsmorethan45yesno))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  scale_x_discrete(labels = c("0" = "No", "1" = "Yes")) +
  xlab("At least a BZD >45 min") +
  ylab("Proportion of patients")
figureproportionmorethan45yesno
```




```
# Number of benzodiazepines received more than 45 minutes by subgroups of
hospital onset
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$preAEDBZDsmorethan45)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |         2 |         3 |         4 |
##           |-----------|-----------|-----------|-----------|-----------|
##           |        90 |        47 |        44 |        11 |         4 |
##           |     0.448 |     0.234 |     0.219 |     0.055 |     0.020 |
##           |-----------|-----------|-----------|-----------|-----------|
##
##
##           |         5 |         6 |        10 |
##           |-----------|-----------|-----------|
##           |         1 |         3 |         1 |
##           |     0.005 |     0.015 |     0.005 |
```

```
##           |-----------|-----------|-----------|
##
##
##
##
```

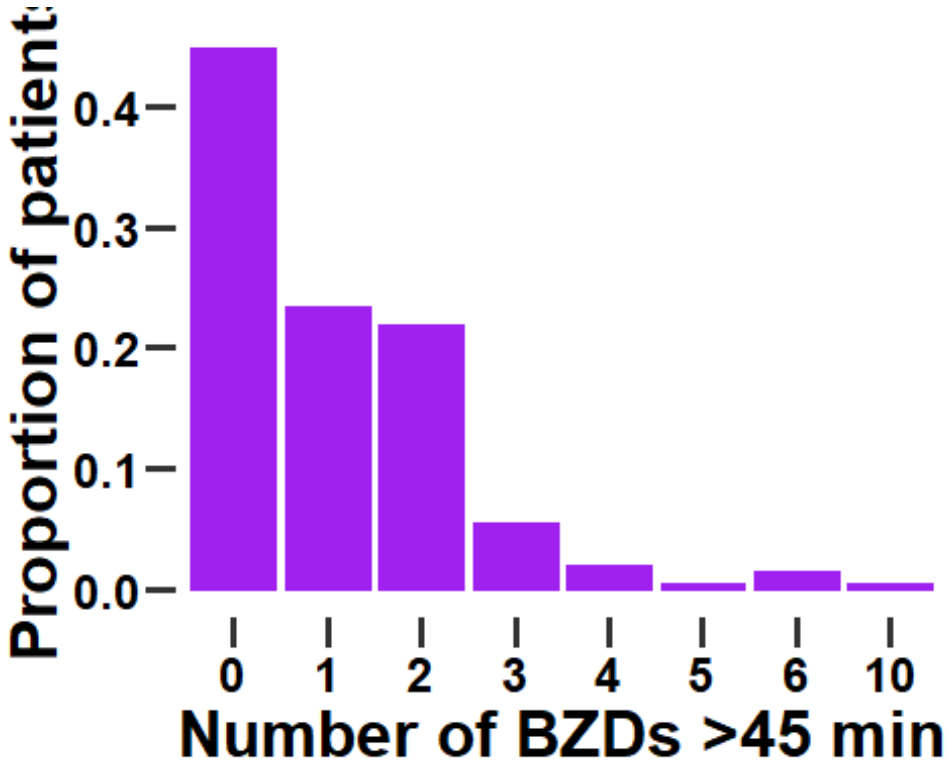
```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$preAEDBZDsmorethan45)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |         2 |         3 |         4 |
##           |-----------|-----------|-----------|-----------|-----------|
##           |        74 |        12 |         4 |         1 |         1 |
##           |     0.804 |     0.130 |     0.043 |     0.011 |     0.011 |
##           |-----------|-----------|-----------|-----------|-----------|
##
##
##
##
```

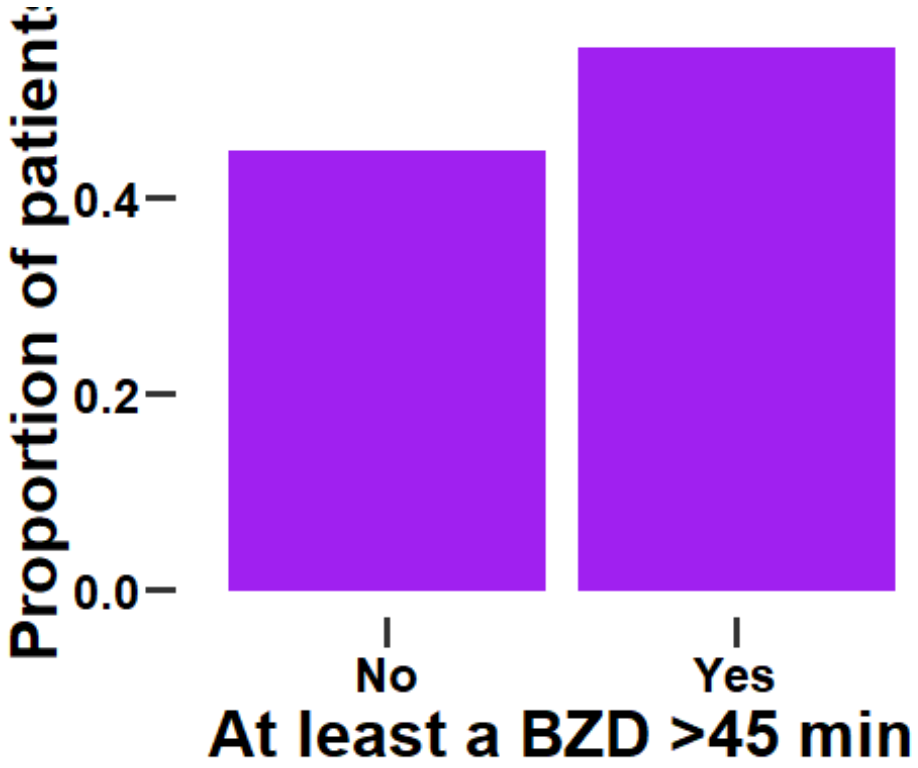
```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"),
]$preAEDBZDsmorethan45yesno)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        90 |       111 |
##           |     0.448 |     0.552 |
##           |-----------|-----------|
##
```

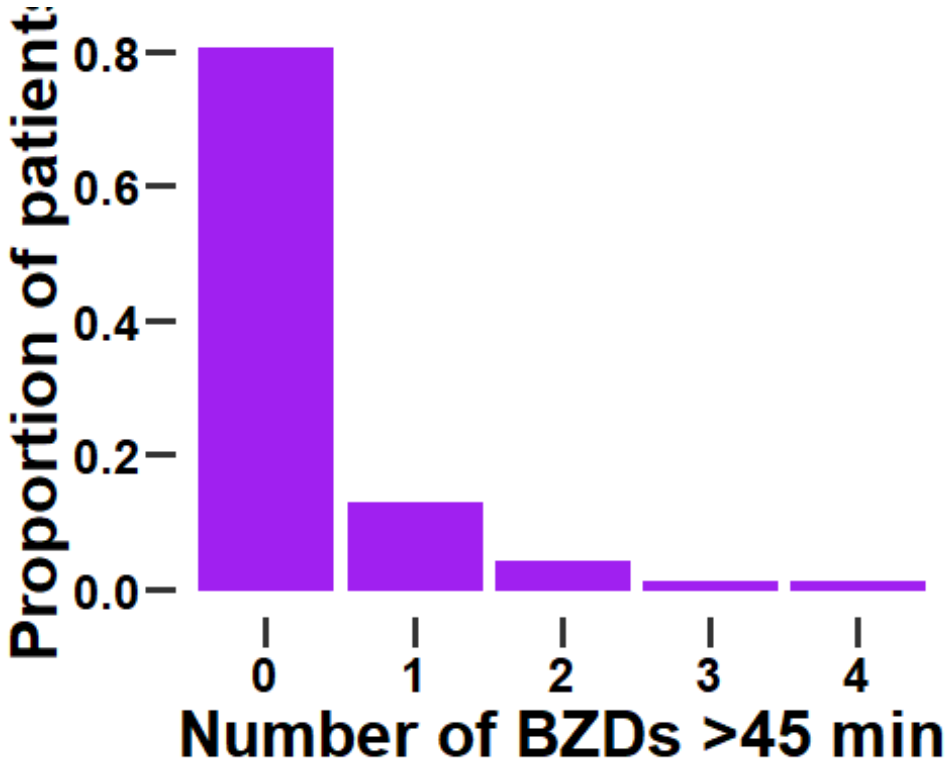
```
##
##
##

CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"),
]$preAEDBZDsmorethan45yesno)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |        74 |        18 |
##            |     0.804 |     0.196 |
##            |-----------|-----------|
##
##
##
##

table(pSERG$preAEDBZDsmorethan45yesno, pSERG$HOSPITALONSET)

##
##      no yes
##   0  90  74
##   1 111  18

# Figure number of benzodiazepines before non-benzodiazepine ASMs given after
45 minutes of seizure onset with onset out of the hospital
figurenumbermorethan45out <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "no"),
], aes(x = as.factor(preAEDBZDsmorethan45))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  xlab("Number of BZDs >45 min") +
  ylab("Proportion of patients")
figurenumbermorethan45out
```



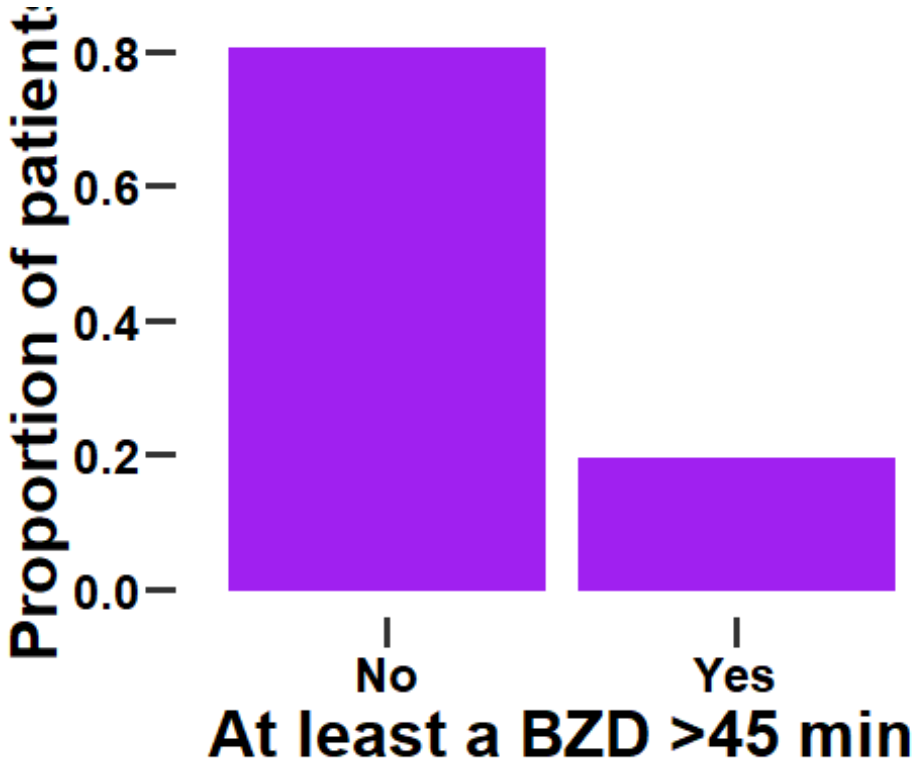

```r
# Figure proportion patients with at least one benzodiazepine given after 45 minutes with onset out of the hospital
figureproportionmorethan45yesnoout <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "no"), ], aes(x = as.factor(preAEDBZDsmorethan45yesno))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill = "purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size = 1.2)) +
  scale_x_discrete(labels = c("0" = "No", "1" = "Yes")) +
  xlab("At least a BZD >45 min") +
  ylab("Proportion of patients")
figureproportionmorethan45yesnoout
```




```
# Figure number of benzodiazepines before non-benzodiazepine ASMs given after
45 minutes of seizure onset with onset in the hospital
figurenumbermorethan45in <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "yes"),
], aes(x = as.factor(preAEDBZDsmorethan45))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill =
"purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size =
1.2)) +
  xlab("Number of BZDs >45 min") +
  ylab("Proportion of patients")
figurenumbermorethan45in
```




```r
# Figure proportion patients with at least one benzodiazepine given after 45 minutes with onset out of the hospital
figureproportionmorethan45yesnoin <- ggplot(pSERG[which(pSERG$HOSPITALONSET == "yes"), ], aes(x = as.factor(preAEDBZDsmorethan45yesno))) +
  geom_bar(aes(y = (..count..) / sum(..count..)), color = "purple", fill = "purple") +
  theme(panel.background = element_rect(fill = "white"),
        axis.text = element_text(size = 18, color = "black", face = "bold"),
        axis.title = element_text(size = 24, color = "black", face = "bold"),
        axis.ticks.length = unit(0.4, "cm"), axis.ticks = element_line(size = 1.2)) +
  scale_x_discrete(labels = c("0" = "No", "1" = "Yes")) +
  xlab("At least a BZD >45 min") +
  ylab("Proportion of patients")
figureproportionmorethan45yesnoin
```



Regression models

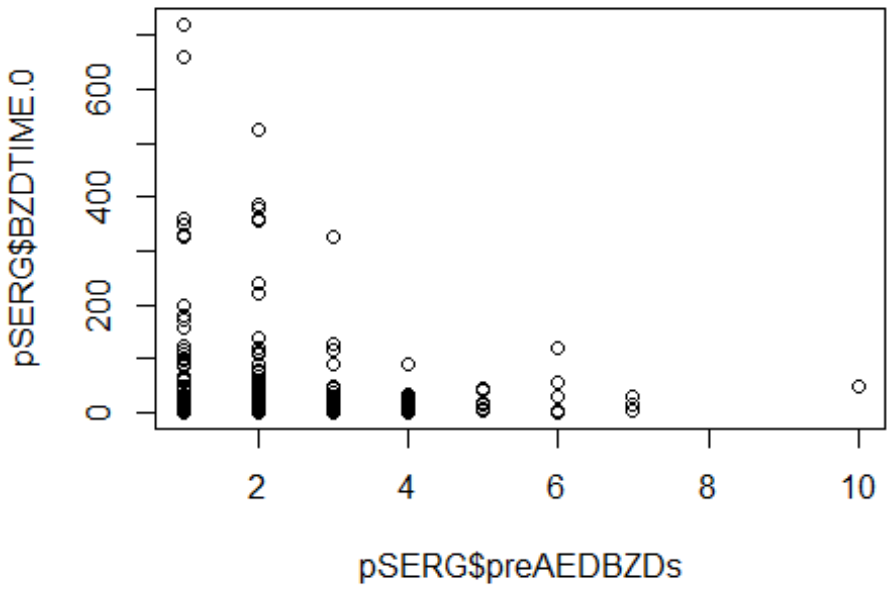
```
pSERG$BZD1stdosinginadequate <- ifelse(pSERG$TOTALDZPINADEQUATESINGLEDOSE ==
1 | pSERG$LZPinadequateSINGLEDOSE == 1 | pSERG$TOTALMDZINADEQUATESINGLEDOSE
== 1 | pSERG$TOTALCLZINADEQUATESINGLEDOSE == 1, 1, 0)
table(pSERG$BZD1stdosinginadequate)

