CGD Data: Recurrent Events Analysis – an analysis using the package `bayesSurv`

Arnošt Komárek

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In this document we describe the analysis of CGD data presented in Section 4.1 of Komárek and Lesaffre (2004).

We consider the following model

$$\begin{aligned}\log(T_{i,l}) = &\beta_1\, trtmt_i + \beta_2\, inherit_i + \beta_3\, age_{i,l} + \beta_4\, cortico_i + \beta_5\, prophy_i + \beta_6\, (gender_i = female) + \\ &+ \beta_7\, (hospital_i = USother) + \beta_8\, (hospit_i = EUAmsterdam) + \beta_9\, (hospit_i = EUother) + \\ &+ b_i + \varepsilon_{i,l},\end{aligned}$$

where $i = 1, \ldots, 128$ indexes patients and l recurrent events on patients.

1 Initial data operations

Firstly we load the package `bayesSurv`, read the data and do some arrangements.

```
> library(bayesSurv)

Loading required package: survival
Loading required package: coda

> datadir <- paste(getwd(), "/cgd1", sep = "")
> data <- read.table(paste(datadir, "/cgd.dat", sep = ""), header = TRUE,
+     colClasses = c(rep("numeric", 2), rep("character", 2), rep("numeric",
+         13)))
> print(data[1:6, ])

  hospit     ID    RDT    IDT trtmt inherit age height weight cortico prophy
1    174 174054 120688 092589     1       2  38 152.20   66.7       2      1
2    174 174077 011389 092589     2       1  14 144.00   32.8       2      1
3    174 174109 022489 092589     2       1  26  81.25   55.0       2      1
4    174 174111 030689 092589     2       1  26 178.50   69.3       2      1
5    204 204001 082888 040489     1       2  12 147.00   62.0       2      2
6    204 204001 040589 090589     1       2  12 147.00   62.0       2      2
  gender hcat  T1  T2 event sequence
1      2    2 293   0     2        1
2      1    2 255   0     2        1
3      1    2 213   0     2        1
4      1    2 203   0     2        1
5      2    2 219   0     1        1
6      2    2 373 220     1        2
```

For our analysis we change all 1-2 variables into 1-0 or 0-1 ones. Such that

Variable	0	1
trtmt	placebo	treatment
gender	male	female
inherit	X-linked	autosomal recessive
cortico	no	yes
prophy	no	yes
event	censored	obsered

```
> data$trtmt <- -(data$trtmt - 2)
> data$gender <- data$gender - 1
> data$inherit <- data$inherit - 1
> data$cortico <- -(data$cortico - 2)
> data$prophy <- -(data$prophy - 2)
> data$gender <- factor(data$gender, labels = c("male", "female"))
> data$inherit <- factor(data$inherit, labels = c("X-l", "AuRec"))
> data$hcat <- factor(data$hcat, labels = c("US-NIH", "US-other",
+     "EU-Am", "EU-other"))
> data$event <- -(data$event - 2)
```

Further we compute times between two consecutive infections and define some additional variables.

```
> data$time <- data$T1 - data$T2
> npatient <- length(unique(data$ID))
> nobs <- dim(data)[1]
> print(data[1:6, ])
```

```
  hospit     ID    RDT    IDT trtmt inherit age height weight cortico prophy
1    174 174054 120688 092589     1   AuRec  38 152.20   66.7       0      1
2    174 174077 011389 092589     0     X-l  14 144.00   32.8       0      1
3    174 174109 022489 092589     0     X-l  26  81.25   55.0       0      1
4    174 174111 030689 092589     0     X-l  26 178.50   69.3       0      1
5    204 204001 082888 040489     1   AuRec  12 147.00   62.0       0      0
6    204 204001 040589 090589     1   AuRec  12 147.00   62.0       0      0
  gender     hcat  T1  T2 event sequence time
1 female US-other 293   0     0        1  293
2   male US-other 255   0     0        1  255
3   male US-other 213   0     0        1  213
4   male US-other 203   0     0        1  203
5 female US-other 219   0     1        1  219
6 female US-other 373 220     1        2  153
```

2 Finding reasonable values for prior hyperparameters

To find reasonable values for prior hyperparameters we fit the log-normal AFT model with and without random intercept using maximum likelihood:

```
> ifit <- survreg(Surv(time, event) ~ trtmt + inherit + age + cortico +
+     prophy + gender + hcat + frailty(ID, dist = "gaussian"),
+     dist = "lognormal", data = data)
> resid <- ifit$y[, 1] - ifit$linear.predictors
> R <- max(resid) - min(resid)
> ifit2 <- survreg(Surv(time, event) ~ trtmt + inherit + age +
+     cortico + prophy + gender + hcat, dist = "lognormal", data = data)
```

