Web-based SupplementaryMaterials for Simultaneous Inference for HIV Dynamic Models with Skew-t Distribution Incorporating Mismeasured Covariate and Multiple Treatment Factors by Y. Huang et al.

Appendix A. Multivariate skew-t distribution

Different versions of the multivariate skew-t (ST) distribution has been considered and used in the literature (Arellano-Valle and Genton, 2005; Azzalini and Capitanio, 2003; Ho and Lin, 2010; Sahu *et al.*, 2003) and among others. A new class of distributions by introducing skewness in multivariate elliptically distributions were developed in publication.[8] The class, which is obtained by using transformation and conditioning, contains many standard families including the multivariate ST distribution. For completeness, this appendix briefly summarizes the multivariate ST distribution that will be used in this paper. Assume an m-dimensional random vector $\boldsymbol{Y}$ follows an m variate ST distribution with location vector $\boldsymbol{\mu}$, $m \times m$ positive (diagonal) dispersion matrix $\boldsymbol{\Sigma}$, $m \times m$ skewness matrix $\boldsymbol{\Delta}(\boldsymbol{\delta}) = diag(\delta_1, \delta_2, \ldots, \delta_m)$ and the degree of freedom ν, where $\boldsymbol{\delta} = (\delta_1, \ldots, \delta_m)^T$ is a vector of skewness parameters. In what follows, we briefly discuss multivariate ST distribution introduced by Sahu *et al.*(2003) which is suitable for a Bayesian inference since it is built using conditional method. For detailed discussions on properties of ST distribution, see Reference (Sahu *et al.*, 2003).

An m-dimensional random vector $\boldsymbol{Y}$ follows an m-variate ST distribution if its probability density function (pdf) is given by

$$f(\boldsymbol{y}|\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Delta}(\boldsymbol{\delta}), \nu) = 2^m t_{m,\nu}(\boldsymbol{y}|\boldsymbol{\mu}, \boldsymbol{A}) P(\boldsymbol{V} > \boldsymbol{0}), \tag{A.1}$$

where $\boldsymbol{A} = \boldsymbol{\Sigma} + \boldsymbol{\Delta}^2(\boldsymbol{\delta})$, we denote the m-variate t distribution with parameters $\boldsymbol{\mu}$, $\boldsymbol{A}$ and degrees of freedom ν by $t_{m,\nu}(\boldsymbol{\mu}, \boldsymbol{A})$ and the corresponding pdf by $t_{m,\nu}(\boldsymbol{y}|\boldsymbol{\mu}, \boldsymbol{A})$ henceforth, the random vector $\boldsymbol{V}$ follows the multivariate t distribution $t_{m,\nu+m}(\cdot)$. We denote this distribution by $ST_{m,\nu}(\boldsymbol{\mu}, \boldsymbol{\Sigma}, \boldsymbol{\Delta}(\boldsymbol{\delta}))$. In particular, when $\boldsymbol{\Sigma} = \sigma^2 \boldsymbol{I}_m$ and $\boldsymbol{\Delta}(\boldsymbol{\delta}) = \delta \boldsymbol{I}_m$, the equation (A.1) simplifies to

$$\begin{aligned} f(\boldsymbol{y}|\boldsymbol{\mu}, \sigma^2, \delta, \nu) = 2^m (\sigma^2 + \delta^2)^{-m/2} \tfrac{\Gamma((\nu+m)/2)}{\Gamma(\nu/2)(\nu\pi)^{m/2}} \left\{1 + \tfrac{(\boldsymbol{y}-\boldsymbol{\mu})^T(\boldsymbol{y}-\boldsymbol{\mu})}{\nu(\sigma^2+\delta^2)}\right\}^{-(\nu+m)/2} \\ \times T_{m,\nu+m}\left[\left\{\tfrac{\nu+(\sigma^2+\delta^2)^{-1}(\boldsymbol{y}-\boldsymbol{\mu})^T(\boldsymbol{y}-\boldsymbol{\mu})}{\nu+m}\right\}^{-1/2} \tfrac{\delta(\boldsymbol{y}-\boldsymbol{\mu})}{\sigma\sqrt{\sigma^2+\delta^2}}\right], \end{aligned} \tag{A.2}$$