##
##   0   1
## 127 166

# by subgroups
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"),
]$BZD1stdosinginadequate)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
```

```
##           |-----------|-----------|
##           |        95 |       106 |
##           |     0.473 |     0.527 |
##           |-----------|-----------|
##
##
##
##
```

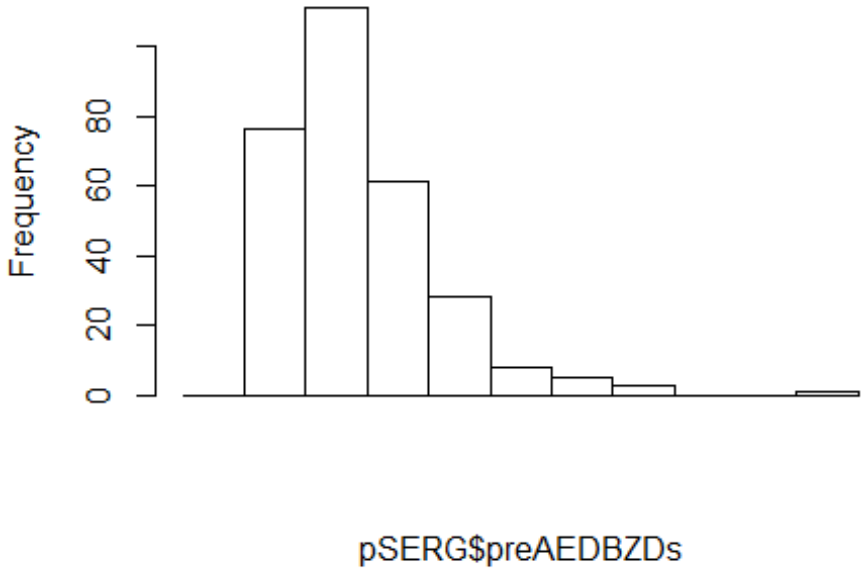
```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"),
]$BZD1stdosinginadequate)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        32 |        60 |
##           |     0.348 |     0.652 |
##           |-----------|-----------|
##
##
##
##
```

```
pSERG$priorSE <- as.factor(as.numeric(pSERG$priorSE))
pSERG$priorepilepsy <- as.factor(as.numeric(pSERG$priorepilepsy))
pSERG$BZD1stdosinginadequate <-
as.factor(as.numeric(pSERG$BZD1stdosinginadequate))
pSERG$delayedtreatmentinitiation <-
as.factor(as.numeric(pSERG$delayedtreatmentinitiation))

plot(pSERG$preAEDBZDs, pSERG$BZDTIME.0)
```




```
# 1.    Outcome = Number of BZD doses before non-BZD ASM

## Distribution of data
hist(pSERG$preAEDBZDs, xlim=c(-1,10), breaks=c(-1,0,1,2,3,4,5,6,7,8,9,10),
main = " ",  xaxt = "n")
```




```
table(pSERG$preAEDBZDs)

##
##   1   2   3   4   5   6   7  10
##  76 111  61  28   8   5   3   1

# Model
t <- glm.nb(pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears + pSERG$TYPESTATUS
+ (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy + pSERG$priorSE +
pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0)

## Warning in theta.ml(Y, mu, sum(w), w, limit = control$maxit, trace =
## control$trace > : iteration limit reached

## Warning in theta.ml(Y, mu, sum(w), w, limit = control$maxit, trace =
## control$trace > : iteration limit reached

summary(t)

##
## Call:
## glm.nb(formula = pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE + pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0,
##     init.theta = 56894.99667, link = log)
##
## Deviance Residuals:
```

```
##     Min       1Q   Median       3Q      Max
## -1.3853  -0.6190  -0.1080   0.3402   3.7225
##
## Coefficients:
##                                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)                     0.7542560  0.1242568   6.070 1.28e-09 ***
## pSERG$SEXmale                   0.0370008  0.0785400   0.471   0.6376
## pSERG$ageyears                 -0.0014457  0.0077079  -0.188   0.8512
## pSERG$TYPESTATUSintermittent   -0.0411815  0.0801379  -0.514   0.6073
## pSERG$HOSPITALONSET == "no"TRUE  0.1608927  0.0877559   1.833   0.0667 .
## pSERG$priorepilepsy1            0.0622880  0.0851427   0.732   0.4644
## pSERG$priorSE1                  0.1462122  0.0959589   1.524   0.1276
## pSERG$BZD1stdosinginadequate1  -0.0007244  0.0801684  -0.009   0.9928
## pSERG$BZDTIME.0                -0.0013930  0.0005556  -2.507   0.0122 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(56895) family taken to be 1)
##
##     Null deviance: 187.54  on 292  degrees of freedom
## Residual deviance: 170.97  on 284  degrees of freedom
## AIC: 968.76
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  56895
##           Std. Err.:  484962
## Warning while fitting theta: iteration limit reached
##
##  2 x log-likelihood:  -948.758
```

```
(bettacoefficients_withCIt <- cbind(Estimate = coef(t), confint(t)))
```

```
## Waiting for profiling to be done...
```

```
##                                    Estimate        2.5 %        97.5 %
## (Intercept)                     0.754255955  0.507488124  0.9946094907
## pSERG$SEXmale                   0.037000819 -0.116510390  0.1914923418
## pSERG$ageyears                 -0.001445710 -0.016739887  0.0134857515
## pSERG$TYPESTATUSintermittent   -0.041181450 -0.197387902  0.1169012632
## pSERG$HOSPITALONSET == "no"TRUE  0.160892702 -0.009468650  0.3347096803
## pSERG$priorepilepsy1            0.062287968 -0.104778340  0.2290838056
## pSERG$priorSE1                  0.146212168 -0.043930860  0.3324226631
## pSERG$BZD1stdosinginadequate1  -0.000724372 -0.157604143  0.1567736231
## pSERG$BZDTIME.0                -0.001392976 -0.002546176 -0.0003635395
```

```
(IR_withCIt <- exp(bettacoefficients_withCIt))
```

```
##                                  Estimate     2.5 %    97.5 %
## (Intercept)                     2.1260291 1.6611134 2.7036683
```

```
## pSERG$SEXmale                    1.0376939 0.8900208 1.2110556
## pSERG$ageyears                   0.9985553 0.9833994 1.0135771
## pSERG$TYPESTATUSintermittent     0.9596550 0.8208722 1.1240084
## pSERG$HOSPITALONSET == "no"TRUE 1.1745589 0.9905760 1.3975346
## pSERG$priorepilepsy1             1.0642688 0.9005241 1.2574474
## pSERG$priorSE1                   1.1574417 0.9570201 1.3943421
## pSERG$BZD1stdosinginadequate1    0.9992759 0.8541879 1.1697308
## pSERG$BZDTIME.0                  0.9986080 0.9974571 0.9996365
```

```
x <- glm(pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears + pSERG$TYPESTATUS +
(pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy + pSERG$priorSE +
pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0, family = "poisson")
summary(x)
```

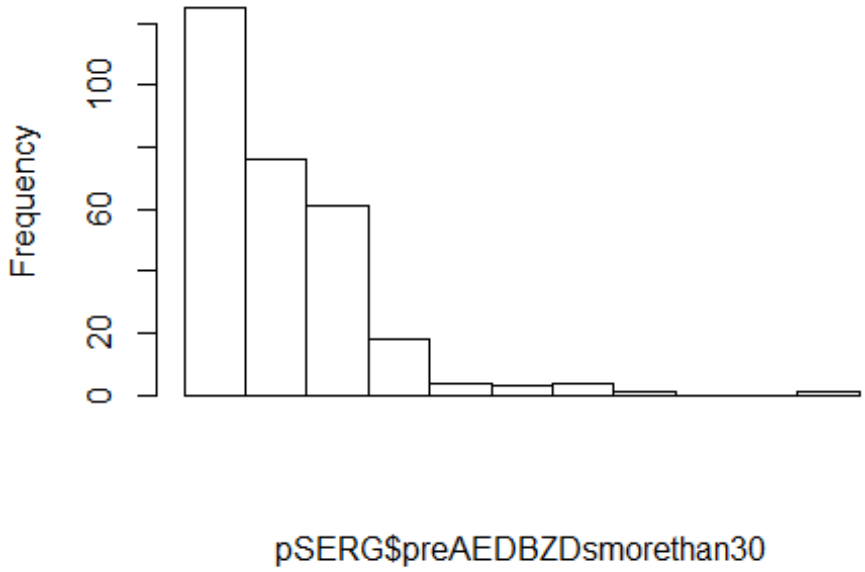
```
##
## Call:
## glm(formula = pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE + pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0,
##     family = "poisson")
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.3854  -0.6190  -0.1080   0.3402   3.7227
##
## Coefficients:
##                                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)                     0.7542563  0.1242528   6.070 1.28e-09 ***
## pSERG$SEXmale                   0.0370008  0.0785372   0.471   0.6376
## pSERG$ageyears                 -0.0014457  0.0077077  -0.188   0.8512
## pSERG$TYPESTATUSintermittent   -0.0411812  0.0801350  -0.514   0.6073
## pSERG$HOSPITALONSET == "no"TRUE  0.1608927  0.0877531   1.833   0.0667 .
## pSERG$priorepilepsy1            0.0622878  0.0851395   0.732   0.4644
## pSERG$priorSE1                  0.1462123  0.0959556   1.524   0.1276
## pSERG$BZD1stdosinginadequate1  -0.0007245  0.0801654  -0.009   0.9928
## pSERG$BZDTIME.0                -0.0013930  0.0005556  -2.507   0.0122 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for poisson family taken to be 1)
##
##     Null deviance: 187.55  on 292  degrees of freedom
## Residual deviance: 170.98  on 284  degrees of freedom
## AIC: 966.75
##
## Number of Fisher Scoring iterations: 4
```

```
confint(x)
```

```
## Waiting for profiling to be done...
```

```
##                                       2.5 %        97.5 %
## (Intercept)                        0.507493197  0.9946046316
## pSERG$SEXmale                     -0.116507068  0.1914890680
## pSERG$ageyears                    -0.016739602  0.0134853809
## pSERG$TYPESTATUSintermittent      -0.197384229  0.1168981259
## pSERG$HOSPITALONSET == "no"TRUE -0.009464926  0.3347062097
## pSERG$priorepilepsy1              -0.104775059  0.2290801335
## pSERG$priorSE1                    -0.043926525  0.3324182471
## pSERG$BZD1stdosinginadequate1     -0.157600929  0.1567701415
## pSERG$BZDTIME.0                   -0.002546191 -0.0003635338

(bettacoefficients_withCI <- cbind(Estimate = coef(x), confint(x)))

## Waiting for profiling to be done...

##                                        Estimate        2.5 %        97.5 %
## (Intercept)                         0.7542562925  0.507493197  0.9946046316
## pSERG$SEXmale                       0.0370007989 -0.116507068  0.1914890680
## pSERG$ageyears                     -0.0014457401 -0.016739602  0.0134853809
## pSERG$TYPESTATUSintermittent       -0.0411812493 -0.197384229  0.1168981259
## pSERG$HOSPITALONSET == "no"TRUE  0.1608927186 -0.009464926  0.3347062097
## pSERG$priorepilepsy1                0.0622877879 -0.104775059  0.2290801335
## pSERG$priorSE1                      0.1462122687 -0.043926525  0.3324182471
## pSERG$BZD1stdosinginadequate1     -0.0007245323 -0.157600929  0.1567701415
## pSERG$BZDTIME.0                   -0.0013929800 -0.002546191 -0.0003635338

(IR_withCI <- exp(bettacoefficients_withCI))

##                                    Estimate     2.5 %    97.5 %
## (Intercept)                       2.1260298 1.6611219 2.7036552
## pSERG$SEXmale                     1.0376938 0.8900238 1.2110516
## pSERG$ageyears                    0.9985553 0.9833997 1.0135767
## pSERG$TYPESTATUSintermittent      0.9596552 0.8208752 1.1240049
## pSERG$HOSPITALONSET == "no"TRUE 1.1745590 0.9905797 1.3975297
## pSERG$priorepilepsy1              1.0642686 0.9005271 1.2574428
## pSERG$priorSE1                    1.1574419 0.9570243 1.3943359
## pSERG$BZD1stdosinginadequate1     0.9992757 0.8541906 1.1697267
## pSERG$BZDTIME.0                   0.9986080 0.9974570 0.9996365

#install.packages("lmtest")
library(lmtest)

## Warning: package 'lmtest' was built under R version 3.5.3

## Loading required package: zoo

## Warning: package 'zoo' was built under R version 3.5.2

##
## Attaching package: 'zoo'
```

```
## The following objects are masked from 'package:base':
##
##     as.Date, as.Date.numeric

# Likelihood ratio test to test the best model
lrtest(t, x)

## Warning in modelUpdate(objects[[i - 1]], objects[[i]]): original model was
## of class "negbin", updated model is of class "glm"

## Likelihood ratio test
##
## Model 1: pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears + pSERG$TYPESTATUS
+
##     (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy + pSERG$priorSE +
##     pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0
## Model 2: pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears + pSERG$TYPESTATUS
+
##     (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy + pSERG$priorSE +
##     pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0
##   #Df  LogLik Df  Chisq Pr(>Chisq)
## 1  10 -474.38
## 2   9 -474.38 -1 0.0041     0.9491

# 2.    Outcome = Number of BZD doses before non-BZD ASM and within the first
30 min

## Distribution of data
hist(pSERG$preAEDBZDsmorethan30, xlim=c(-1,10), breaks=c(-
1,0,1,2,3,4,5,6,7,8,9,10), main = " ",  xaxt = "n")
```