Summary for the model with the random intercept and the range of residuals:

```
> summary(ifit)

Call:
survreg(formula = Surv(time, event) ~ trtmt + inherit + age +
    cortico + prophy + gender + hcat + frailty(ID, dist = "gaussian"),
    data = data, dist = "lognormal")
               Value Std. Error     z        p
(Intercept)   3.9152     0.6611  5.92 3.18e-09
trtmt         1.1040     0.3037  3.63 2.78e-04
inheritAuRec -0.6560     0.3793 -1.73 8.38e-02
age           0.0366     0.0176  2.08 3.73e-02
cortico      -1.7607     0.9307 -1.89 5.85e-02
prophy        0.9390     0.4516  2.08 3.76e-02
genderfemale  1.0256     0.5137  2.00 4.59e-02
hcatUS-other  0.3695     0.3807  0.97 3.32e-01
hcatEU-Am     1.2154     0.5881  2.07 3.88e-02
hcatEU-other  0.8248     0.5191  1.59 1.12e-01
Log(scale)    0.1776     0.0907  1.96 5.03e-02

Scale= 1.19

Log Normal distribution
Loglik(model)= -491.7   Loglik(intercept only)= -548.5
        Chisq= 113.44 on 36.3 degrees of freedom, p= 7e-10
Number of Newton-Raphson Iterations:  6 25
n= 203

> print(R)

[1] 6.40232
```

Summary for the model without the random intercept:

```
> summary(ifit2)

Call:
survreg(formula = Surv(time, event) ~ trtmt + inherit + age +
    cortico + prophy + gender + hcat, data = data, dist = "lognormal")
               Value Std. Error      z        p
(Intercept)   3.6570     0.6658  5.493 3.96e-08
trtmt         1.3531     0.3226  4.195 2.73e-05
inheritAuRec -0.9582     0.3646 -2.628 8.58e-03
age           0.0451     0.0185  2.429 1.51e-02
cortico      -2.3894     0.9599 -2.489 1.28e-02
prophy        1.1071     0.4540  2.439 1.47e-02
genderfemale  1.4679     0.5300  2.770 5.61e-03
hcatUS-other  0.2463     0.4030  0.611 5.41e-01
hcatEU-Am     1.4157     0.6451  2.194 2.82e-02
hcatEU-other  0.9850     0.5673  1.736 8.25e-02
Log(scale)    0.5223     0.0864  6.046 1.48e-09

Scale= 1.69

Log Normal distribution
Loglik(model)= -526.3   Loglik(intercept only)= -548.5
        Chisq= 44.31 on 9 degrees of freedom, p= 1.2e-06
Number of Newton-Raphson Iterations: 4
n= 203
```

3 Specification of priors

To specify correctly the prior hyperparameters for β parameters we have to know how the covariates are sorted in the design matrix. Normally, the same order should be used as in the `formula` specification. However, one never knows...

The following command returns the design matrix and we look at first few rows to see how are the covariates sorted in the columns. We also define the variable `nregres` (number of covariates). The same model `formula` is used as in the future function call.

```
> X <- bayessurvreg1(Surv(time, event) ~ trtmt + inherit + age +
+     cortico + prophy + gender + hcat + cluster(ID), random = ~1,
+     data = data, onlyX = TRUE)
> nregres <- dim(X)[2]
> X[1:3, ]
```

```
  trtmt inheritAuRec age cortico prophy genderfemale hcatUS-other hcatEU-Am
1     1            1  38       0      1            1            1         0
2     0            0  14       0      1            0            1         0
3     0            0  26       0      1            0            1         0
  hcatEU-other
1            0
2            0
3            0
```

We see that $\beta_1 = trtmt$, $\beta_2 = inherit \ldots \beta_7 = hcat(US - other)$, $\beta_8 = hcat(EU - Am)$, $\beta_9 = hcat(EU - other)$.

Now, we can start to specify the prior choices. These will be stored in `lists`. For illustration purposes, we show also some other prior choices than these used in Komárek and Lesaffre (2004).

3.1 Priors for the mixture

```
> prior <- list()
```

Prior for the number of mixture components k will be truncated Poisson(λ, k_{max}) with $k_{max} = 30$ and $\lambda = 5$. Alternative prior distribution would be uniform specified by

```
prior$k.prior = ``uniform"
```

```
> prior$kmax <- 30
> prior$k.prior <- "poisson"
> prior$poisson.k <- 5
```

Prior for mixture weights $w_1, \ldots, w_k$ will be Dirichlet($\delta, \ldots, \delta$) with $\delta = 1$.

```
> prior$dirichlet.w <- 1
```

Prior for mixture means $\mu_1, \ldots, \mu_k$ will be N(ξ, κ) with $\xi = 3.66$ (taken from `survreg(dist = "lognormal")` fit (approx intercept)) and $\kappa = 5^2 \approx (3 \times 1.69)^2$ (1.69 was estimated scale parameter by `survreg`).

```
> prior$mean.mu <- 3.66
> prior$var.mu <- 5^2
```

Prior for mixture inverse-variances $\sigma_1^{-2}, \ldots, \sigma_k^{-2}$ will be Gamma(ζ, η) and prior for η will be Gamma(g, h), with $\zeta = 2.0$, $g = 0.2$ and $h = 0.1$.

```
> prior$shape.invsig2 <- 2
> prior$shape.hyper.invsig2 <- 0.2
> prior$rate.hyper.invsig2 <- 0.1
```