where $T_{m,\nu+m}(\cdot)$ denotes the cumulative distribution function (cdf) of $t_{m,\nu+m}(\mathbf{0}, \boldsymbol{I}_m)$. However, unlike in the SN distribution discussed by Huang and Dagne (2011), the ST density can not be written as the product of univariate ST densities. Here $\boldsymbol{Y}$ are dependent but uncorrelated.

The mean and covariance matrix of the ST distribution $ST_{m,\nu}(\boldsymbol{\mu}, \sigma^2\boldsymbol{I}_m, \boldsymbol{\Delta}(\boldsymbol{\delta}))$ are given by

$$
\begin{aligned}
E(\boldsymbol{Y}) &= \boldsymbol{\mu} + (\nu/\pi)^{1/2}\tfrac{\Gamma((\nu-1)/2)}{\Gamma(\nu/2)}\boldsymbol{\delta}, \\
cov(\boldsymbol{Y}) &= \left[\sigma^2\boldsymbol{I}_m + \boldsymbol{\Delta}^2(\boldsymbol{\delta})\right]\tfrac{\nu}{\nu-2} - \tfrac{\nu}{\pi}\left[\tfrac{\Gamma\{(\nu-1)/2\}}{\Gamma(\nu/2)}\right]^2\boldsymbol{\Delta}^2(\boldsymbol{\delta}).
\end{aligned} \tag{A.3}
$$

It is noted that when $\boldsymbol{\delta} = \mathbf{0}$, the ST distribution reduces to usual t distribution. In order to have a zero mean vector, we should assume the location parameter $\boldsymbol{\mu} = -(\nu/\pi)^{1/2}\frac{\Gamma((\nu-1)/2)}{\Gamma(\nu/2)}\boldsymbol{\delta}$, which is what we assume in the paper.

By the proposition discussed by Sahu *et al.*(2003) and Ho and Lin (2010) the ST distribution of $\boldsymbol{Y}$ has a convenient stochastic representation as follows.

$$\boldsymbol{Y} = \boldsymbol{\mu} + \boldsymbol{\Delta}(\boldsymbol{\delta})|\boldsymbol{X}_0| + \boldsymbol{\Sigma}^{1/2}\boldsymbol{X}_1, \tag{A.4}$$

where $\boldsymbol{X}_0$ and $\boldsymbol{X}_1$ are two independent random vectors following $t_{m,\nu}(\mathbf{0}, \boldsymbol{I}_m)$. Note that the expression (A.4) provides a convenience device for random number generation and for implementation purpose. Let $\boldsymbol{w} = |\boldsymbol{X}_0|$; then $\boldsymbol{w}$ follows an m-dimensional standard half-t distribution. Thus, a hierarchical representation of (A.4) is given by

$$\boldsymbol{Y}|\boldsymbol{w} \sim t_{m,\nu}(\boldsymbol{\mu} + \boldsymbol{\Delta}(\boldsymbol{\delta})\boldsymbol{w}, c\boldsymbol{\Sigma}), \ \boldsymbol{w} \sim t_{m,\nu}(\mathbf{0}, \boldsymbol{I}_m)\boldsymbol{I}(\boldsymbol{w} > \mathbf{0}), \tag{A.5}$$

where $c = (\nu + \boldsymbol{w}^T\boldsymbol{w})/(\nu + m)$.