```
table(pSERG$preAEDBZDsmorethan30)

##
##   0   1   2   3   4   5   6   7  10
## 125  76  61  18   4   3   4   1   1

# Model
a <- glm.nb(pSERG$preAEDBZDsmorethan30 ~ pSERG$SEX + pSERG$ageyears +
pSERG$TYPESTATUS + (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy +
pSERG$priorSE)
summary(a)

##
## Call:
## glm.nb(formula = pSERG$preAEDBZDsmorethan30 ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE, init.theta = 2.485299922, link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.5698  -1.0306  -0.2961   0.4115   3.1695
##
## Coefficients:
##                                Estimate Std. Error z value Pr(>|z|)
## (Intercept)                   -0.786868   0.224908  -3.499 0.000468 ***
## pSERG$SEXmale                  0.103165   0.139683   0.739 0.460174
```

```
## pSERG$ageyears                     0.004639   0.013289   0.349 0.727019
## pSERG$TYPESTATUSintermittent       0.135908   0.145238   0.936 0.349397
## pSERG$HOSPITALONSET == "no"TRUE    0.888142   0.174695   5.084  3.7e-07 ***
## pSERG$priorepilepsy1               0.085555   0.145837   0.587 0.557442
## pSERG$priorSE1                    -0.080348   0.179303  -0.448 0.654073
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(2.4853) family taken to be 1)
##
##     Null deviance: 342.20  on 292  degrees of freedom
## Residual deviance: 309.85  on 286  degrees of freedom
## AIC: 832.71
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  2.485
##           Std. Err.:  0.730
##
##  2 x log-likelihood:  -816.706
```

```
confint(a)
```

```
## Waiting for profiling to be done...
```

```
##                                       2.5 %      97.5 %
## (Intercept)                      -1.23429868 -0.35569482
## pSERG$SEXmale                    -0.17047067  0.37830294
## pSERG$ageyears                   -0.02138531  0.03034669
## pSERG$TYPESTATUSintermittent     -0.14742656  0.42287399
## pSERG$HOSPITALONSET == "no"TRUE   0.55069535  1.24056156
## pSERG$priorepilepsy1             -0.20122341  0.37232157
## pSERG$priorSE1                   -0.43691297  0.26908085
```

```
(abettacoefficients_withCI <- cbind(Estimate = coef(a), confint(a)))
```

```
## Waiting for profiling to be done...
```

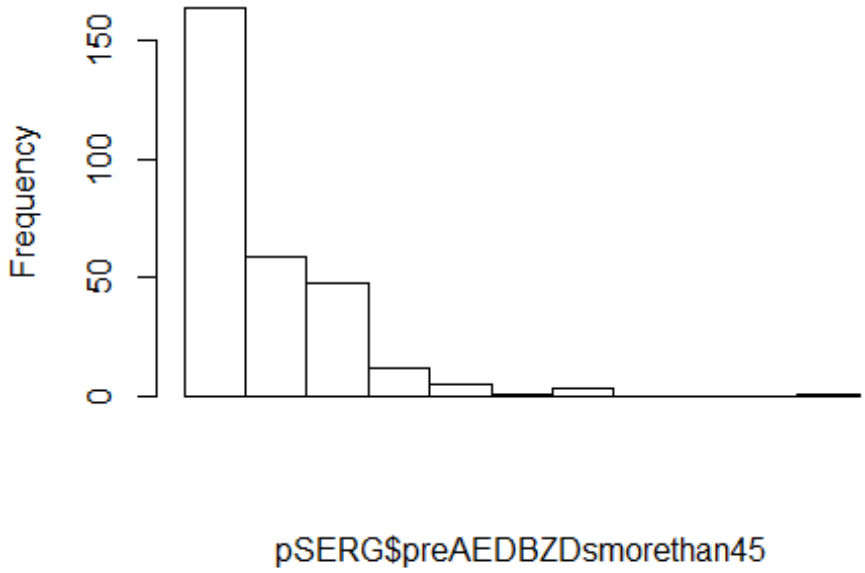
```
##                                      Estimate       2.5 %      97.5 %
## (Intercept)                      -0.786868057 -1.23429868 -0.35569482
## pSERG$SEXmale                     0.103164524 -0.17047067  0.37830294
## pSERG$ageyears                    0.004639142 -0.02138531  0.03034669
## pSERG$TYPESTATUSintermittent      0.135907776 -0.14742656  0.42287399
## pSERG$HOSPITALONSET == "no"TRUE   0.888142496  0.55069535  1.24056156
## pSERG$priorepilepsy1              0.085554538 -0.20122341  0.37232157
## pSERG$priorSE1                   -0.080347640 -0.43691297  0.26908085
```

```
(aIR_withCI <- exp(abettacoefficients_withCI))
```

```
##                                    Estimate     2.5 %    97.5 %
## (Intercept)                      0.4552684 0.2910388 0.7006864
```

```
## pSERG$SEXmale                    1.1086738 0.8432678 1.4598051
## pSERG$ageyears                   1.0046499 0.9788417 1.0308118
## pSERG$TYPESTATUSintermittent     1.1455762 0.8629258 1.5263420
## pSERG$HOSPITALONSET == "no"TRUE 2.4306106 1.7344587 3.4575546
## pSERG$priorepilepsy1             1.0893210 0.8177297 1.4510995
## pSERG$priorSE1                   0.9227955 0.6460277 1.3087610
```

```
# 3.    Outcome = Number of BZD doses before non-BZD ASM and within the first 45 min

## Distribution of data
hist(pSERG$preAEDBZDsmorethan45, xlim=c(-1,10), breaks=c(-1,0,1,2,3,4,5,6,7,8,9,10), main = " ",  xaxt = "n")
```




```
table(pSERG$preAEDBZDsmorethan45)

##
##   0   1   2   3   4   5   6  10
## 164  59  48  12   5   1   3   1

# Model
b <- glm.nb(pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears + pSERG$TYPESTATUS + (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy + pSERG$priorSE)
summary(b)

##
## Call:
```

```
## glm.nb(formula = pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE, init.theta = 1.478189662, link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.4147  -1.1428  -0.6648   0.3748   3.2284
##
## Coefficients:
##                                 Estimate Std. Error z value Pr(>|z|)
## (Intercept)                     -1.57173    0.29324  -5.360 8.33e-08 ***
## pSERG$SEXmale                    0.04449    0.16961   0.262   0.7931
## pSERG$ageyears                   0.01054    0.01603   0.658   0.5108
## pSERG$TYPESTATUSintermittent     0.36239    0.18131   1.999   0.0456 *
## pSERG$HOSPITALONSET == "no"TRUE  1.32128    0.23233   5.687 1.29e-08 ***
## pSERG$priorepilepsy1             0.06443    0.17641   0.365   0.7150
## pSERG$priorSE1                  -0.18989    0.22298  -0.852   0.3944
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(1.4782) family taken to be 1)
##
##     Null deviance: 322.07  on 292  degrees of freedom
## Residual deviance: 277.20  on 286  degrees of freedom
## AIC: 714.7
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  1.478
##           Std. Err.:  0.408
##
##  2 x log-likelihood:  -698.700
```

```
confint(b)
```

```
## Waiting for profiling to be done...
```

```
##                                      2.5 %      97.5 %
## (Intercept)                     -2.156830696 -1.01717709
## pSERG$SEXmale                   -0.288106330  0.37793635
## pSERG$ageyears                  -0.020758038  0.04168883
## pSERG$TYPESTATUSintermittent     0.008479591  0.72245346
## pSERG$HOSPITALONSET == "no"TRUE  0.877137274  1.79691521
## pSERG$priorepilepsy1            -0.285585698  0.41429525
## pSERG$priorSE1                  -0.635034544  0.24596676
```

```
(bbettacoefficients_withCI <- cbind(Estimate = coef(b), confint(b)))
```

```
## Waiting for profiling to be done...
```

```
##                                    Estimate        2.5 %      97.5 %
## (Intercept)                     -1.57173065 -2.156830696 -1.01717709
## pSERG$SEXmale                    0.04449135 -0.288106330  0.37793635
## pSERG$ageyears                   0.01053825 -0.020758038  0.04168883
## pSERG$TYPESTATUSintermittent     0.36239111  0.008479591  0.72245346
## pSERG$HOSPITALONSET == "no"TRUE  1.32128357  0.877137274  1.79691521
## pSERG$priorepilepsy1             0.06442568 -0.285585698  0.41429525
## pSERG$priorSE1                  -0.18988510 -0.635034544  0.24596676
```

```
(bIR_withCI <- exp(bbettacoefficients_withCI))
```

```
##                                   Estimate     2.5 %    97.5 %
## (Intercept)                     0.2076854 0.1156912 0.3616143
## pSERG$SEXmale                   1.0454959 0.7496819 1.4592701
## pSERG$ageyears                  1.0105940 0.9794559 1.0425700
## pSERG$TYPESTATUSintermittent    1.4367608 1.0085156 2.0594799
## pSERG$HOSPITALONSET == "no"TRUE 3.7482294 2.4040078 6.0310143
## pSERG$priorepilepsy1            1.0665463 0.7515739 1.5133039
## pSERG$priorSE1                  0.8270542 0.5299172 1.2788571
```

```
v <- glm.nb(pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
pSERG$TYPESTATUS + pSERG$HOSPITALONSET + pSERG$priorepilepsy + pSERG$priorSE
+ pSERG$TYPESTATUS*pSERG$HOSPITALONSET)
summary(v)
```

```
##
## Call:
## glm.nb(formula = pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + pSERG$HOSPITALONSET + pSERG$priorepilepsy +
##     pSERG$priorSE + pSERG$TYPESTATUS * pSERG$HOSPITALONSET, init.theta =
1.478237345,
##     link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.4144  -1.1435  -0.6618   0.3752   3.2381
##
## Coefficients:
##                                                    Estimate Std. Error
## (Intercept)                                       -0.24925    0.22375
## pSERG$SEXmale                                      0.04471    0.16962
## pSERG$ageyears                                     0.01055    0.01605
## pSERG$TYPESTATUSintermittent                       0.36048    0.19468
## pSERG$HOSPITALONSETyes                            -1.33220    0.46721
## pSERG$priorepilepsy1                               0.06442    0.17643
## pSERG$priorSE1                                    -0.19021    0.22325
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes  0.01451    0.53668
##                                                   z value Pr(>|z|)
## (Intercept)                                        -1.114  0.26528
## pSERG$SEXmale                                       0.264  0.79211
## pSERG$ageyears                                      0.657  0.51121
```

```
## pSERG$TYPESTATUSintermittent                              1.852  0.06407 .
## pSERG$HOSPITALONSETyes                                   -2.851  0.00435 **
## pSERG$priorepilepsy1                                      0.365  0.71503
## pSERG$priorSE1                                           -0.852  0.39420
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes       0.027  0.97843
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(1.4782) family taken to be 1)
##
##     Null deviance: 322.07  on 292  degrees of freedom
## Residual deviance: 277.20  on 285  degrees of freedom
## AIC: 716.7
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  1.478
##           Std. Err.:  0.408
##
##  2 x log-likelihood:  -698.699
```

```
confint(v)
```

```
## Waiting for profiling to be done...
```

```
##                                                           2.5 %
## (Intercept)                                          -0.68314310
## pSERG$SEXmale                                        -0.28825942
## pSERG$ageyears                                       -0.02075514
## pSERG$TYPESTATUSintermittent                         -0.02002705
## pSERG$HOSPITALONSETyes                               -2.34452714
## pSERG$priorepilepsy1                                 -0.28558289
## pSERG$priorSE1                                       -0.63594567
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes -0.99528352
##                                                          97.5 %
## (Intercept)                                           0.17577057
## pSERG$SEXmale                                         0.37851459
## pSERG$ageyears                                        0.04170022
## pSERG$TYPESTATUSintermittent                          0.74626282
## pSERG$HOSPITALONSETyes                               -0.48200659
## pSERG$priorepilepsy1                                  0.41427807
## pSERG$priorSE1                                        0.24630610
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes   1.13851037
```

```
(vbettacoefficients_withCI <- cbind(Estimate = coef(v), confint(v)))
```

```
## Waiting for profiling to be done...
```

```
##                                                        Estimate
## (Intercept)                                          -0.24925473
```

```
## pSERG$SEXmale                                          0.04470830
## pSERG$ageyears                                         0.01054564
## pSERG$TYPESTATUSintermittent                           0.36047651
## pSERG$HOSPITALONSETyes                                -1.33220006
## pSERG$priorepilepsy1                                   0.06441622
## pSERG$priorSE1                                        -0.19021049
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes    0.01450730
##                                                             2.5 %
## (Intercept)                                           -0.68314310
## pSERG$SEXmale                                         -0.28825942
## pSERG$ageyears                                        -0.02075514
## pSERG$TYPESTATUSintermittent                          -0.02002705
## pSERG$HOSPITALONSETyes                                -2.34452714
## pSERG$priorepilepsy1                                  -0.28558289
## pSERG$priorSE1                                        -0.63594567
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes   -0.99528352
##                                                            97.5 %
## (Intercept)                                            0.17577057
## pSERG$SEXmale                                          0.37851459
## pSERG$ageyears                                         0.04170022
## pSERG$TYPESTATUSintermittent                           0.74626282
## pSERG$HOSPITALONSETyes                                -0.48200659
## pSERG$priorepilepsy1                                   0.41427807
## pSERG$priorSE1                                         0.24630610
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes    1.13851037

(vIR_withCI <- exp(vbettacoefficients_withCI))

##                                                        Estimate      2.5 %
## (Intercept)                                           0.7793814 0.50502715
## pSERG$SEXmale                                         1.0457228 0.74956711
## pSERG$ageyears                                        1.0106014 0.97945877
## pSERG$TYPESTATUSintermittent                          1.4340126 0.98017216
## pSERG$HOSPITALONSETyes                                0.2638960 0.09589254
## pSERG$priorepilepsy1                                  1.0665362 0.75157604
## pSERG$priorSE1                                        0.8267851 0.52943458
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes   1.0146130 0.36961864
##                                                         97.5 %
## (Intercept)                                           1.192165
## pSERG$SEXmale                                         1.460114
## pSERG$ageyears                                        1.042582
## pSERG$TYPESTATUSintermittent                          2.109103
## pSERG$HOSPITALONSETyes                                0.617543
## pSERG$priorepilepsy1                                  1.513278
## pSERG$priorSE1                                        1.279291
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes   3.122114
```

First non-benzodiazepine ASM

Description of the first non-benzodiazepine ASM.