Probabilities of the split move (given current value of k) will be always 0.5 except when $k = 1$ or $k = k_{max}$.

```
> prior$pi.split <- c(1, rep(0.5, prior$kmax - 2), 0)
```

Probabilities of the birth move (given current value of k) will be always 0.5 except when $k = 1$ or $k = k_{max}$.

```
> prior$pi.birth <- c(1, rep(0.5, prior$kmax - 2), 0)
```

The last component of the `list prior` should be always set to `FALSE`. Its value equal to `TRUE` served only for some exploratory purposes of the author.

```
> prior$Eb0.depend.mix <- FALSE
```

Look how it looks like:

```
> print(prior)

$kmax
[1] 30

$k.prior
[1] "poisson"

$poisson.k
[1] 5

$dirichlet.w
[1] 1

$mean.mu
[1] 3.66

$var.mu
[1] 25

$shape.invsig2
[1] 2

$shape.hyper.invsig2
[1] 0.2

$rate.hyper.invsig2
[1] 0.1

$pi.split
 [1] 1.0 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5
[20] 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.0

$pi.birth
 [1] 1.0 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5
[20] 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.0

$Eb0.depend.mix
[1] FALSE
```

3.2 Priors for regression parameters β

For illustration purposes, we define several `list`s with the same prior specification (all $\boldsymbol{\beta}$ parameters are assigned $\mathrm{N}(0, 1000)$ prior) however with different possibilities how to update the $\boldsymbol{\beta}$ parameters in the MCMC simulation.

3.2.1 All β parameters updated using the Gibbs step

With the first specification, all $\boldsymbol{\beta}$ will be updated in one block using the Gibbs move. This is usually a recommended choice and was also used to get results presented in Komárek and Lesaffre (2004).

```
> prior.beta.gibbs <- list()
> prior.beta.gibbs$mean.prior <- rep(0, nregres)
> prior.beta.gibbs$var.prior <- rep(1000, nregres)
```

Look how it looks like:

```
> print(prior.beta.gibbs)

$mean.prior
[1] 0 0 0 0 0 0 0 0 0

$var.prior
[1] 1000 1000 1000 1000 1000 1000 1000 1000 1000
```

3.2.2 All β parameters updated in one block using random walk Metropolis-Hastings step

With the second specification, all $\boldsymbol{\beta}$ parameters would be updated in one block using a random walk Metropolis-Hastings step with a proposal covariance matrix `covm`.

```
> prior.beta.mh1 <- list()
> prior.beta.mh1$mean.prior <- rep(0, nregres)
> prior.beta.mh1$var.prior <- rep(1000, nregres)
```

Definition of blocks in which beta parameters will be updated and the way in which they will be updated:

```
> prior.beta.mh1$blocks <- list()
> prior.beta.mh1$blocks$ind.block <- list()
```

There is only one block that contains beta[1:9]:

```
> prior.beta.mh1$blocks$ind.block[[1]] <- 1:9
> nblock <- length(prior.beta.mh1$blocks$ind.block)
```

Further we define a proposal covariance matrix.

`vars`	=	proposal variances for each beta parameter
`cors`	=	lower triangle of the proposal correlation matrix
`corsm`	=	proposal correlation matrix itself
`covm`	=	proposal covariance matrix

```
> vars <- c(0.15, 0.2, 3e-04, 1.3, 0.08, 0.25, 0.1, 0.35, 0.35)
> cors <- c(1, 0.1, 0, 0.1, 0.15, 0, 0.4, 0.1, 0.2, 1, -0.15, 0.15,
+     -0.2, -0.3, 0.2, -0.1, 0, 1, -0.2, 0.15, 0.2, 0.3, 0.2, 0.1,
+     1, 0.2, -0.5, 0.2, -0.4, 0.4, 1, 0.15, 0.5, 0.3, 0.4, 1,
```

```
+     0.15, 0.15, 0, 1, 0.35, 0.65, 1, 0.2, 1)
> corsm <- diag(9)
> corsm[lower.tri(corsm, diag = TRUE)] <- cors
> corsm[upper.tri(corsm, diag = FALSE)] <- t(corsm)[upper.tri(t(corsm),
+     diag = FALSE)]
> covm <- diag(sqrt(vars)) %*% corsm %*% diag(sqrt(vars))
```

Here is the proposal correlation matrix:

```
> print(corsm)
```

```
      [,1]  [,2]  [,3]  [,4]  [,5]  [,6] [,7]  [,8] [,9]
 [1,] 1.00  0.10  0.00  0.10  0.15  0.00 0.40  0.10 0.20
 [2,] 0.10  1.00 -0.15  0.15 -0.20 -0.30 0.20 -0.10 0.00
 [3,] 0.00 -0.15  1.00 -0.20  0.15  0.20 0.30  0.20 0.10
 [4,] 0.10  0.15 -0.20  1.00  0.20 -0.50 0.20 -0.40 0.40
 [5,] 0.15 -0.20  0.15  0.20  1.00  0.15 0.50  0.30 0.40
 [6,] 0.00 -0.30  0.20 -0.50  0.15  1.00 0.15  0.15 0.00
 [7,] 0.40  0.20  0.30  0.20  0.50  0.15 1.00  0.35 0.65
 [8,] 0.10 -0.10  0.20 -0.40  0.30  0.15 0.35  1.00 0.20
 [9,] 0.20  0.00  0.10  0.40  0.40  0.00 0.65  0.20 1.00
```