Appendix B: WinBUGS code of ST Model I for the analysis of AIDS data

```
## Begin of Model
model{
for (i in 1:n)  # n=number of subjects
    {
 ## Random-Effects with Normal Distribution
      b0[i,1]<-0
      b0[i,2]<-0
      b0[i,3]<-0
      b0[i,4]<-0
      b[i,1:4]~dmnorm(b0[i,1:4],Omega1[,])
      a0[i,1]<-0
      a0[i,2]<-0
      a0[i,3]<-0
      a[i,1:3]~dmnorm(a0[i,1:3],Omega2[,])
      L44[i]<-beta[2]+b[i,2]
     }

for (j in 1 : M) # M= total number of measurements
    {
 ## CD4 Measurement Errors Model with ST Distribution
 ## Z[,]= values of spline basis function
    w2[j]~dt(0,1,nu2)I(0,)
    c2[j]<-(nu2+w2[j]*w2[j])/n2
    aau2[j]<-1/(c2[j]*tau2*tau2)
    z.star[j]<-(alpha[1]+a[y[j,2],1])+(alpha[2]+a[y[j,2],2])*Z[j,2]
               +(alpha[3]+a[y[j,2],3])*Z[j,3]          # y[j,2]=id
    z.mean[j]<-z.star[j]+delta2*(w2[j]-mue2)            # ST distribution
    y[j,3] ~dt(z.mean[j],aau2[j],n2)            # y[j,3]=Standardized cd4

 ## Viral Load Response NLME Model with ST Distribution
    p1[j]<-beta[1] +b[y[j,2],1]
    p2[j]<-beta[3] +b[y[j,2],3]
    lambda1[j]<-beta[2] +b[y[j,2],2]
    lambda2[j]<-beta[4]+beta[5]*z.mean[j]
              +beta[6]*y[j,4]+b[y[j,2],4]               # y[j,4]=drug efficacy
    dm1[j]<-p1[j]-step(lambda1[j]-lambda2[j])*lambda1[j]*y[j,5]  # y[j,5]=time
    dm2[j]<-p2[j]-step(lambda1[j]-lambda2[j])*lambda2[j]*y[j,5]
    dm3[j]<-exp(dm1[j])
    dm4[j]<-exp(dm2[j])
    dm5[j]<-dm3[j]+dm4[j]

    w1[j]~dt(0,1,nu1)I(0,)
    c1[j]<-(nu+w1[j]*w1[j])/n1
    aau1[j]<-1/(c1[j]*tau*tau)
    mu[j]<-log(dm5[j])+ delta*(w1[j]-mue1)              # ST distribution
    y[j,6]~dt(mu[j],aau1[j],n1)                         # y[j,6]=log(RNA)
```

```
 ## Fitted Values and Residuals
    fit[j]<-mu[j]
    resid[j]<-y[j,6]-fit[j]
    }

 ## Prior Distributions of the Hyperparameters
 #(1) Degree of freedom
   nu0<-0.5
   nu~dexp(nu0)I(2,)
   n1<-nu+1
   mue1<-exp(loggam(0.5*(nu-1.))-loggam(0.5*nu))*sqrt(nu/3.14159)

   nu20<-0.5
   nu2~dexp(nu20)I(2,)
   n2<-nu2+1
   mue2<-exp(loggam(0.5*(nu2-1.))-loggam(0.5*nu2))*sqrt(nu2/3.14159)

 #(2) Coefficients
   for (l in 1:6){beta[l]~dnorm(0,1.0E-2)}
   for (k in 1:3){alpha[k]~dnorm(0,1.0E-2)}

 #(3) Skewness parameters
   delta~dnorm(0.0, 0.01)
   delta2~dnorm(0.0, 0.01)

 #(4) Variance-covariance matrices
   Omega1[1:4,1:4]~dwish(R1[,],5)
   v1[1:4,1:4]<-inverse(Omega1[,])
   Omega2[1:3,1:3]~dwish(R2[,],5)
   v2[1:3,1:3]<-inverse(Omega2[,])

 #(5) Precision parameters
   tau~dunif(0,100)
   sigma.tau<-tau*tau
   tau2~dunif(0,100)
   sigma.tau2<-tau2*tau2
}
##End of model
```