```r
# Time to first non-benzodiazepine ASM
summary(pSERG$AEDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##     3.0    35.0    63.0   143.5   126.0  4320.0
```

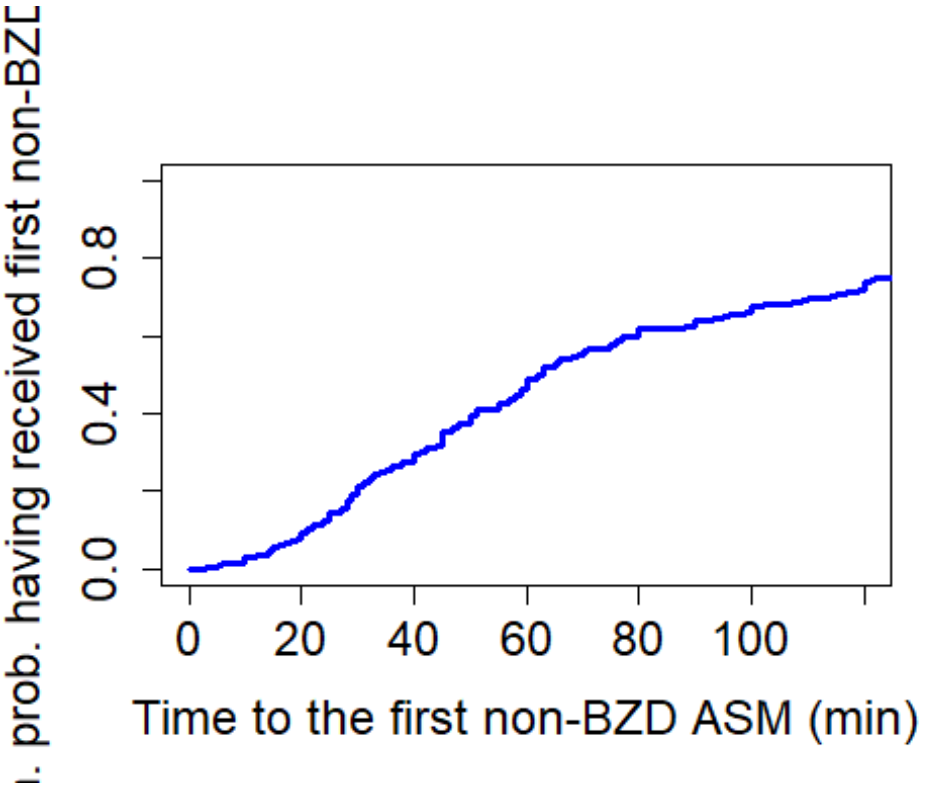
```r
sd(pSERG$AEDTIME.0)
```

```
## [1] 317.0263
```

```r
survfit(Surv(pSERG$AEDTIME.0) ~ 1)
```

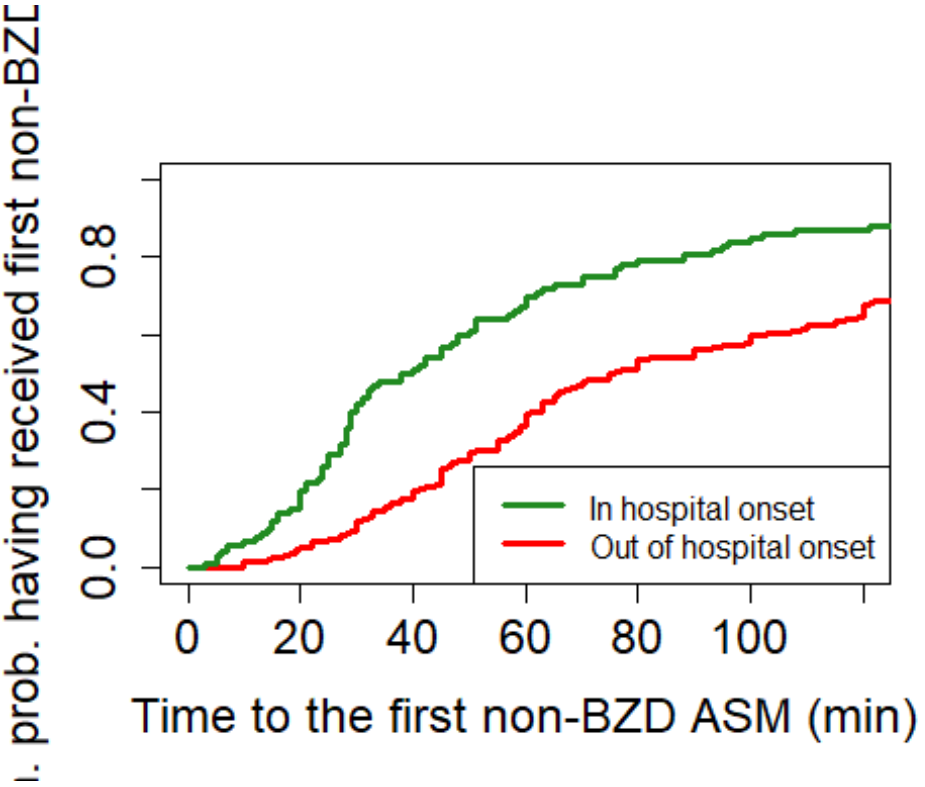
```
## Call: survfit(formula = Surv(pSERG$AEDTIME.0) ~ 1)
##
##       n  events  median 0.95LCL 0.95UCL
##     293     293      63      58      70
```

```r
# Figure time to first non-benzodiazepine ASM
plot(survfit(Surv(pSERG$AEDTIME.0) ~ 1), fun = "event",
     conf.int = FALSE, xlim = c(0, 120), col = "blue", lwd = 3,
     cex.axis = 1.5, cex.lab = 1.5,
     xlab="Time to the first non-BZD ASM (min)", ylab="Cum. prob. having
received first non-BZD ASM")
```




```r
# Time to first non-benzodiazepine ASM by hospital onset group
summary(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$AEDTIME.0)
```

```
##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    10.0    45.0    76.0   171.1   155.0  4320.0

summary(pSERG[which(pSERG$HOSPITALONSET == "yes"), ]$AEDTIME.0)

##    Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
##    3.00   24.00   39.00   83.27   71.50 1488.00

survdiff(Surv(pSERG$AEDTIME.0) ~ pSERG$hospitalonsetnumeric, rho = 1)

## Call:
## survdiff(formula = Surv(pSERG$AEDTIME.0) ~ pSERG$hospitalonsetnumeric,
##     rho = 1)
##
##                                 N Observed Expected (O-E)^2/E (O-E)^2/V
## pSERG$hospitalonsetnumeric=0 201     88.2    115.1      6.26      40.8
## pSERG$hospitalonsetnumeric=1  92     60.0     33.1     21.78      40.8
##
##  Chisq= 40.8  on 1 degrees of freedom, p= 2e-10

# Figure time to first non-BZD by hospital onset
plot(survfit(Surv(pSERG$AEDTIME.0) ~ pSERG$hospitalonsetnumeric), fun =
"event",
     conf.int = FALSE, xlim = c(0, 120), col = c("red", "forestgreen"), lwd =
3,
     cex.axis = 1.5, cex.lab = 1.5,
     xlab="Time to the first non-BZD ASM (min)", ylab="Cum. prob. having
received first non-BZD ASM")
legend(x = "bottomright", legend = c("In hospital onset", "Out of hospital
onset"), col = c("forestgreen", "red"), lty = 1, lwd = 3)
```



Reasons for the distribution of medications

Number of benzodiazepines before non-benzodiazepine ASMs or continuous infusions.

```
## Patients who did not receive any treatment before arriving into the
hospital
# Create variable first benzodiazepine in hospital
pSERG$firstBZDinhospital[pSERG$BZDLOCATION.0 == "home"] <- 0
pSERG$firstBZDinhospital[pSERG$BZDLOCATION.0 == "EMS"] <- 0
pSERG$firstBZDinhospital[pSERG$BZDLOCATION.0 == "outsideh"] <- 1
pSERG$firstBZDinhospital[pSERG$BZDLOCATION.0 == "studyh"] <- 1

# No medication before hospital arrival
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$BZDLOCATION.0)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
```

```
##            |       EMS |      home |  outsideh |    studyh |
##            |-----------|-----------|-----------|-----------|
##            |        51 |        56 |        47 |        47 |
##            |     0.254 |     0.279 |     0.234 |     0.234 |
##            |-----------|-----------|-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$firstBZDinhospital)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##            |         0 |         1 |
##            |-----------|-----------|
##            |       107 |        94 |
##            |     0.532 |     0.468 |
##            |-----------|-----------|
##
##
##
##
```

```
# Prior epilepsy in patients who did not receive any treatment before
arriving into the hospital
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no" & pSERG$firstBZDinhospital
== 1), ]$priorepilepsy)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  94
##
##
```

```
##           |         0 |         1 |
##           |-----------|-----------|
##           |        54 |        40 |
##           |     0.574 |     0.426 |
##           |-----------|-----------|
##
##
##
##

## Prior status epilepticus in patients who did not receive any treatment
before arriving into the hospital
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no" & pSERG$firstBZDinhospital
== 1), ]$priorSE)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  94
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        84 |        10 |
##           |     0.894 |     0.106 |
##           |-----------|-----------|
##
##
##
##

## Three or more benzodiazepines before the first non-benzodiazepine ASM
# Patients who received 3 or more doses of benzodiazepines prior to a non-
benzodiazepine ASM
CrossTable(pSERG$threeormorepreAEDBZDs)

##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
```

```
## Total Observations in Table:  293
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       187 |       106 |
##           |     0.638 |     0.362 |
##           |-----------|-----------|
##
##
##
##
```

```
# Patients who received 3 or more doses of benzodiazepines prior to a non-
benzodiazepine ASM by subgroup of hospital onset
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "no"), ]$threeormorepreAEDBZDs)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  201
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |       123 |        78 |
##           |     0.612 |     0.388 |
##           |-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$HOSPITALONSET == "yes"),
]$threeormorepreAEDBZDs)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
```

```
## Total Observations in Table:  92
##
##
##           |         0 |         1 |
##           |-----------|-----------|
##           |        64 |        28 |
##           |     0.696 |     0.304 |
##           |-----------|-----------|
##
##
##
##
```

```
# Location of the third benzodiazepine administered before a non-
benzodiazepine ASM
CrossTable(pSERG[which(pSERG$threeormorepreAEDBZDs == 1), ]$BZDLOCATION.2)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  106
##
##
##           |       EMS |      home |  outsideh |    studyh |
##           |-----------|-----------|-----------|-----------|
##           |        23 |         4 |        31 |        48 |
##           |     0.217 |     0.038 |     0.292 |     0.453 |
##           |-----------|-----------|-----------|-----------|
##
##
##
##
```

```
# Location of the third benzodiazepine administered before a non-
benzodiazepine ASM by subgroup of hospital onset
CrossTable(pSERG[which(pSERG$threeormorepreAEDBZDs == 1 & pSERG$HOSPITALONSET
== "no"), ]$BZDLOCATION.2)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
```

```
##
##
## Total Observations in Table:  78
##
##
##           |       EMS |      home |  outsideh |    studyh |
##           |-----------|-----------|-----------|-----------|
##           |        23 |         4 |        28 |        23 |
##           |     0.295 |     0.051 |     0.359 |     0.295 |
##           |-----------|-----------|-----------|-----------|
##
##
##
##
```

```
CrossTable(pSERG[which(pSERG$threeormorepreAEDBZDs == 1 & pSERG$HOSPITALONSET
== "yes"), ]$BZDLOCATION.2)
```

```
##
##
##    Cell Contents
## |-------------------------|
## |                       N |
## |         N / Table Total |
## |-------------------------|
##
##
## Total Observations in Table:  28
##
##
##           |  outsideh |    studyh |
##           |-----------|-----------|
##           |         3 |        25 |
##           |     0.107 |     0.893 |
##           |-----------|-----------|
##
##
##
##
```

```
## Number of benzodiazepines in the hospital once they have received at least
one benzodiazepine out of the hospital
# Create location of benzodiazepine only for benzodiazepines given before
first non-BZD ASM
for (i in 1 : dim(pSERG)[1]) {
    if (pSERG$preAEDBZDs[i] >= 1) {
    pSERG$preAEDBZDlocation0[i] <- as.character(pSERG$BZDLOCATION.0[i])
  } else {
    pSERG$preAEDBZDlocation0[i] <- NA
  }
```

```
}
pSERG$preAEDBZDlocation0 <- as.factor(pSERG$preAEDBZDlocation0)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 2) {
    pSERG$preAEDBZDlocation1[i] <- as.character(pSERG$BZDLOCATION.1[i])
  }  else {
    pSERG$preAEDBZDlocation1[i] <- NA
  }
}
pSERG$preAEDBZDlocation1 <- as.factor(pSERG$preAEDBZDlocation1)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 3) {
    pSERG$preAEDBZDlocation2[i] <- as.character(pSERG$BZDLOCATION.2[i])
  }  else {
    pSERG$preAEDBZDlocation2[i] <- NA
  }
}
pSERG$preAEDBZDlocation2 <- as.factor(pSERG$preAEDBZDlocation2)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 4) {
    pSERG$preAEDBZDlocation3[i] <- as.character(pSERG$BZDLOCATION.3[i])
  }  else {
    pSERG$preAEDBZDlocation3[i] <- NA
  }
}
pSERG$preAEDBZDlocation3 <- as.factor(pSERG$preAEDBZDlocation3)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 5) {
    pSERG$preAEDBZDlocation4[i] <- as.character(pSERG$BZDLOCATION.4[i])
  }  else {
    pSERG$preAEDBZDlocation4[i] <- NA
  }
}
pSERG$preAEDBZDlocation4 <- as.factor(pSERG$preAEDBZDlocation4)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 6) {
    pSERG$preAEDBZDlocation5[i] <- as.character(pSERG$BZDLOCATION.5[i])
  }  else {
    pSERG$preAEDBZDlocation5[i] <- NA
  }
}
pSERG$preAEDBZDlocation5 <- as.factor(pSERG$preAEDBZDlocation5)

for (i in 1 : dim(pSERG)[1]) {
```

```
  if (pSERG$preAEDBZDs[i] >= 7) {
    pSERG$preAEDBZDlocation6[i] <- as.character(pSERG$BZDLOCATION.6[i])
  }  else {
    pSERG$preAEDBZDlocation6[i] <- NA
  }
}
pSERG$preAEDBZDlocation6 <- as.factor(pSERG$preAEDBZDlocation6)


for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 8) {
    pSERG$preAEDBZDlocation7[i] <- as.character(pSERG$BZDLOCATION.7[i])
  }  else {
    pSERG$preAEDBZDlocation7[i] <- NA
  }
}
pSERG$preAEDBZDlocation7 <- as.factor(pSERG$preAEDBZDlocation7)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 9) {
    pSERG$preAEDBZDlocation8[i] <- as.character(pSERG$BZDLOCATION.8[i])
  }  else {
    pSERG$preAEDBZDlocation8[i] <- NA
  }
}
pSERG$preAEDBZDlocation8 <- as.factor(pSERG$preAEDBZDlocation8)

for (i in 1 : dim(pSERG)[1]) {
  if (pSERG$preAEDBZDs[i] >= 10) {
    pSERG$preAEDBZDlocation9[i] <- as.character(pSERG$BZDLOCATION.9[i])
  }  else {
    pSERG$preAEDBZDlocation9[i] <- NA
  }
}
pSERG$preAEDBZDlocation9 <- as.factor(pSERG$preAEDBZDlocation9)