Here is the proposal covariance matrix:

```
> print(round(covm, digits = 3))
```

```
       [,1]   [,2]   [,3]   [,4]   [,5]   [,6]  [,7]   [,8]  [,9]
 [1,] 0.150  0.017  0.000  0.044  0.016  0.000 0.049  0.023 0.046
 [2,] 0.017  0.200 -0.001  0.076 -0.025 -0.067 0.028 -0.026 0.000
 [3,] 0.000 -0.001  0.000 -0.004  0.001  0.002 0.002  0.002 0.001
 [4,] 0.044  0.076 -0.004  1.300  0.064 -0.285 0.072 -0.270 0.270
 [5,] 0.016 -0.025  0.001  0.064  0.080  0.021 0.045  0.050 0.067
 [6,] 0.000 -0.067  0.002 -0.285  0.021  0.250 0.024  0.044 0.000
 [7,] 0.049  0.028  0.002  0.072  0.045  0.024 0.100  0.065 0.122
 [8,] 0.023 -0.026  0.002 -0.270  0.050  0.044 0.065  0.350 0.070
 [9,] 0.046  0.000  0.001  0.270  0.067  0.000 0.122  0.070 0.350
```

Now we put a lower triangle of the proposal covariance matrix to the resulting list. `cov.prop` component of the resulting list is again a list, now with only one component since there is only one block of regression parameters. Observe that only lower traingle of each proposal covariance matrix must be supplied.

```
> prior.beta.mh1$blocks$cov.prop <- list()
> prior.beta.mh1$blocks$cov.prop[[1]] <- covm[lower.tri(covm, diag = TRUE)]
```

Further, we have to say that all blocks (one here) will be updated using a random-walk Metropolis algorithm (default would be Gibbs).

```
> prior.beta.mh1$type.upd <- rep("random.walk.metropolis", nblock)
```

Subsequently, we have to say how a normal proposal will be mixed with a uniform proposal when updating each block of parameters. We specify weights of a uniform component (here 0.05 for our one block). You can set each weight to zero if you do not want to mix normal and uniform proposals

```
> prior.beta.mh1$weight.unif <- rep(0.05, nblock)
```

Finally, we have to specify half of a range of a uniform component proposal for each regression parameter, i.e. we have to supply a vector of length 9.

```
> prior.beta.mh1$half.range.unif <- c(0.25, 0.25, 0.01, 1, 0.15,
+     0.25, 0.3, 1, 1)
```

Look how it looks like:

```
> print(prior.beta.mh1)

$mean.prior
[1] 0 0 0 0 0 0 0 0 0

$var.prior
[1] 1000 1000 1000 1000 1000 1000 1000 1000 1000

$blocks
$blocks$ind.block
$blocks$ind.block[[1]]
[1] 1 2 3 4 5 6 7 8 9


$blocks$cov.prop
$blocks$cov.prop[[1]]
 [1]  0.1500000000  0.0173205081  0.0000000000  0.0441588043  0.0164316767
 [6]  0.0000000000  0.0489897949  0.0229128785  0.0458257569  0.2000000000
[11] -0.0011618950  0.0764852927 -0.0252982213 -0.0670820393  0.0282842712
[16] -0.0264575131  0.0000000000  0.0003000000 -0.0039496835  0.0007348469
[21]  0.0017320508  0.0016431677  0.0020493902  0.0010246951  1.3000000000
[26]  0.0644980620 -0.2850438563  0.0721110255 -0.2698147513  0.2698147513
[31]  0.0800000000  0.0212132034  0.0447213595  0.0501996016  0.0669328021
[36]  0.2500000000  0.0237170825  0.0443705984  0.0000000000  0.1000000000
[41]  0.0654790043  0.1216038651  0.3500000000  0.0700000000  0.3500000000



$type.upd
[1] "random.walk.metropolis"

$weight.unif
[1] 0.05

$half.range.unif
[1] 0.25 0.25 0.01 1.00 0.15 0.25 0.30 1.00 1.00
```

3.2.3 β updated in two blocks using random walk Metropolis-Hastings step

Finally, we show how to specify the prior `list` for the situation we wish to update $\boldsymbol{\beta}$ parameters in two blocks, first of them updated using a Gibbs step, the second one using a random walk Metropolis-Hastings step.

```
> prior.beta.mh2 <- list()
> prior.beta.mh2$mean.prior <- rep(0, nregres)
> prior.beta.mh2$var.prior <- rep(1000, nregres)
```

Definition of blocks in which beta parameters will be updated (two blocks – `beta[1:6]` and `beta[7:9]`) and the way in which they will be updated.

```
> prior.beta.mh2$blocks <- list()
> prior.beta.mh2$blocks$ind.block <- list()
> prior.beta.mh2$blocks$ind.block[[1]] <- 1:6
```

```
> prior.beta.mh2$blocks$ind.block[[2]] <- 7:9
> nblock <- length(prior.beta.mh2$blocks$ind.block)
```

Further we define a proposal covariance matrix for the second block. Note that the proposal covariance matrix for the first block does not have to be defined since the first block is updated using a Gibbs move.

