1. Frequentist ZIP Model in SAS (assumes vertical dataset where each row is a person-observation)

```sas
*zero inflated poisson,;
titl 'NLMIXe ED of ZIP Model for Midazolam';
proc nlmixed data=temC.Midaz3Vert;
  parameters b1=0 b2=0 b3=0 b4=0 b5=0 b6=0 b7=0 b8=0 b9=0 b10=0 b11=0
                   a1=0 a2=0 a3=0 a4=0 a5=0 a6=0 a7=0 a8=0 a9=0 a10=0 a11=0 s2u=1;
  /* linear predictor for the inflation probability */
  linpinfl = a1 + a2*shift + a3*night + a4*nonwhite + a5*male + a6*iqcodeA +
                       + a7*intubated + a8*APS
                   + a9*icudeath + a10*age + a11*LOSlt5d ;
  /* infprob = inflation probability for zeros */
  /*         = logistic transform of the linear predictor*/
  infprob  = 1/(1+exp(-linpinfl));
  /* Poisson mean */
  lambda   = exp(b1 + b1R + b2*shift + b3*night + b4*nonwhite + b5*male +
                   b6*iqcodeA +
                       + b7*intubated + b8*APS
                   + b9*icudeath5 + b10*age + b11*LOSlt5d );
  /* Build the ZIP log likelihood */
  if MidazDose=0 then
    ll = log(infprob + (1-infprob)*exp(-lambda));
  else ll = log((1-infprob)) - lambda + MidazDose*log(lambda) -
                   lgamma(MidazDose + 1);
  model MidazDose ~ general(ll);
  random b1R  ~ normal(0,s2u) subject=studyid;
run;
```

2. Bayesian ZIP Model in WinBUGS (assumes horizontal dataset with single row per person)

```r
model {

  # we nest the 15 shifts within each studyid among the cohort of ICU survivors
  # who were in ICU >= 3 days and received Midazolam during that time
  # the Midazolam doses have been rounded to nearest unit for use with Poisson
  # this is the classic mixture form of the ZIP model where occurrences of zeroes
  # are modeled with a logistic regression and the positive integers with a Poisson
  # and final likelihood is a mix of the two distributions

  for(studyid in 1:N){
    for(shift in 1:NumShifts[studyid]) {
      # a column called NumShifts is person specific
      # logistic likelihood for extra zeroes
      # coefficients centered around the sample mean of study population to facilitate convergence
    }
  }
}
```

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\[
\text{logExtraZ}[\text{studyid}, \text{shift}] \leftarrow \beta[1] \\
+ \beta[2]*(\text{shift} - 8) \\
+ \beta[3]*(\text{nigh}[\text{shift}] - 0.33) \\
+ \beta[4]*(\text{nonwhite}[\text{studyid}] - 0.17) \\
+ \beta[5]*(\text{male}[\text{studyid}] - 0.55) \\
+ \beta[6]*(\text{iqcodea}[\text{studyid}] - 0.3) \\
+ \beta[7]*(\text{intubated}[\text{studyid}] - 0.17) \\
+ \beta[8]*(\text{aps}[\text{studyid}] - 24.3) \\
+ \beta[9]*(\text{icudeath}[\text{studyid}] - 0.17) \\
+ \beta[10]*(\text{age}[\text{studyid}] - 73.4) \\
+ \beta[11]*(\text{losLT5d}[\text{studyid}] - 0.29) \\
+ \text{Rint}[\text{studyid}, 1] \quad \# \text{this is the random intercept for each person in logistic model}
\]

\[
\text{probZ}[\text{studyid}, \text{shift}] \leftarrow 1/(1 + \exp(-\text{logExtraZ}[\text{studyid}, \text{shift}]))) \quad \# \text{probZ = probability of a zero dose}
\]

\# Poisson likelihood for positive integers

\[
\text{log}(\text{lambda}[\text{studyid}, \text{shift}]) \leftarrow \alpha[1] \\
+ \alpha[2]*(\text{shift} - 8) \\
+ \alpha[3]*(\text{nigh}[\text{shift}] - 0.33) \\
+ \alpha[4]*(\text{nonwhite}[\text{studyid}] - 0.17) \\
+ \alpha[5]*(\text{male}[\text{studyid}] - 0.55) \\
+ \alpha[6]*(\text{iqcodea}[\text{studyid}] - 0.3) \\
+ \alpha[7]*(\text{intubated}[\text{studyid}] - 0.17) \\
+ \alpha[8]*(\text{aps}[\text{studyid}] - 24.3) \\
+ \alpha[9]*(\text{icudeath}[\text{studyid}] - 0.17) \\
+ \alpha[10]*(\text{age}[\text{studyid}] - 73.4) \\
+ \alpha[11]*(\text{losLT5d}[\text{studyid}] - 0.29) \\
+ \text{Rint}[\text{studyid}, 1] \quad \# \text{this is the random intercept for each person in Poisson model}
\]

\[
\text{probGTZ}[\text{studyid}, \text{shift}] \leftarrow \text{probZ}[\text{studyid}, \text{shift}]*1(1 - \exp(-\text{lambda}[\text{studyid}, \text{shift}]))) \quad \# \text{prob of MidazDose} > 0
\]

\[
\text{d}[\text{studyid}, \text{shift}] \leftarrow \text{step}(\text{MidazDose}[\text{studyid}, \text{shift}] - 1)
\]