# Detail of the findings
pSERG[which(pSERG$firstBZDinhospital == 0), c("preAEDBZDs",
"preAEDBZDlocation0", "preAEDBZDlocation1", "preAEDBZDlocation2",
"preAEDBZDlocation3", "preAEDBZDlocation4", "preAEDBZDlocation5",
"preAEDBZDlocation6", "preAEDBZDlocation7", "preAEDBZDlocation8",
"preAEDBZDlocation9")]

##     preAEDBZDs preAEDBZDlocation0 preAEDBZDlocation1 preAEDBZDlocation2
## 2            3                EMS                EMS                EMS
## 9            4               home                EMS                EMS
## 18           4               home               home                EMS
## 22           4               home               home               home
```

```
## 29           1          EMS          <NA>          <NA>
## 31           2         home           EMS          <NA>
## 36           1          EMS          <NA>          <NA>
## 43           2         home        studyh          <NA>
## 53           2         home        studyh          <NA>
## 56           1          EMS          <NA>          <NA>
## 69           4         home           EMS           EMS
## 71           3          EMS           EMS           EMS
## 72           4          EMS           EMS           EMS
## 78           3         home        studyh        studyh
## 81           2          EMS        studyh          <NA>
## 101          3          EMS        studyh        studyh
## 107          2          EMS        studyh          <NA>
## 112          2         home        studyh          <NA>
## 117          3          EMS        studyh        studyh
## 143          3          EMS        studyh        studyh
## 146          2          EMS     outsideh          <NA>
## 147          3         home           EMS        studyh
## 151          2          EMS     outsideh          <NA>
## 153          3          EMS           EMS     outsideh
## 158          2         home           EMS          <NA>
## 162          3         home        studyh        studyh
## 176          2         home        studyh          <NA>
## 185          1          EMS          <NA>          <NA>
## 193          4          EMS     outsideh     outsideh
## 206          4         home          home           EMS
## 209          3         home           EMS     outsideh
## 211          1         home          <NA>          <NA>
## 217          4         home           EMS     outsideh
## 222          2         home          home          <NA>
## 230          2         home          home          <NA>
## 234          4         home     outsideh     outsideh
## 239          2          EMS           EMS          <NA>
## 248          3          EMS     outsideh     outsideh
## 257          3         home        studyh        studyh
## 267          5         home           EMS           EMS
## 280          5         home     outsideh     outsideh
## 281          2          EMS           EMS          <NA>
## 282          7          EMS           EMS           EMS
## 284          5          EMS     outsideh     outsideh
## 286          3         home           EMS           EMS
## 288          3          EMS           EMS     outsideh
## 289          3         home     outsideh     outsideh
## 294          2          EMS     outsideh          <NA>
## 319          1         home          <NA>          <NA>
## 322          3         home           EMS           EMS
## 331          3         home        studyh        studyh
## 335          2         home          home          <NA>
## 348          6          EMS           EMS           EMS
## 349          4         home          home           EMS
```

```
## 354          2              home            studyh             <NA>
## 361          2              home              home             <NA>
## 363          1              home              <NA>             <NA>
## 369          3              home              home           studyh
## 409          2               EMS               EMS             <NA>
## 411          2               EMS          outsideh             <NA>
## 412          2              home          outsideh             <NA>
## 413          3               EMS            studyh           studyh
## 415          3               EMS          outsideh         outsideh
## 427          2               EMS          outsideh             <NA>
## 431          2               EMS               EMS             <NA>
## 437          2               EMS               EMS             <NA>
## 438          2               EMS               EMS             <NA>
## 440          1               EMS              <NA>             <NA>
## 442          3              home            studyh           studyh
## 448          2               EMS          outsideh             <NA>
## 450          4               EMS          outsideh         outsideh
## 451          7               EMS               EMS         outsideh
## 457          5               EMS               EMS         outsideh
## 459          4               EMS               EMS              EMS
## 462          3              home               EMS              EMS
## 469          6              home               EMS         outsideh
## 473          4              home              home              EMS
## 474          4               EMS          outsideh         outsideh
## 475          2              home          outsideh             <NA>
## 483          4               EMS          outsideh         outsideh
## 493          2               EMS          outsideh             <NA>
## 497          3              home          outsideh         outsideh
## 504          4               EMS               EMS              EMS
## 508          3               EMS          outsideh         outsideh
## 521          2               EMS            studyh             <NA>
## 553          4              home               EMS              EMS
## 554          3               EMS               EMS              EMS
## 559          1               EMS              <NA>             <NA>
## 560          2               EMS               EMS             <NA>
## 561          1               EMS              <NA>             <NA>
## 562          2              home               EMS             <NA>
## 571          2              home          outsideh             <NA>
## 611          1               EMS              <NA>             <NA>
## 629          4              home               EMS              EMS
## 647          1              home              <NA>             <NA>
## 663          3              home              home           studyh
## 672          2              home               EMS             <NA>
## 685          7              home               EMS           studyh
## 686          6              home              home             home
## 687          3              home              home           studyh
## 693          6               EMS               EMS              EMS
## 697          2              home              home             <NA>
## 701          3               EMS            studyh           studyh
## 724          5              home              home           studyh
```

```
## 730          4               home               home               home
## 741          1                EMS               <NA>               <NA>
## 743          3                EMS                EMS                EMS
## 744          3               home               home               home
## 760          3               home          outsideh           outsideh
##     preAEDBZDlocation3 preAEDBZDlocation4 preAEDBZDlocation5
## 2                 <NA>               <NA>               <NA>
## 9               studyh               <NA>               <NA>
## 18              studyh               <NA>               <NA>
## 22                 EMS               <NA>               <NA>
## 29                <NA>               <NA>               <NA>
## 31                <NA>               <NA>               <NA>
## 36                <NA>               <NA>               <NA>
## 43                <NA>               <NA>               <NA>
## 53                <NA>               <NA>               <NA>
## 56                <NA>               <NA>               <NA>
## 69                 EMS               <NA>               <NA>
## 71                <NA>               <NA>               <NA>
## 72           outsideh               <NA>               <NA>
## 78                <NA>               <NA>               <NA>
## 81                <NA>               <NA>               <NA>
## 101               <NA>               <NA>               <NA>
## 107               <NA>               <NA>               <NA>
## 112               <NA>               <NA>               <NA>
## 117               <NA>               <NA>               <NA>
## 143               <NA>               <NA>               <NA>
## 146               <NA>               <NA>               <NA>
## 147               <NA>               <NA>               <NA>
## 151               <NA>               <NA>               <NA>
## 153               <NA>               <NA>               <NA>
## 158               <NA>               <NA>               <NA>
## 162               <NA>               <NA>               <NA>
## 176               <NA>               <NA>               <NA>
## 185               <NA>               <NA>               <NA>
## 193          outsideh               <NA>               <NA>
## 206            studyh               <NA>               <NA>
## 209               <NA>               <NA>               <NA>
## 211               <NA>               <NA>               <NA>
## 217          outsideh               <NA>               <NA>
## 222               <NA>               <NA>               <NA>
## 230               <NA>               <NA>               <NA>
## 234            studyh               <NA>               <NA>
## 239               <NA>               <NA>               <NA>
## 248               <NA>               <NA>               <NA>
## 257               <NA>               <NA>               <NA>
## 267                EMS             studyh               <NA>
## 280          outsideh           outsideh               <NA>
## 281               <NA>               <NA>               <NA>
## 282            studyh             studyh             studyh
## 284          outsideh           outsideh               <NA>
```

```
## 286              <NA>              <NA>              <NA>
## 288              <NA>              <NA>              <NA>
## 289              <NA>              <NA>              <NA>
## 294              <NA>              <NA>              <NA>
## 319              <NA>              <NA>              <NA>
## 322              <NA>              <NA>              <NA>
## 331              <NA>              <NA>              <NA>
## 335              <NA>              <NA>              <NA>
## 348               EMS            studyh            studyh
## 349          outsideh              <NA>              <NA>
## 354              <NA>              <NA>              <NA>
## 361              <NA>              <NA>              <NA>
## 363              <NA>              <NA>              <NA>
## 369              <NA>              <NA>              <NA>
## 409              <NA>              <NA>              <NA>
## 411              <NA>              <NA>              <NA>
## 412              <NA>              <NA>              <NA>
## 413              <NA>              <NA>              <NA>
## 415              <NA>              <NA>              <NA>
## 427              <NA>              <NA>              <NA>
## 431              <NA>              <NA>              <NA>
## 437              <NA>              <NA>              <NA>
## 438              <NA>              <NA>              <NA>
## 440              <NA>              <NA>              <NA>
## 442              <NA>              <NA>              <NA>
## 448              <NA>              <NA>              <NA>
## 450          outsideh              <NA>              <NA>
## 451          outsideh          outsideh          outsideh
## 457          outsideh          outsideh              <NA>
## 459            studyh              <NA>              <NA>
## 462              <NA>              <NA>              <NA>
## 469          outsideh          outsideh          outsideh
## 473          outsideh              <NA>              <NA>
## 474          outsideh              <NA>              <NA>
## 475              <NA>              <NA>              <NA>
## 483          outsideh              <NA>              <NA>
## 493              <NA>              <NA>              <NA>
## 497              <NA>              <NA>              <NA>
## 504          outsideh              <NA>              <NA>
## 508              <NA>              <NA>              <NA>
## 521              <NA>              <NA>              <NA>
## 553               EMS              <NA>              <NA>
## 554              <NA>              <NA>              <NA>
## 559              <NA>              <NA>              <NA>
## 560              <NA>              <NA>              <NA>
## 561              <NA>              <NA>              <NA>
## 562              <NA>              <NA>              <NA>
## 571              <NA>              <NA>              <NA>
## 611              <NA>              <NA>              <NA>
## 629               EMS              <NA>              <NA>
```

```
## 647                <NA>                <NA>                <NA>
## 663                <NA>                <NA>                <NA>
## 672                <NA>                <NA>                <NA>
## 685              studyh              studyh              studyh
## 686                home                home              studyh
## 687                <NA>                <NA>                <NA>
## 693                 EMS                 EMS              studyh
## 697                <NA>                <NA>                <NA>
## 701                <NA>                <NA>                <NA>
## 724              studyh              studyh                <NA>
## 730                 EMS                <NA>                <NA>
## 741                <NA>                <NA>                <NA>
## 743                <NA>                <NA>                <NA>
## 744                <NA>                <NA>                <NA>
## 760                <NA>                <NA>                <NA>
##     preAEDBZDlocation6 preAEDBZDlocation7 preAEDBZDlocation8
## 2                  <NA>                <NA>                <NA>
## 9                  <NA>                <NA>                <NA>
## 18                 <NA>                <NA>                <NA>
## 22                 <NA>                <NA>                <NA>
## 29                 <NA>                <NA>                <NA>
## 31                 <NA>                <NA>                <NA>
## 36                 <NA>                <NA>                <NA>
## 43                 <NA>                <NA>                <NA>
## 53                 <NA>                <NA>                <NA>
## 56                 <NA>                <NA>                <NA>
## 69                 <NA>                <NA>                <NA>
## 71                 <NA>                <NA>                <NA>
## 72                 <NA>                <NA>                <NA>
## 78                 <NA>                <NA>                <NA>
## 81                 <NA>                <NA>                <NA>
## 101                <NA>                <NA>                <NA>
## 107                <NA>                <NA>                <NA>
## 112                <NA>                <NA>                <NA>
## 117                <NA>                <NA>                <NA>
## 143                <NA>                <NA>                <NA>
## 146                <NA>                <NA>                <NA>
## 147                <NA>                <NA>                <NA>
## 151                <NA>                <NA>                <NA>
## 153                <NA>                <NA>                <NA>
## 158                <NA>                <NA>                <NA>
## 162                <NA>                <NA>                <NA>
## 176                <NA>                <NA>                <NA>
## 185                <NA>                <NA>                <NA>
## 193                <NA>                <NA>                <NA>
## 206                <NA>                <NA>                <NA>
## 209                <NA>                <NA>                <NA>
## 211                <NA>                <NA>                <NA>
## 217                <NA>                <NA>                <NA>
## 222                <NA>                <NA>                <NA>
```