`vars`	=	proposal variances for each beta[7:9] parameter
`cors`	=	lower triangle of the proposal correlation matrix
`corsm`	=	proposal correlation matrix itself
`covm`	=	proposal covariance matrix

```
> vars <- c(0.1, 0.35, 0.35)
> cors <- c(1, 0.9, 0.9, 1, 0.9, 1)
> corsm <- diag(3)
> corsm[lower.tri(corsm, diag = TRUE)] <- cors
> corsm[upper.tri(corsm, diag = FALSE)] <- t(corsm)[upper.tri(t(corsm),
+     diag = FALSE)]
> covm <- diag(sqrt(vars)) %*% corsm %*% diag(sqrt(vars))
```

Here is the proposal correlation matrix for the second block of `beta` parameters:

```
> print(corsm)
```

```
     [,1] [,2] [,3]
[1,]  1.0  0.9  0.9
[2,]  0.9  1.0  0.9
[3,]  0.9  0.9  1.0
```

Here is the proposal covariance matrix for the second block of `beta` parameters:

```
> print(covm)
```

```
          [,1]      [,2]      [,3]
[1,] 0.1000000 0.1683746 0.1683746
[2,] 0.1683746 0.3500000 0.3150000
[3,] 0.1683746 0.3150000 0.3500000
```

Now we put a lower triangle of the proposal covariance matrix to the resulting list. `cov.prop` component of the resulting list is again a list, now with two components (we have 2 blocks). Note that the first component of `cov.prop` may be set to `NULL` since we intend to use Gibbs step for the first block and no proposal covariance matrix is thus needed. Further, only lower traingle of each proposal covariance matrix must be supplied.

```
> prior.beta.mh2$blocks$cov.prop <- list()
> prior.beta.mh2$blocks$cov.prop[[1]] <- NULL
> prior.beta.mh2$blocks$cov.prop[[2]] <- covm[lower.tri(covm, diag = TRUE)]
```

Further, we have to say that the first block will be updated using the Gibbs move and the second block using random-walk Metropolis.

```
> prior.beta.mh2$type.upd <- c("gibbs", "random.walk.metropolis")
```

Subsequently, we have to say how a normal proposal will be mixed with a uniform proposal when updating each block of parameters. So we specify weights of a uniform component (here 0.05 for our second block). Note that the first component of this vector will be ignored since the first block is updated using Gibbs move.

```
> prior.beta.mh2$weight.unif <- c(0.05, 0.05)
```

Finally, we have to specify half of a range of a uniform component proposal for each regression parameter, i.e. we have to supply a vector of length 9. Again, first 6 components of this vector will be ignored since the first block is updated using the Gibbs move.

```
> prior.beta.mh2$half.range.unif <- c(0.25, 0.25, 0.01, 1, 0.15,
+     0.25, 0.3, 1, 1)
```

Look how it looks like:

```
> print(prior.beta.mh2)

$mean.prior
[1] 0 0 0 0 0 0 0 0 0

$var.prior
[1] 1000 1000 1000 1000 1000 1000 1000 1000 1000

$blocks
$blocks$ind.block
$blocks$ind.block[[1]]
[1] 1 2 3 4 5 6

$blocks$ind.block[[2]]
[1] 7 8 9


$blocks$cov.prop
$blocks$cov.prop[[1]]
NULL

$blocks$cov.prop[[2]]
[1] 0.1000000 0.1683746 0.1683746 0.3500000 0.3150000 0.3500000



$type.upd
[1] "gibbs"                  "random.walk.metropolis"

$weight.unif
[1] 0.05 0.05

$half.range.unif
[1] 0.25 0.25 0.01 1.00 0.15 0.25 0.30 1.00 1.00
```

4 Prior specification for the random intercept b_i related parameters

The following `list` has only to specify two prior hyperparameters for the covariance matrix $\mathbb{D}$ (which is a scalar here, let say d) and to say how the individual random effects will be updated.

