

A Appendix: simulation code and model files

A.1 R code to simulate data

```
1 #####
2 ##### function to simulate survival time #####
3 #####
4 # survival function is given by:  $S(t) = \exp(-\exp(B) * (\exp(A*t) - 1) / A)$ 
5 sim_Ti = function(n=250, alpha1, alpha2, delta=c(1,1), gamma=c(1,1)){
6   # random effects
7   Sigma=matrix(c(0.09, 0.09*0.16, 0.09*0.16, 0.09), nrow=2, byrow=T)
8   u=rmvnorm(n,c(0,0),Sigma)
9   H = matrix(rnorm(2*n),n,2)
10  W = matrix(rnorm(2*n),n,2)
11
12  # define the survival function
13  surv = function(t) {
14    if(alpha1==0 & alpha2==0) {res=t*exp(W*%gamma)}
15    else{
16      res = ((exp(alpha2*u[,1]+alpha2*t*u[,2]+alpha1*delta[1]*H[,1]+alpha1*
17        delta[2]*H[,2]*t+W*%gamma)-exp(alpha1*H[,1]*delta[1]+W*%gamma+alpha2*u
18        [,1]))/(alpha2*u[,2]+alpha1*H[,2]*delta[2]))
19    }
20    return(exp(-res))
21  }
22  rnd =runif(n)
23  Ti = rep(Inf,n)
24  # w = which(surv(1e8)-rnd < 0)
25  w = which(1-surv(101)-rnd > 0)
26  Ti[w] = sapply(w,function(j) uniroot(function(x) 1-surv(x)[j]-rnd[j],lower
27    =0,upper=101)$root)
28  Ti[Ti==0] = min(Ti[Ti>0])/2
29  Ci = 5*rbeta(n,4,1)
30  Delta = as.numeric(Ti < Ci)
31  Ti2 = pmin(Ti, Ci)
32  list(Ti=Ti2, event=Delta, H=H, W=W, U=u)
33 }
34
35 #####
36 ##### function to simulate longitudinal data #####
37 #####
38 sim_longitudinal_data = function(survival_data=surdata, n=250, time=c(0, 0.25,
39   0.5, 0.75, 1, 3), tau, sigma=1, beta=c(1,1), delta=c(1,1)){
40   # survival_data - data simulated from survival model
41   # n - # of subjects
42   # time - time points of observations
43   # tau - quantile
44   # sigma - scale parameter
```

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44
45 # random generation of ALD(0,sigma,p)
46 rald = function(n, location=0, scale, p){
47   u = rnorm(n)
48   z = rexp(n)
49   v = scale*z
50   theta = (1-2*p)/(p*(1-p))
51   tau = sqrt(2/(p*(1-p)))
52   sample = theta * z + tau * sqrt(z) * u
53 }
54
55 time = time # at most # = length(time) observations per patient
56 y = matrix(NA, nrow=n, ncol=length(time)) # wide format
57 Ti = survival_data$Ti
58 U = survival_data$U # random effects
59 H = survival_data$H
60 X = cbind(1, rnorm(n))
61 count = sapply(Ti, function(x) sum(x > time)) # number of observations after
drop-outs
62
63 for (i in 1:n){
64   for (j in 1:count[i]){
65     location = beta %*% X[i, ] + delta %*% c(H[i,1], H[i,2]*time[j]) + U[i,]
66     %*% c(1, time[j])
67     y[i,j] = location + rald(1, scale=sigma, p=tau)
68   }
69 }
70 list(y = y, X = X, J=count)
71 }
72
73 #####
74 ##### function to simulate multiple joint data sets #####
75 #####
76 sim_multiple_data = function(N, sur_fun=sim_Ti, longi_fun=sim_longitudinal_
data, alpha, tau){
77   # N - number of data sets to generate
78   # sur_fun - function to simulate survival data
79   # longi_fun - function to simulate longitudinal data
80   # alpha - association mechanism for JM
81   # tau - quantile
82
83   outdata = vector(mode='list', N)
84   for (i in 1:N){
85     sur_data = sur_fun(alpha1=alpha[1], alpha2=alpha[2])
86     longi_data = longi_fun(sur_data, tau=tau)
87     outdata[[i]] = list(survival_data=sur_data, longitudinal_data=longi_data)
88   }
89   outdata
90 }

```

A.2 JAGS model file

```

1 model{
2   zero[1] <- 0
3   zero[2] <- 0
4   k1 <- (1-2*qt)/(qt*(1-qt))
5   k2 <- 2/(qt*(1-qt))
6
7   for (i in 1:I){
8     # prior for random effects
9     u[i, 1:2] ~ dmnorm(zero[], precision[,])
10
11    # longitudinal process, BQR mixed model using ALD representation
12    for (j in 1:J[i]){
13      er[i,j] ~ dexp(sigma)
14      mu[i,j] <- u[i,1] + u[i,2]*t[j] + inprod(X[i,], beta[]) + delta[1]*H[i
15      ,1] + delta[2]*H[i,2]*t[j] + k1*er[i,j]
16      prec[i,j] <- sigma/(k2*er[i,j])
17      y[i,j] ~ dnorm(mu[i,j], prec[i,j])
18    } #end of j loop
19
20    # survival process, baseline hazard is set to 1
21    A[i] <- alpha2*u[i,2] + alpha1*delta[2]*H[i,2]
22    B[i] <- alpha1*delta[1]*H[i,1] + alpha2*u[i,1] + inprod(gamma, W[i,])
23    S[i] <- exp(- c*exp(B[i])*(pow(exp(A[i]), Ti[i])-1)/A[i])
24    h[i] <- c*exp(inprod(gamma, W[i,]) + alpha1*(delta[1]*H[i,1] + delta[2]*H[i
25    ,2]*Ti[i]) + alpha2*(u[i,1] + u[i,2]*Ti[i]))
26    L[i] <- pow(h[i], event[i])*S[i]/1.0E+08
27
28    # zero trick
29    phi[i] <- -log(L[i])
30    zeros[i] ~ dpois(phi[i])
31
32  }#end of i loop
33
34  precision[1:2,1:2] <- inverse(Sigma[,])
35  Sigma[1,1] <- 1
36  Sigma[1,2] <- rho*sig1
37  Sigma[2,1] <- Sigma[1,2]
38  Sigma[2,2] <- sig1*sig1
39
40  # priors for other parameters
41  alpha1 ~ dnorm(0, 0.001)
42  alpha2 ~ dnorm(0, 0.001)
43  beta[1] ~ dnorm(0, 0.001)
44  beta[2] ~ dnorm(0, 0.001)
45  delta[1] ~ dnorm(0, 0.001)
46  delta[2] ~ dnorm(0, 0.001)
47  gamma[1] ~ dnorm(0, 0.001)
48  gamma[2] ~ dnorm(0, 0.001)
49  sigma ~ dgamma(0.001, 0.001)

```

```
48 rho ~ dunif(-1, 1)
49 sig1 ~ dgamma(0.01, 0.01)
50 c ~ dunif(0.01, 10)
51 }
```