```
## 230              <NA>              <NA>              <NA>
## 234              <NA>              <NA>              <NA>
## 239              <NA>              <NA>              <NA>
## 248              <NA>              <NA>              <NA>
## 257              <NA>              <NA>              <NA>
## 267              <NA>              <NA>              <NA>
## 280              <NA>              <NA>              <NA>
## 281              <NA>              <NA>              <NA>
## 282            studyh              <NA>              <NA>
## 284              <NA>              <NA>              <NA>
## 286              <NA>              <NA>              <NA>
## 288              <NA>              <NA>              <NA>
## 289              <NA>              <NA>              <NA>
## 294              <NA>              <NA>              <NA>
## 319              <NA>              <NA>              <NA>
## 322              <NA>              <NA>              <NA>
## 331              <NA>              <NA>              <NA>
## 335              <NA>              <NA>              <NA>
## 348              <NA>              <NA>              <NA>
## 349              <NA>              <NA>              <NA>
## 354              <NA>              <NA>              <NA>
## 361              <NA>              <NA>              <NA>
## 363              <NA>              <NA>              <NA>
## 369              <NA>              <NA>              <NA>
## 409              <NA>              <NA>              <NA>
## 411              <NA>              <NA>              <NA>
## 412              <NA>              <NA>              <NA>
## 413              <NA>              <NA>              <NA>
## 415              <NA>              <NA>              <NA>
## 427              <NA>              <NA>              <NA>
## 431              <NA>              <NA>              <NA>
## 437              <NA>              <NA>              <NA>
## 438              <NA>              <NA>              <NA>
## 440              <NA>              <NA>              <NA>
## 442              <NA>              <NA>              <NA>
## 448              <NA>              <NA>              <NA>
## 450              <NA>              <NA>              <NA>
## 451          outsideh              <NA>              <NA>
## 457              <NA>              <NA>              <NA>
## 459              <NA>              <NA>              <NA>
## 462              <NA>              <NA>              <NA>
## 469              <NA>              <NA>              <NA>
## 473              <NA>              <NA>              <NA>
## 474              <NA>              <NA>              <NA>
## 475              <NA>              <NA>              <NA>
## 483              <NA>              <NA>              <NA>
## 493              <NA>              <NA>              <NA>
## 497              <NA>              <NA>              <NA>
## 504              <NA>              <NA>              <NA>
## 508              <NA>              <NA>              <NA>
```

```
## 521                <NA>                <NA>                <NA>
## 553                <NA>                <NA>                <NA>
## 554                <NA>                <NA>                <NA>
## 559                <NA>                <NA>                <NA>
## 560                <NA>                <NA>                <NA>
## 561                <NA>                <NA>                <NA>
## 562                <NA>                <NA>                <NA>
## 571                <NA>                <NA>                <NA>
## 611                <NA>                <NA>                <NA>
## 629                <NA>                <NA>                <NA>
## 647                <NA>                <NA>                <NA>
## 663                <NA>                <NA>                <NA>
## 672                <NA>                <NA>                <NA>
## 685              studyh                <NA>                <NA>
## 686                <NA>                <NA>                <NA>
## 687                <NA>                <NA>                <NA>
## 693                <NA>                <NA>                <NA>
## 697                <NA>                <NA>                <NA>
## 701                <NA>                <NA>                <NA>
## 724                <NA>                <NA>                <NA>
## 730                <NA>                <NA>                <NA>
## 741                <NA>                <NA>                <NA>
## 743                <NA>                <NA>                <NA>
## 744                <NA>                <NA>                <NA>
## 760                <NA>                <NA>                <NA>
##     preAEDBZDlocation9
## 2                  <NA>
## 9                  <NA>
## 18                 <NA>
## 22                 <NA>
## 29                 <NA>
## 31                 <NA>
## 36                 <NA>
## 43                 <NA>
## 53                 <NA>
## 56                 <NA>
## 69                 <NA>
## 71                 <NA>
## 72                 <NA>
## 78                 <NA>
## 81                 <NA>
## 101                <NA>
## 107                <NA>
## 112                <NA>
## 117                <NA>
## 143                <NA>
## 146                <NA>
## 147                <NA>
## 151                <NA>
## 153                <NA>
```

```
## 158              <NA>
## 162              <NA>
## 176              <NA>
## 185              <NA>
## 193              <NA>
## 206              <NA>
## 209              <NA>
## 211              <NA>
## 217              <NA>
## 222              <NA>
## 230              <NA>
## 234              <NA>
## 239              <NA>
## 248              <NA>
## 257              <NA>
## 267              <NA>
## 280              <NA>
## 281              <NA>
## 282              <NA>
## 284              <NA>
## 286              <NA>
## 288              <NA>
## 289              <NA>
## 294              <NA>
## 319              <NA>
## 322              <NA>
## 331              <NA>
## 335              <NA>
## 348              <NA>
## 349              <NA>
## 354              <NA>
## 361              <NA>
## 363              <NA>
## 369              <NA>
## 409              <NA>
## 411              <NA>
## 412              <NA>
## 413              <NA>
## 415              <NA>
## 427              <NA>
## 431              <NA>
## 437              <NA>
## 438              <NA>
## 440              <NA>
## 442              <NA>
## 448              <NA>
## 450              <NA>
## 451              <NA>
## 457              <NA>
## 459              <NA>
```

```
## 462                <NA>
## 469                <NA>
## 473                <NA>
## 474                <NA>
## 475                <NA>
## 483                <NA>
## 493                <NA>
## 497                <NA>
## 504                <NA>
## 508                <NA>
## 521                <NA>
## 553                <NA>
## 554                <NA>
## 559                <NA>
## 560                <NA>
## 561                <NA>
## 562                <NA>
## 571                <NA>
## 611                <NA>
## 629                <NA>
## 647                <NA>
## 663                <NA>
## 672                <NA>
## 685                <NA>
## 686                <NA>
## 687                <NA>
## 693                <NA>
## 697                <NA>
## 701                <NA>
## 724                <NA>
## 730                <NA>
## 741                <NA>
## 743                <NA>
## 744                <NA>
## 760                <NA>
```

```
# Among patients with first non benzodiazepine ASM in the hospital, how many
received an extra benzodiazepine dose at hospital arrival
for (i in 1 : dim(pSERG)[1]) {
  if (
    (is.na(pSERG$preAEDBZDlocation0[i]) == FALSE &
(pSERG$preAEDBZDlocation0[i] == "home" | pSERG$preAEDBZDlocation0[i] ==
"EMS")) &
      (is.na(pSERG$preAEDBZDlocation1[i]) == FALSE &
(pSERG$preAEDBZDlocation1[i] == "home" | pSERG$preAEDBZDlocation1[i] ==
"EMS")) &
      (
        (is.na(pSERG$preAEDBZDlocation2[i]) == FALSE &
(pSERG$preAEDBZDlocation2[i] == "outsideh" | pSERG$preAEDBZDlocation2[i] ==
"studyh")) |
```

```
      (is.na(pSERG$preAEDBZDlocation3[i]) == FALSE &
(pSERG$preAEDBZDlocation3[i] == "outsideh" | pSERG$preAEDBZDlocation3[i] ==
"studyh")) |
      (is.na(pSERG$preAEDBZDlocation4[i]) == FALSE &
(pSERG$preAEDBZDlocation4[i] == "outsideh" | pSERG$preAEDBZDlocation4[i] ==
"studyh")) |
      (is.na(pSERG$preAEDBZDlocation5[i]) == FALSE &
(pSERG$preAEDBZDlocation5[i] == "outsideh" | pSERG$preAEDBZDlocation5[i] ==
"studyh")) |
      (is.na(pSERG$preAEDBZDlocation6[i]) == FALSE &
(pSERG$preAEDBZDlocation6[i] == "outsideh" | pSERG$preAEDBZDlocation6[i] ==
"studyh")) |
      (is.na(pSERG$preAEDBZDlocation7[i]) == FALSE &
(pSERG$preAEDBZDlocation7[i] == "outsideh" | pSERG$preAEDBZDlocation7[i] ==
"studyh")) |
      (is.na(pSERG$preAEDBZDlocation8[i]) == FALSE &
(pSERG$preAEDBZDlocation8[i] == "outsideh" | pSERG$preAEDBZDlocation8[i] ==
"studyh")) |
      (is.na(pSERG$preAEDBZDlocation9[i]) == FALSE &
(pSERG$preAEDBZDlocation9[i] == "outsideh" | pSERG$preAEDBZDlocation9[i] ==
"studyh"))
      )
      ) {
    pSERG$extradoseinthehospital[i] <- 1
  } else {
    pSERG$extradoseinthehospital[i] <- 0
      }
}

# Patients with extra benzodiazepine in the hospital after some treatment
outside
table(pSERG[which(pSERG$HOSPITALONSET == "no" & pSERG$firstBZDinhospital ==
0), ]$extradoseinthehospital)

##
##  0  1
## 81 26

# Detail of the findings
dim(pSERG[which(pSERG$HOSPITALONSET == "no" & pSERG$firstBZDinhospital == 0 &
pSERG$preAEDBZDs >1 & (pSERG$BZDLOCATION.1 == "home" | pSERG$BZDLOCATION.1 ==
"EMS")),])  # 54 patients out of 201 patients with out-of-hospital onset
received at least 2 BZDs before hospital arrival. 26 out of those 54 patients
received an additional BZD dose at hospital arrival.

## [1]   54 1643

pSERG[which(pSERG$HOSPITALONSET == "no" & pSERG$firstBZDinhospital == 0 &
pSERG$preAEDBZDs >1 & (pSERG$BZDLOCATION.1 == "home" | pSERG$BZDLOCATION.1 ==
"EMS")), c("preAEDBZDs",  "preAEDBZDlocation2", "preAEDBZDlocation3",
```

```
"preAEDBZDlocation4", "preAEDBZDlocation5", "preAEDBZDlocation6",
"preAEDBZDlocation7", "preAEDBZDlocation8", "preAEDBZDlocation9")]

##     preAEDBZDs preAEDBZDlocation2 preAEDBZDlocation3 preAEDBZDlocation4
## 2            3                EMS               <NA>               <NA>
## 9            4                EMS             studyh               <NA>
## 18           4                EMS             studyh               <NA>
## 22           4               home                EMS               <NA>
## 31           2               <NA>               <NA>               <NA>
## 69           4                EMS                EMS               <NA>
## 71           3                EMS               <NA>               <NA>
## 72           4                EMS           outsideh               <NA>
## 147          3             studyh                <NA>               <NA>
## 153          3           outsideh                <NA>               <NA>
## 158          2               <NA>               <NA>               <NA>
## 206          4                EMS             studyh               <NA>
## 209          3           outsideh                <NA>               <NA>
## 217          4           outsideh           outsideh               <NA>
## 222          2               <NA>                <NA>               <NA>
## 230          2               <NA>                <NA>               <NA>
## 267          5                EMS                EMS             studyh
## 281          2               <NA>                <NA>               <NA>
## 282          7                EMS             studyh             studyh
## 286          3                EMS                <NA>               <NA>
## 288          3           outsideh                <NA>               <NA>
## 322          3                EMS                <NA>               <NA>
## 335          2               <NA>                <NA>               <NA>
## 348          6                EMS                EMS             studyh
## 349          4                EMS           outsideh               <NA>
## 361          2               <NA>                <NA>               <NA>
## 369          3             studyh                <NA>               <NA>
## 409          2               <NA>                <NA>               <NA>
## 431          2               <NA>                <NA>               <NA>
## 437          2               <NA>                <NA>               <NA>
## 438          2               <NA>                <NA>               <NA>
## 451          7           outsideh           outsideh           outsideh
## 457          5           outsideh           outsideh           outsideh
## 459          4                EMS             studyh               <NA>
## 462          3                EMS                <NA>               <NA>
## 469          6           outsideh           outsideh           outsideh
## 473          4                EMS           outsideh               <NA>
## 504          4                EMS           outsideh               <NA>
## 553          4                EMS                EMS               <NA>
## 554          3                EMS                <NA>               <NA>
## 560          2               <NA>                <NA>               <NA>
## 562          2               <NA>                <NA>               <NA>
## 629          4                EMS                EMS               <NA>
## 663          3             studyh                <NA>               <NA>
## 672          2               <NA>                <NA>               <NA>
## 685          7             studyh             studyh             studyh
```

```
## 686          6               home               home               home
## 687          3             studyh               <NA>               <NA>
## 693          6                EMS                EMS                EMS
## 697          2               <NA>               <NA>               <NA>
## 724          5             studyh             studyh             studyh
## 730          4               home                EMS               <NA>
## 743          3                EMS               <NA>               <NA>
## 744          3               home               <NA>               <NA>
##     preAEDBZDlocation5 preAEDBZDlocation6 preAEDBZDlocation7
## 2                <NA>               <NA>               <NA>
## 9                <NA>               <NA>               <NA>
## 18               <NA>               <NA>               <NA>
## 22               <NA>               <NA>               <NA>
## 31               <NA>               <NA>               <NA>
## 69               <NA>               <NA>               <NA>
## 71               <NA>               <NA>               <NA>
## 72               <NA>               <NA>               <NA>
## 147              <NA>               <NA>               <NA>
## 153              <NA>               <NA>               <NA>
## 158              <NA>               <NA>               <NA>
## 206              <NA>               <NA>               <NA>
## 209              <NA>               <NA>               <NA>
## 217              <NA>               <NA>               <NA>
## 222              <NA>               <NA>               <NA>
## 230              <NA>               <NA>               <NA>
## 267              <NA>               <NA>               <NA>
## 281              <NA>               <NA>               <NA>
## 282            studyh             studyh               <NA>
## 286              <NA>               <NA>               <NA>
## 288              <NA>               <NA>               <NA>
## 322              <NA>               <NA>               <NA>
## 335              <NA>               <NA>               <NA>
## 348            studyh               <NA>               <NA>
## 349              <NA>               <NA>               <NA>
## 361              <NA>               <NA>               <NA>
## 369              <NA>               <NA>               <NA>
## 409              <NA>               <NA>               <NA>
## 431              <NA>               <NA>               <NA>
## 437              <NA>               <NA>               <NA>
## 438              <NA>               <NA>               <NA>
## 451          outsideh           outsideh               <NA>
## 457              <NA>               <NA>               <NA>
## 459              <NA>               <NA>               <NA>
## 462              <NA>               <NA>               <NA>
## 469          outsideh               <NA>               <NA>
## 473              <NA>               <NA>               <NA>
## 504              <NA>               <NA>               <NA>
## 553              <NA>               <NA>               <NA>
## 554              <NA>               <NA>               <NA>
## 560              <NA>               <NA>               <NA>
```