4.1 Inverse-gamma prior distribution for d

```
> prior.b.gamma <- list()
```

Hyperparameters for d are degrees of freedom τ and scale parameter $\mathbb{S} = s$. Here, $\tau = 0.002$ and $s = 0.002$ which results in inverse-gamma$(0.001, 0.001)$ prior for d. Remember that inverse-Wishart(τ, invscale $= 1/s$) = inverse-gamma($\tau/2$, scale $= s/2$) and Wishart(τ, scale $= s$) = gamma($\tau/2$, scale $= 2/s$) = gamma($\tau/2$, rate $= s/2$).

```
> prior.b.gamma$prior.D <- "inv.wishart"
> prior.b.gamma$df.D <- 0.002
> prior.b.gamma$scale.D <- 0.002
```

Type of the update of the random intercept will be Gibbs move (this could be omitted since it is a default choice).

```
> prior.b.gamma$type.upd <- "gibbs"
```

Look how it looks like:

```
> print(prior.b.gamma)

$prior.D
[1] "inv.wishart"

$df.D
[1] 0.002

$scale.D
[1] 0.002

$type.upd
[1] "gibbs"
```

4.2 Uniform distribution for $\sqrt{d}$

This prior choice gives much better results than the previous one. A uniform prior (here Unif$(0, 100)$) is used for the standard deviation ($\sqrt{d}$) of the random intercept.

```
> prior.b.unif <- list()
> prior.b.unif$prior.D <- "sduniform"
```

Upper limit for the prior uniform distribution of $\sqrt{d}$:

```
> prior.b.unif$scale.D <- 100
```

Type of the update of individual random effects:

```
> prior.b.unif$type.upd <- "gibbs"
```

Look how it looks like:

```
> print(prior.b.unif)

$prior.D
[1] "sduniform"

$scale.D
[1] 100

$type.upd
[1] "gibbs"
```

4.3 Parameters to perform reversible jumps

```
> prop.revjump <- list()
```

Type of the algorithm:

```
> prop.revjump$algorithm <- "correlated.av"
```

Parameters of a moody ring (ϵ, *delta*, see paper Brooks et al. (2003) for details). Remember, ϵ = time dependence, δ = component dependence.

```
> prop.revjump$moody.ring <- c(0.1, 0.05)
```

Transformation of a canonical seed for split-combine move:

```
> prop.revjump$transform.split.combine <- "brooks"
> prop.revjump$transform.split.combine.parms <- c(2, 2, 2, 2, 1,
+     1)
```

Transformation of a canonical seed for birth-death move:

```
> prop.revjump$transform.birth.death <- "richardson.green"
```

Look how it looks like:

```
> print(prop.revjump)

$algorithm
[1] "correlated.av"

$moody.ring
[1] 0.10 0.05

$transform.split.combine
[1] "brooks"

$transform.split.combine.parms
[1] 2 2 2 2 1 1

$transform.birth.death
[1] "richardson.green"
```

5 Specification of initial values for the MCMC

We give two sets of initial values to run two chains. Undefined initials are sampled automatically by the program.

5.1 Initials for chain 1

```
> init1 <- list()
```

Iteration number of the nulth iteration:

```
> init1$iter <- 0
```

Initial mixture (from `survreg(dist = "lognormal")`). It will have one component with $w_1 = 1$, $\mu_1 = 3.9$ and $\sigma_1^2 = 1.2$.

```
> init1$mixture <- c(1, 1, rep(0, prior$kmax - 1), 3.9, rep(0,
+     prior$kmax - 1), 1.2, rep(0, prior$kmax - 1))
```

Initial regression parameters $\boldsymbol{\beta}$ (from `survreg(dist = "lognormal")`):

```
> init1$beta <- c(1.1, -0.66, 0.04, -1.76, 0.94, 1.03, 0.37, 1.22,
+     0.82)
```

Initial variance d of the random intercept b_i:

```
> init1$D <- 0.16
```

Initial values of a random intercept for each of 128 patients. Here, use zero for all patients.

```
> init1$b <- rep(0, npatient)
```

Initial (augmented) log(event) times – let the program sample them:

```
> init1$y <- NULL
```

Initial component pertinence of the observations to the mixture (all observations belong to the first component):

```
> init1$r <- rep(1, nobs)
```

Initial value of a hyperparameter η (sample it from a prior distribution):

```
> init1$otherp <- rgamma(1, shape = prior$shape.hyper.invsig2,
+     rate = prior$rate.hyper.invsig2)
```

Initial values of canonical variables for reversible move (sample it from a uniform distribution):

```
> init1$u <- c(runif(1), 0, 0, runif(3 * (prior$kmax - 1)))
```