\# Log Likelihood is a Mixture of logistic and Poisson

\[
\text{LogLLH}[\text{studyid}, \text{shift}] \leftarrow (1 - \text{d}[\text{studyid}, \text{shift}])*\log(1 - \text{probGTZ}[\text{studyid}, \text{shift}])) \quad \# \text{for all zero doses} \\
+ \text{d}[\text{studyid}, \text{shift}]*\log(\text{probGTZ}[\text{studyid}, \text{shift}]) + \text{MidazDose}[\text{studyid}, \text{shift}]*\log(\text{lambda}[\text{studyid}, \text{shift}]) \\
- \text{lambda}[\text{studyid}, \text{shift}] - \text{loggam}(\text{MidazDose}[\text{studyid}, \text{shift}] + 1) - \log(1 - \exp(-\text{lambda}[\text{studyid}, \text{shift}]))) \\
\]

\# following lines employ the zeroes trick, i.e., WinBUGS’ equivalent of general() in SAS 
\]

K <= 10000 \quad \# \text{constant required for “zeros trick”} 
zeros[studyid,shift] ~ dpois(0) 
zeros[studyid,shift] ~ dpois(\phi[studyid,shift]) 
\phi[studyid,shift] ~ -LogLLH[studyid,shift] + K 

\} \quad \# \text{close shift loop} 
\} \quad \# \text{close studyid loop} 

# prior distributions for fixed model terms

for (i in 1:11) 
{ 
\alpha[i] ~ dnorm(0,0.1) 
}

for (i in 1:11) 
{ 
\beta[i] ~ dnorm(0,0.1) 
}
### prior distributions for random terms

# first for normal locations
for (i in 1:113) {
  Rint[i,1] ~ dnorm(0,tau1)
  m[i] <- psi*Rint[i,1]
  Rint[i,2] ~ dnorm(m[i], tau2)
}

psi~dnorm(0, 0.001)
tau1 ~ dgamma(0.1,0.1)
tau2 ~ dgamma(0.1,0.1)

# second for variances

sigma1 <- 1/sqrt(tau1)   # SD of Rint[,1]
denom1 <- pow(psi,2)/tau1 + 1/tau2
sigma2 <- sqrt(denom1)  # SD of Rint[,2]
denom2 <- sqrt(denom1/tau1)
num <- psi/tau1
rho <- num/denom2  # corr(Rint[,1],Rint[,2])

###

3. Bayesian Random Effects Poisson Model in WinBUGS (assumes horizontal dataset with single row per person)

```c
model
{
  # we nest the 15 shifts within each studyid among the cohort of ICU survivors
  # who were in ICU >= 3 days and received Midazolam during that time

  for(studyid in 1 : N) {
    for(shift in 1 : NumShifts[studyid]) { # a column called NumShifts is person specific

      # Poisson likelihood for observed doses
      MidazDose[studyid,shift] ~ dpois(mu[studyid,shift])
      log(mu[studyid,shift]) <-
        + alpha[4]*(nonwhite[studyid] - 0.17) + alpha[5]*(male[studyid] - 0.55)
        + alpha[6]*(night[shift] - 0.33) + alpha[7]*(intubated[studyid] - 0.75)
        + alpha[8]*(aps[studyid] - 24.3) + alpha[9]*(icudeath[studyid] - 0.17)
        + alpha[10]*(age[studyid] - 73.4) + alpha[11]*(losLT5d[studyid] - 0.29)
        + theta[studyid] + perShift[studyid,shift] # random effects person-shift
    }
  }
}
```
# Prior distribution for the person-shift intercepts
for(studyid in 1 : N) {
  for(shift in 1 : 15) {
    perShift[studyid,shift] ~ dnorm(0,tau.perShift)
  }
}

# Prior distribution for the random intercepts
for (studyid in 1:N) {
  theta[studyid]~dnorm(0,tau.theta)
}

# prior distributions for the model coefficients
alpha[1:11]~dmnorm(alphamu[,],Sigma[,])

#Hyperprior distributions on inverse variance parameter of random effects
  tau.theta ~ dgamma(1,1)
  tau.perShift ~ dgamma(1,1)
}