```
## 562                <NA>                <NA>                <NA>
## 629                <NA>                <NA>                <NA>
## 663                <NA>                <NA>                <NA>
## 672                <NA>                <NA>                <NA>
## 685              studyh              studyh                <NA>
## 686              studyh                <NA>                <NA>
## 687                <NA>                <NA>                <NA>
## 693              studyh                <NA>                <NA>
## 697                <NA>                <NA>                <NA>
## 724                <NA>                <NA>                <NA>
## 730                <NA>                <NA>                <NA>
## 743                <NA>                <NA>                <NA>
## 744                <NA>                <NA>                <NA>
##     preAEDBZDlocation8 preAEDBZDlocation9
## 2                  <NA>                <NA>
## 9                  <NA>                <NA>
## 18                 <NA>                <NA>
## 22                 <NA>                <NA>
## 31                 <NA>                <NA>
## 69                 <NA>                <NA>
## 71                 <NA>                <NA>
## 72                 <NA>                <NA>
## 147                <NA>                <NA>
## 153                <NA>                <NA>
## 158                <NA>                <NA>
## 206                <NA>                <NA>
## 209                <NA>                <NA>
## 217                <NA>                <NA>
## 222                <NA>                <NA>
## 230                <NA>                <NA>
## 267                <NA>                <NA>
## 281                <NA>                <NA>
## 282                <NA>                <NA>
## 286                <NA>                <NA>
## 288                <NA>                <NA>
## 322                <NA>                <NA>
## 335                <NA>                <NA>
## 348                <NA>                <NA>
## 349                <NA>                <NA>
## 361                <NA>                <NA>
## 369                <NA>                <NA>
## 409                <NA>                <NA>
## 431                <NA>                <NA>
## 437                <NA>                <NA>
## 438                <NA>                <NA>
## 451                <NA>                <NA>
## 457                <NA>                <NA>
## 459                <NA>                <NA>
## 462                <NA>                <NA>
## 469                <NA>                <NA>
```

```
## 473                <NA>                <NA>
## 504                <NA>                <NA>
## 553                <NA>                <NA>
## 554                <NA>                <NA>
## 560                <NA>                <NA>
## 562                <NA>                <NA>
## 629                <NA>                <NA>
## 663                <NA>                <NA>
## 672                <NA>                <NA>
## 685                <NA>                <NA>
## 686                <NA>                <NA>
## 687                <NA>                <NA>
## 693                <NA>                <NA>
## 697                <NA>                <NA>
## 724                <NA>                <NA>
## 730                <NA>                <NA>
## 743                <NA>                <NA>
## 744                <NA>                <NA>

# Among the 201 patients with out-of-hospital rSE onset, 94 did not receive
any medication until hospital arrival, 53 received 1 BZD and 54 received two
or more BZDs.
```

Additional numbers [] for the tables

```
# Table of 30 min

pSERG$the_BZD_received_before_30_min_were <- pSERG$preAEDBZDs -
pSERG$preAEDBZDsmorethan30
table(pSERG$the_BZD_received_before_30_min_were)

##
##   0   1   2   3   4
##  82 101  72  27  11

table(pSERG$the_BZD_received_before_30_min_were, pSERG$preAEDBZDsmorethan30)

##
##      0  1  2  3  4  5  6  7 10
##   0  0 32 32  9  2  2  3  1  1
##   1 44 26 22  6  1  1  1  0  0
##   2 53 10  6  3  0  0  0  0  0
##   3 20  6  0  0  1  0  0  0  0
##   4  8  2  1  0  0  0  0  0  0

table(pSERG[which(pSERG$HOSPITALONSET ==
"no"),]$the_BZD_received_before_30_min_were, pSERG[which(pSERG$HOSPITALONSET
== "no"),]$preAEDBZDsmorethan30)

##
##      0  1  2  3  4  5  6  7 10
##   0  0 27 28  8  2  2  3  1  1
```

```
##   1 24 15 18  6  1  0  1  0  0
##   2 29  9  3  2  0  0  0  0  0
##   3  8  5  0  0  1  0  0  0  0
##   4  4  2  1  0  0  0  0  0  0

table(pSERG[which(pSERG$HOSPITALONSET ==
"yes"),]$the_BZD_received_before_30_min_were, pSERG[which(pSERG$HOSPITALONSET
== "yes"),]$preAEDBZDsmorethan30)

##
##      0  1  2  3  5
##   0  0  5  4  1  0
##   1 20 11  4  0  1
##   2 24  1  3  1  0
##   3 12  1  0  0  0
##   4  4  0  0  0  0

# Table of 45 min

pSERG$the_BZD_received_before_45_min_were <- pSERG$preAEDBZDs -
pSERG$preAEDBZDsmorethan45
table(pSERG$the_BZD_received_before_45_min_were)

##
##  0  1  2  3  4  5
## 61 90 84 43 12  3

table(pSERG$the_BZD_received_before_45_min_were, pSERG$preAEDBZDsmorethan45)

##
##      0  1  2  3  4  5  6 10
##   0  0 25 27  5  1  0  2  1
##   1 51 16 15  5  2  0  1  0
##   2 68 10  3  1  1  1  0  0
##   3 31  7  3  1  1  0  0  0
##   4 12  0  0  0  0  0  0  0
##   5  2  1  0  0  0  0  0  0

table(pSERG[which(pSERG$HOSPITALONSET ==
"no"),]$the_BZD_received_before_45_min_were, pSERG[which(pSERG$HOSPITALONSET
== "no"),]$preAEDBZDsmorethan45)

##
##      0  1  2  3  4  5  6 10
##   0  0 22 26  5  1  0  2  1
##   1 29 11 12  5  2  0  1  0
##   2 35  9  3  0  0  1  0  0
##   3 17  4  3  1  1  0  0  0
##   4  7  0  0  0  0  0  0  0
##   5  2  1  0  0  0  0  0  0
```

```
table(pSERG[which(pSERG$HOSPITALONSET ==
"yes"),]$the_BZD_received_before_45_min_were, pSERG[which(pSERG$HOSPITALONSET
== "yes"),]$preAEDBZDsmorethan45)

##
##      0  1  2  3  4
##   0  0  3  1  0  0
##   1 22  5  3  0  0
##   2 33  1  0  1  1
##   3 14  3  0  0  0
##   4  5  0  0  0  0
```

Additional analyses requested by one reviewer (inclusion of etiology in the models)

```
# Create variable structural etiology

pSERG$structural_etiology[pSERG$ETIOLOGY == "structural"] <- 1
pSERG$structural_etiology[pSERG$ETIOLOGY == "metabolic" | pSERG$ETIOLOGY ==
"genetic" | pSERG$ETIOLOGY == "unknown" | pSERG$ETIOLOGY == "other"] <- 0
table(pSERG$structural_etiology)

##
##   0   1
## 222  70

# 1.    Outcome = Number of BZD doses before non-BZD ASM

# Model
tplus <- glm.nb(pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears +
pSERG$TYPESTATUS + (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy +
pSERG$priorSE + pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0 +
pSERG$structural_etiology)

## Warning in theta.ml(Y, mu, sum(w), w, limit = control$maxit, trace =
## control$trace > : iteration limit reached

## Warning in theta.ml(Y, mu, sum(w), w, limit = control$maxit, trace =
## control$trace > : iteration limit reached

summary(tplus)

##
## Call:
## glm.nb(formula = pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE + pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0 +
##     pSERG$structural_etiology, init.theta = 57385.42108, link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
```

```
## -1.3934  -0.6116  -0.1181   0.3228   3.6938
##
## Coefficients:
##                                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)                     0.7690689  0.1263900   6.085 1.17e-09 ***
## pSERG$SEXmale                   0.0322031  0.0787384   0.409   0.6825
## pSERG$ageyears                 -0.0024129  0.0077940  -0.310   0.7569
## pSERG$TYPESTATUSintermittent   -0.0354768  0.0803282  -0.442   0.6587
## pSERG$HOSPITALONSET == "no"TRUE  0.1613353  0.0881057   1.831   0.0671 .
## pSERG$priorepilepsy1            0.0634947  0.0854438   0.743   0.4574
## pSERG$priorSE1                  0.1409026  0.0962788   1.463   0.1433
## pSERG$BZD1stdosinginadequate1   0.0064781  0.0804512   0.081   0.9358
## pSERG$BZDTIME.0                -0.0014063  0.0005541  -2.538   0.0112 *
## pSERG$structural_etiology      -0.0494466  0.0920732  -0.537   0.5912
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(57385.42) family taken to be
1)
##
##     Null deviance: 186.52  on 291  degrees of freedom
## Residual deviance: 169.80  on 282  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 967.59
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  57385
##           Std. Err.:  490071
## Warning while fitting theta: iteration limit reached
##
##  2 x log-likelihood:  -945.588
```

```
(bettacoefficients_withCItplus <- cbind(Estimate = coef(tplus),
confint(tplus)))
```

```
## Waiting for profiling to be done...
```

```
##                                    Estimate        2.5 %        97.5 %
## (Intercept)                     0.769068856  0.518013369  1.0134953275
## pSERG$SEXmale                   0.032203070 -0.121686554  0.1870938613
## pSERG$ageyears                 -0.002412908 -0.017868137  0.0126954173
## pSERG$TYPESTATUSintermittent   -0.035476771 -0.192057757  0.1229765330
## pSERG$HOSPITALONSET == "no"TRUE  0.161335346 -0.009734827  0.3358138136
## pSERG$priorepilepsy1            0.063494655 -0.104168507  0.2308742908
## pSERG$priorSE1                  0.140902637 -0.049863246  0.3277407565
## pSERG$BZD1stdosinginadequate1   0.006478109 -0.150964028  0.1645215596
## pSERG$BZDTIME.0                -0.001406297 -0.002556225 -0.0003792151
## pSERG$structural_etiology      -0.049446618 -0.232728632  0.1284440852
```

```
(IR_withCItplus <- exp(bettacoefficients_withCItplus))
```

```
##                                    Estimate     2.5 %    97.5 %
## (Intercept)                       2.1577561 1.6786894 2.7552146
## pSERG$SEXmale                     1.0327272 0.8854259 1.2057405
## pSERG$ageyears                    0.9975900 0.9822906 1.0127763
## pSERG$TYPESTATUSintermittent      0.9651452 0.8252592 1.1308579
## pSERG$HOSPITALONSET == "no"TRUE   1.1750790 0.9903124 1.3990785
## pSERG$priorepilepsy1              1.0655538 0.9010734 1.2597009
## pSERG$priorSE1                    1.1513125 0.9513595 1.3878291
## pSERG$BZD1stdosinginadequate1     1.0064991 0.8598786 1.1788290
## pSERG$BZDTIME.0                   0.9985947 0.9974470 0.9996209
## pSERG$structural_etiology         0.9517560 0.7923686 1.1370578
```

```
xplus <- glm(pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears + pSERG$TYPESTATUS
+ (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy + pSERG$priorSE +
pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0 + pSERG$structural_etiology,
family = "poisson")
summary(xplus)
```

```
##
## Call:
## glm(formula = pSERG$preAEDBZDs ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE + pSERG$BZD1stdosinginadequate + pSERG$BZDTIME.0 +
##     pSERG$structural_etiology, family = "poisson")
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.3935  -0.6116  -0.1181   0.3228   3.6939
##
## Coefficients:
##                                    Estimate Std. Error z value Pr(>|z|)
## (Intercept)                       0.7690693  0.1263860   6.085 1.16e-09 ***
## pSERG$SEXmale                     0.0322030  0.0787357   0.409   0.6825
## pSERG$ageyears                   -0.0024129  0.0077938  -0.310   0.7569
## pSERG$TYPESTATUSintermittent     -0.0354766  0.0803253  -0.442   0.6587
## pSERG$HOSPITALONSET == "no"TRUE  0.1613353  0.0881029   1.831   0.0671 .
## pSERG$priorepilepsy1              0.0634945  0.0854407   0.743   0.4574
## pSERG$priorSE1                    0.1409027  0.0962754   1.464   0.1433
## pSERG$BZD1stdosinginadequate1     0.0064779  0.0804482   0.081   0.9358
## pSERG$BZDTIME.0                  -0.0014063  0.0005541  -2.538   0.0111 *
## pSERG$structural_etiology        -0.0494464  0.0920699  -0.537   0.5912
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for poisson family taken to be 1)
##
##     Null deviance: 186.53  on 291  degrees of freedom
```

```
## Residual deviance: 169.81  on 282  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 965.58
##
## Number of Fisher Scoring iterations: 4
```

```
confint(xplus)
```

```
## Waiting for profiling to be done...
```

```
##                                       2.5 %        97.5 %
## (Intercept)                       0.518018526  1.0134905384
## pSERG$SEXmale                    -0.121683280  0.1870905592
## pSERG$ageyears                   -0.017867866  0.0126950467
## pSERG$TYPESTATUSintermittent     -0.192054148  0.1229733654
## pSERG$HOSPITALONSET == "no"TRUE  -0.009731216  0.3358103011
## pSERG$priorepilepsy1             -0.104165242  0.2308706054
## pSERG$priorSE1                   -0.049858944  0.3277363709
## pSERG$BZD1stdosinginadequate1    -0.150960840  0.1645180801
## pSERG$BZDTIME.0                  -0.002556239 -0.0003792089
## pSERG$structural_etiology        -0.232724708  0.1284402961
```

```
(bettacoefficients_withCIplus <- cbind(Estimate = coef(xplus),
confint(xplus)))
```

```
## Waiting for profiling to be done...
```

```
##                                      Estimate        2.5 %        97.5 %
## (Intercept)                       0.769069286  0.518018526  1.0134905384
## pSERG$SEXmale                     0.032203010 -0.121683280  0.1870905592
## pSERG$ageyears                   -0.002412946 -0.017867866  0.0126950467
## pSERG$TYPESTATUSintermittent     -0.035476617 -0.192054148  0.1229733654
## pSERG$HOSPITALONSET == "no"TRUE   0.161335286 -0.009731216  0.3358103011
## pSERG$priorepilepsy1              0.063494462 -0.104165242  0.2308706054
## pSERG$priorSE1                    0.140902735 -0.049858944  0.3277363709
## pSERG$BZD1stdosinginadequate1     0.006477938 -0.150960840  0.1645180801
## pSERG$BZDTIME.0                  -0.001406300 -0.002556239 -0.0003792089
## pSERG$structural_etiology        -0.049446387 -0.232724708  0.1284402961
```

```
(IR_withCIplus <- exp(bettacoefficients_withCIplus))
```

```
##                                   Estimate     2.5 %    97.5 %
## (Intercept)                      2.1577571 1.6786981 2.7552014
## pSERG$SEXmale                    1.0327271 0.8854288 1.2057365
## pSERG$ageyears                   0.9975900 0.9822908 1.0127760
## pSERG$TYPESTATUSintermittent     0.9651453 0.8252622 1.1308543
## pSERG$HOSPITALONSET == "no"TRUE 1.1750789 0.9903160 1.3990736
## pSERG$priorepilepsy1             1.0655536 0.9010764 1.2596962
## pSERG$priorSE1                   1.1513127 0.9513636 1.3878231
## pSERG$BZD1stdosinginadequate1    1.0064990 0.8598814 1.1788249
## pSERG$BZDTIME.0                  0.9985947 0.9974470 0.9996209
## pSERG$structural_etiology        0.9517562 0.7923717 1.1370535
```