Look how it look like:

```
> print(init1)
```

```
$iter
[1] 0

$mixture
 [1] 1.0 1.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0
[20] 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 3.9 0.0 0.0 0.0 0.0 0.0 0.0
[39] 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0
[58] 0.0 0.0 0.0 0.0 1.2 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0
[77] 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0

$beta
[1]  1.10 -0.66  0.04 -1.76  0.94  1.03  0.37  1.22  0.82

$D
[1] 0.16
```

```
$b
  [1] 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
 [38] 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
 [75] 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
[112] 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

$r
  [1] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
 [38] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
 [75] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
[112] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
[149] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
[186] 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

$otherp
[1] 6.300993

$u
 [1] 0.174304877 0.000000000 0.000000000 0.836317423 0.022461188 0.605111721
 [7] 0.051642385 0.854546962 0.445194034 0.857326345 0.135352092 0.547420292
[13] 0.676557139 0.847755976 0.120215760 0.814491668 0.623330991 0.969478300
[19] 0.872148183 0.333888454 0.856516252 0.626130563 0.778769636 0.204476710
[25] 0.925465756 0.390777498 0.910897769 0.862282692 0.190846605 0.226227179
[31] 0.432498947 0.524690561 0.012644746 0.807842303 0.439268866 0.583867981
[37] 0.644169420 0.268751388 0.183528103 0.802373542 0.762259574 0.464848898
[43] 0.037185794 0.108571416 0.415030675 0.182302093 0.305950307 0.959535294
[49] 0.798008798 0.523724933 0.600240209 0.021356639 0.540641743 0.327153018
[55] 0.496169003 0.672482854 0.086821235 0.411459669 0.356708388 0.520788439
[61] 0.159800542 0.003116311 0.165676917 0.070549568 0.629290880 0.655733954
[67] 0.397797680 0.348051859 0.851586298 0.929080901 0.868754459 0.371755116
[73] 0.194385185 0.719732701 0.896157837 0.950442448 0.028348952 0.304985804
[79] 0.858374389 0.856361844 0.083502175 0.446745432 0.726752041 0.137075475
[85] 0.568598263 0.923452544 0.338440747 0.022347172 0.054090315 0.210331626
```

5.2 Initials for chain 2

```
> init2 <- list()
```

Iteration number of the nulth iteration:

```
> init2$iter <- 0
```

Initial mixture, now with two components and $w_1 = w_2 = 0.5$, $\mu_1 = 2.5$, $\mu_2 = 5.5$, $\sigma_1^2 = \sigma_2^2 = 1$:

```
> init2$mixture <- c(2, 0.5, 0.5, rep(0, prior$kmax - 2), 2.5,
+     5.5, rep(0, prior$kmax - 2), 1, 1, rep(0, prior$kmax - 2))
```

Initial regression parameters $\boldsymbol{\beta}$ (all zeros here):

```
> init2$beta <- rep(0, nregres)
```

Initial variance d of the random intercept b_i:

```
> init2$D <- 0.05
```

Initial values of a random intercept for each of 128 patients (sample it from a normal distribution):

```
> init2$b <- rnorm(npatient, 0, sqrt(init2$D))
```

Initial (augmented) log(event) times – let the program sample them:

```
> init2$y <- NULL
```

Initial component pertinence of the observations to the mixture (half observations to the first component, half to the second component):

```
> init2$r <- c(rep(1, 102), rep(2, 101))
```

Initial value of a hyperparameter η (sample it from a prior distribution):

```
> init2$otherp <- rgamma(1, shape = prior$shape.hyper.invsig2,
+     rate = prior$rate.hyper.invsig2)
```

Initial values of canonical variables for reversible move (sample it from a uniform distribution):

```
> init2$u <- c(runif(1), 0, 0, runif(3 * (prior$kmax - 1)))
```

6 Running the MCMC simulation

Now we are ready to run the MCMC to sample from the posterior distribution.

Here we define which quantities that are not neccessarily needed for the inference will be stored. With this specification, we store only sampled values of individual values of random effects for each patient.

```
> store <- list(y = FALSE, r = FALSE, u = FALSE, b = TRUE, MHb = FALSE,
+     regresres = FALSE)
```

How long simulation we want to run? For testing purposes, only limited simulation is specified here.

```
> nsimul <- list(niter = 1000, nthin = 3, nburn = 500, nnoadapt = 0,
+     nwrite = 500)
```

For the analysis presented in Komárek and Lesaffre (2004) we used

```
> nsimul <- list(niter = 60000, nthin = 6, nburn = 30000, nnoadapt = 0, nwrite = 1000)
```

which performed $6 \times 30\,000$ iterations of burn-in and additionally $6 \times 30\,000$ iterations from which each 6th value was stored. Further, after cumulating 1 000 sampled values, these were stored on a disk. This would last about 15 minutes on 2GHz machine.

Define directories where first and second chain will be stored. We first create these directories:

```
> dir.create("cgdchain1")
> dir.create("cgdchain2")
> dirsim1 <- paste(getwd(), "/cgdchain1", sep = "")
> dirsim2 <- paste(getwd(), "/cgdchain2", sep = "")
```

Run the simulation for the first and the second chain.

```
> simul1 <- bayessurvreg1(Surv(time, event) ~ trtmt + inherit +
+     age + cortico + prophy + gender + hcat + cluster(ID), random = ~1,
+     data = data, dir = dirsim1, nsimul = nsimul, prior = prior,
+     prior.beta = prior.beta.gibbs, prior.b = prior.b.unif, prop.revjump = prop.revjump,
+     init = init1, store = store)
```

```
Simulation started on                       Fri Sep 10 11:39:19 2004
Iteration 500
Simulation without adaptation finished on   Fri Sep 10 11:39:21 2004   (iteration 500)
Iteration 1000
Simulation finished on                      Fri Sep 10 11:39:24 2004   (iteration 1000)
```

```
> simul2 <- bayessurvreg1(Surv(time, event) ~ trtmt + inherit +
+     age + cortico + prophy + gender + hcat + cluster(ID), random = ~1,
+     data = data, dir = dirsim2, nsimul = nsimul, prior = prior,
+     prior.beta = prior.beta.gibbs, prior.b = prior.b.unif, prop.revjump = prop.revjump,
+     init = init2, store = store)
```

```
Simulation started on                       Fri Sep 10 11:39:24 2004
Iteration 500
Simulation without adaptation finished on   Fri Sep 10 11:39:27 2004   (iteration 500)
Iteration 1000
Simulation finished on                      Fri Sep 10 11:39:29 2004   (iteration 1000)
```