```r
# 2.    Outcome = Number of BZD doses before non-BZD ASM and within the first
30 min


# Model
aplus <- glm.nb(pSERG$preAEDBZDsmorethan30 ~ pSERG$SEX + pSERG$ageyears +
pSERG$TYPESTATUS + (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy +
pSERG$priorSE + pSERG$structural_etiology)
summary(aplus)

##
## Call:
## glm.nb(formula = pSERG$preAEDBZDsmorethan30 ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE + pSERG$structural_etiology, init.theta = 2.450287234,
##     link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.5746  -1.0347  -0.3079   0.4151   3.1321
##
## Coefficients:
##                                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)                     -0.770357   0.231701  -3.325 0.000885 ***
## pSERG$SEXmale                    0.100976   0.140473   0.719 0.472246
## pSERG$ageyears                   0.004046   0.013499   0.300 0.764369
## pSERG$TYPESTATUSintermittent     0.139493   0.145859   0.956 0.338892
## pSERG$HOSPITALONSET == "no"TRUE  0.886179   0.175652   5.045 4.53e-07 ***
## pSERG$priorepilepsy1             0.086368   0.146855   0.588 0.556455
## pSERG$priorSE1                  -0.084921   0.180290  -0.471 0.637624
## pSERG$structural_etiology       -0.048914   0.165413  -0.296 0.767454
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(2.4503) family taken to be 1)
##
##     Null deviance: 341.00  on 291  degrees of freedom
## Residual deviance: 308.65  on 284  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 832.21
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  2.450
##           Std. Err.:  0.716
##
##  2 x log-likelihood:  -814.214
```

```
confint(aplus)

## Waiting for profiling to be done...

##                                       2.5 %      97.5 %
## (Intercept)                     -1.22893757 -0.32856099
## pSERG$SEXmale                   -0.17425528  0.37770924
## pSERG$ageyears                  -0.02223984  0.03003416
## pSERG$TYPESTATUSintermittent    -0.14520393  0.42778552
## pSERG$HOSPITALONSET == "no"TRUE  0.54712325  1.24005207
## pSERG$priorepilepsy1            -0.20205021  0.37485438
## pSERG$priorSE1                  -0.44349980  0.26654205
## pSERG$structural_etiology       -0.37337518  0.26907322

(abettacoefficients_withCIplus <- cbind(Estimate = coef(aplus),
confint(aplus)))

## Waiting for profiling to be done...

##                                    Estimate       2.5 %      97.5 %
## (Intercept)                     -0.770357302 -1.22893757 -0.32856099
## pSERG$SEXmale                    0.100976019 -0.17425528  0.37770924
## pSERG$ageyears                   0.004046437 -0.02223984  0.03003416
## pSERG$TYPESTATUSintermittent     0.139493249 -0.14520393  0.42778552
## pSERG$HOSPITALONSET == "no"TRUE  0.886178586  0.54712325  1.24005207
## pSERG$priorepilepsy1             0.086367752 -0.20205021  0.37485438
## pSERG$priorSE1                  -0.084920514 -0.44349980  0.26654205
## pSERG$structural_etiology       -0.048913885 -0.37337518  0.26907322

(aIR_withCIplus <- exp(abettacoefficients_withCIplus))

##                                   Estimate     2.5 %   97.5 %
## (Intercept)                     0.4628477 0.2926033 0.719959
## pSERG$SEXmale                   1.1062501 0.8400824 1.458939
## pSERG$ageyears                  1.0040546 0.9780056 1.030490
## pSERG$TYPESTATUSintermittent    1.1496910 0.8648459 1.533857
## pSERG$HOSPITALONSET == "no"TRUE 2.4258418 1.7282740 3.455793
## pSERG$priorepilepsy1            1.0902072 0.8170539 1.454780
## pSERG$priorSE1                  0.9185853 0.6417864 1.305442
## pSERG$structural_etiology       0.9522631 0.6884069 1.308751

# 3.    Outcome = Number of BZD doses before non-BZD ASM and within the first
45 min



# Model
bplus <- glm.nb(pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
pSERG$TYPESTATUS + (pSERG$HOSPITALONSET=="no") + pSERG$priorepilepsy +
pSERG$priorSE + pSERG$structural_etiology)
summary(bplus)
```

```
##
## Call:
## glm.nb(formula = pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + (pSERG$HOSPITALONSET == "no") + pSERG$priorepilepsy
+
##     pSERG$priorSE + pSERG$structural_etiology, init.theta = 1.454079284,
##     link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.4240  -1.1413  -0.6645   0.3589   3.1785
##
## Coefficients:
##                                 Estimate Std. Error z value Pr(>|z|)
## (Intercept)                    -1.527514   0.300855  -5.077 3.83e-07 ***
## pSERG$SEXmale                   0.041845   0.170914   0.245   0.8066
## pSERG$ageyears                  0.009258   0.016306   0.568   0.5702
## pSERG$TYPESTATUSintermittent    0.368245   0.182288   2.020   0.0434 *
## pSERG$HOSPITALONSET == "no"TRUE  1.313065   0.233576   5.622 1.89e-08 ***
## pSERG$priorepilepsy1            0.069159   0.177891   0.389   0.6974
## pSERG$priorSE1                 -0.202706   0.224505  -0.903   0.3666
## pSERG$structural_etiology      -0.143315   0.205648  -0.697   0.4859
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(1.4541) family taken to be 1)
##
##     Null deviance: 320.53  on 291  degrees of freedom
## Residual deviance: 275.41  on 284  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 713.62
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  1.454
##           Std. Err.:  0.399
##
##  2 x log-likelihood:  -695.623

confint(bplus)

## Waiting for profiling to be done...

##                                      2.5 %      97.5 %
## (Intercept)                    -2.12497826 -0.96084419
## pSERG$SEXmale                  -0.29335199  0.37780293
## pSERG$ageyears                 -0.02235681  0.04074423
## pSERG$TYPESTATUSintermittent    0.01232780  0.73028143
## pSERG$HOSPITALONSET == "no"TRUE  0.86675993  1.79055271
```

```
## pSERG$priorepilepsy1            -0.28328362  0.42158422
## pSERG$priorSE1                  -0.65088919  0.23612950
## pSERG$structural_etiology       -0.54495270  0.25044103

(bbettacoefficients_withCIplus <- cbind(Estimate = coef(bplus),
confint(bplus)))

## Waiting for profiling to be done...

##                                     Estimate       2.5 %      97.5 %
## (Intercept)                     -1.527514436 -2.12497826 -0.96084419
## pSERG$SEXmale                    0.041845368 -0.29335199  0.37780293
## pSERG$ageyears                   0.009258456 -0.02235681  0.04074423
## pSERG$TYPESTATUSintermittent     0.368244978  0.01232780  0.73028143
## pSERG$HOSPITALONSET == "no"TRUE  1.313065060  0.86675993  1.79055271
## pSERG$priorepilepsy1             0.069158735 -0.28328362  0.42158422
## pSERG$priorSE1                  -0.202706394 -0.65088919  0.23612950
## pSERG$structural_etiology       -0.143315158 -0.54495270  0.25044103

(bIR_withCIplus <- exp(bbettacoefficients_withCIplus))

##                                    Estimate     2.5 %    97.5 %
## (Intercept)                     0.2170746 0.1194356 0.3825698
## pSERG$SEXmale                   1.0427332 0.7457596 1.4590754
## pSERG$ageyears                  1.0093014 0.9778913 1.0415857
## pSERG$TYPESTATUSintermittent    1.4451960 1.0124041 2.0756647
## pSERG$HOSPITALONSET == "no"TRUE 3.7175508 2.3791896 5.9927638
## pSERG$priorepilepsy1            1.0716063 0.7533061 1.5243746
## pSERG$priorSE1                  0.8165179 0.5215818 1.2663383
## pSERG$structural_etiology       0.8664809 0.5798692 1.2845918

vplus <- glm.nb(pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
pSERG$TYPESTATUS + pSERG$HOSPITALONSET + pSERG$priorepilepsy + pSERG$priorSE
+ pSERG$TYPESTATUS*pSERG$HOSPITALONSET + pSERG$structural_etiology)
summary(vplus)

##
## Call:
## glm.nb(formula = pSERG$preAEDBZDsmorethan45 ~ pSERG$SEX + pSERG$ageyears +
##     pSERG$TYPESTATUS + pSERG$HOSPITALONSET + pSERG$priorepilepsy +
##     pSERG$priorSE + pSERG$TYPESTATUS * pSERG$HOSPITALONSET +
##     pSERG$structural_etiology, init.theta = 1.454116304, link = log)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -1.4235  -1.1424  -0.6594   0.3599   3.1954
##
## Coefficients:
##                                                  Estimate Std. Error
## (Intercept)                                     -0.212293   0.231117
## pSERG$SEXmale                                    0.042236   0.170930
```

```
## pSERG$ageyears                                          0.009269   0.016330
## pSERG$TYPESTATUSintermittent                            0.364894   0.195781
## pSERG$HOSPITALONSETyes                                 -1.332012   0.468801
## pSERG$priorepilepsy1                                    0.069145   0.177913
## pSERG$priorSE1                                         -0.203336   0.224847
## pSERG$structural_etiology                              -0.143601   0.205678
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes     0.025243   0.538524
##                                                        z value Pr(>|z|)
## (Intercept)                                             -0.919  0.35833
## pSERG$SEXmale                                            0.247  0.80483
## pSERG$ageyears                                           0.568  0.57029
## pSERG$TYPESTATUSintermittent                             1.864  0.06235 .
## pSERG$HOSPITALONSETyes                                  -2.841  0.00449 **
## pSERG$priorepilepsy1                                     0.389  0.69754
## pSERG$priorSE1                                          -0.904  0.36582
## pSERG$structural_etiology                               -0.698  0.48506
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes      0.047  0.96261
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for Negative Binomial(1.4541) family taken to be 1)
##
##     Null deviance: 320.53  on 291  degrees of freedom
## Residual deviance: 275.41  on 283  degrees of freedom
##   (1 observation deleted due to missingness)
## AIC: 715.62
##
## Number of Fisher Scoring iterations: 1
##
##
##               Theta:  1.454
##           Std. Err.:  0.399
##
##  2 x log-likelihood:  -695.620
```

```
confint(vplus)
```

```
## Waiting for profiling to be done...
```

```
##                                                             2.5 %
## (Intercept)                                            -0.65923012
## pSERG$SEXmale                                          -0.29335702
## pSERG$ageyears                                         -0.02234918
## pSERG$TYPESTATUSintermittent                           -0.01789567
## pSERG$HOSPITALONSETyes                                 -2.34555520
## pSERG$priorepilepsy1                                   -0.28327555
## pSERG$priorSE1                                         -0.65228021
## pSERG$structural_etiology                              -0.54537200
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes    -0.98744760
##                                                            97.5 %
```

```
## (Intercept)                                          0.22652439
## pSERG$SEXmale                                        0.37858335
## pSERG$ageyears                                       0.04075732
## pSERG$TYPESTATUSintermittent                         0.75289614
## pSERG$HOSPITALONSETyes                              -0.48002926
## pSERG$priorepilepsy1                                 0.42155474
## pSERG$priorSE1                                       0.23629865
## pSERG$structural_etiology                            0.25034148
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes  1.15160686

(vbettacoefficients_withCIplus <- cbind(Estimate = coef(vplus),
confint(vplus)))

## Waiting for profiling to be done...

##                                                        Estimate
## (Intercept)                                          -0.21229325
## pSERG$SEXmale                                         0.04223603
## pSERG$ageyears                                        0.00926897
## pSERG$TYPESTATUSintermittent                          0.36489424
## pSERG$HOSPITALONSETyes                               -1.33201162
## pSERG$priorepilepsy1                                  0.06914520
## pSERG$priorSE1                                       -0.20333618
## pSERG$structural_etiology                            -0.14360097
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes   0.02524337
##                                                            2.5 %
## (Intercept)                                          -0.65923012
## pSERG$SEXmale                                        -0.29335702
## pSERG$ageyears                                       -0.02234918
## pSERG$TYPESTATUSintermittent                         -0.01789567
## pSERG$HOSPITALONSETyes                               -2.34555520
## pSERG$priorepilepsy1                                 -0.28327555
## pSERG$priorSE1                                       -0.65228021
## pSERG$structural_etiology                            -0.54537200
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes  -0.98744760
##                                                           97.5 %
## (Intercept)                                           0.22652439
## pSERG$SEXmale                                         0.37858335
## pSERG$ageyears                                        0.04075732
## pSERG$TYPESTATUSintermittent                          0.75289614
## pSERG$HOSPITALONSETyes                               -0.48002926
## pSERG$priorepilepsy1                                  0.42155474
## pSERG$priorSE1                                        0.23629865
## pSERG$structural_etiology                             0.25034148
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes   1.15160686

(vIR_withCIplus <- exp(vbettacoefficients_withCIplus))

##                                                       Estimate     2.5 %
## (Intercept)                                          0.8087275 0.5172494
## pSERG$SEXmale                                        1.0431407 0.7457558
```

```
## pSERG$ageyears                                          1.0093121 0.9778987
## pSERG$TYPESTATUSintermittent                            1.4403617 0.9822635
## pSERG$HOSPITALONSETyes                                  0.2639458 0.0957940
## pSERG$priorepilepsy1                                    1.0715918 0.7533122
## pSERG$priorSE1                                          0.8160039 0.5208568
## pSERG$structural_etiology                               0.8662333 0.5796261
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes 1.0255647 0.3725263
##                                                            97.5 %
## (Intercept)                                             1.2542332
## pSERG$SEXmale                                           1.4602145
## pSERG$ageyears                                          1.0415993
## pSERG$TYPESTATUSintermittent                            2.1231400
## pSERG$HOSPITALONSETyes                                  0.6187653
## pSERG$priorepilepsy1                                    1.5243297
## pSERG$priorSE1                                          1.2665525
## pSERG$structural_etiology                               1.2844640
## pSERG$TYPESTATUSintermittent:pSERG$HOSPITALONSETyes 3.1632718
```