7 Running additional MCMC simulation to compute predictive quantities

First we have to define covariate values for which we want to do a prediction. Here, we want 8 predictive distributions, for each combination of treatment/placebo × X-linked/autosomal recessive pattern of inheritance × male/female. Remaining covariates are set to modus/mean values (age = 14.6, no corticosteroids, yes prophylactic antibiotica, hospital category = US-other). Time (response) variable is set to 1 for all 'new' patients (it does not matter what it is set to). Event variable is set to 0 for all 'new' patients (again, it does not matter, provided that `Surv` is subsequently able to create a survival object from such 'new' data).

```
> nnewpat <- 8
> nID <- 1:nnewpat
> ntrtmt <- c(0, 1, 0, 1, 0, 1, 0, 1)
> ninherit <- factor(c(0, 0, 1, 1, 0, 0, 1, 1), levels = 0:1, labels = c("X-l",
+     "AuRec"))
> nage <- rep(14.6, nnewpat)
> ncortico <- rep(0, nnewpat)
> nprophy <- rep(1, nnewpat)
> ngender <- factor(c(0, 0, 0, 0, 1, 1, 1, 1), levels = 0:1, labels = c("male",
+     "female"))
> nhcat <- factor(rep(2, nnewpat), levels = 1:4, labels = c("US-NIH",
+     "US-other", "EU-Am", "EU-other"))
> ntime <- rep(1, nnewpat)
> nevent <- rep(0, nnewpat)
```

Data frame with 'new' data:

```
> preddata <- data.frame(ID = nID, trtmt = ntrtmt, inherit = ninherit,
+     age = nage, cortico = ncortico, prophy = nprophy, gender = ngender,
+     hcat = nhcat, time = ntime, event = nevent)
> print(preddata)
```

```
  ID trtmt inherit  age cortico prophy gender     hcat time event
1  1     0     X-l 14.6       0      1   male US-other    1     0
2  2     1     X-l 14.6       0      1   male US-other    1     0
3  3     0   AuRec 14.6       0      1   male US-other    1     0
4  4     1   AuRec 14.6       0      1   male US-other    1     0
```

```
5  5     0     X-l 14.6       0      1 female US-other    1     0
6  6     1     X-l 14.6       0      1 female US-other    1     0
7  7     0   AuRec 14.6       0      1 female US-other    1     0
8  8     1   AuRec 14.6       0      1 female US-other    1     0
```

Further, we specify what we want to predict (with this, survivor function and hazard function). Also, specify whether sampled quantities should be stored, otherwise, only quantiles and predictive means are computed (which usually suffice).

```
> predict <- list(Et = TRUE, t = FALSE, Surv = TRUE, hazard = TRUE,
+     cum.hazard = FALSE)
> store <- list(Et = FALSE, t = FALSE, Surv = FALSE, hazard = FALSE,
+     cum.hazard = FALSE)
```

Grid of values in which predictive survivor and hazard curves should be computed:

```
> grid <- seq(1, 401, by = 2.5)
```

How many MCMC iterations we want to perform (`niter` should be $\leq$ length of already sampled chain) and how often should sampled quantities be written to disk

```
> nsimul.pred <- list(niter = nsimul$niter - nsimul$nburn, nwrite = nsimul$niter -
+     nsimul$nburn)
```

Run MCMC simulation to sample from the predictive distribution (only chain 1 will be used here):

```
> simulp <- predictive(Surv(time, event) ~ trtmt + inherit + age +
+     cortico + prophy + gender + hcat + cluster(ID), random = ~1,
+     data = preddata, dir = dirsim1, quantile = c(0, 0.025, 0.5,
+         0.975, 1), nsimul = nsimul.pred, predict = predict, store = store,
+     grid = grid, Eb0.depend.mix = FALSE, type = "mixture")

Simulation started on                       Fri Sep 10 11:39:30 2004
Iteration 500
Computing quantiles.
Storing quantiles.
Simulation finished on                      Fri Sep 10 11:39:35 2004
```

In a directory `./cgdchain1` few new files should appear:

- `quantS1.sim` – `quantS8.sim`;
- `quanthazard1.sim` – `quanthazard8.sim`;
- `quantET.sim`.

Files `quantS*.sim` and `quanthazard*.sim` contain pointwise (evaluated at the grid specified above) posterior predictive quantiles and means of the survivor and hazard function for each combination of covariates specified in `preddata`. File `quantET.sim` contains posterior predictive quantiles and mean for expected survivor time of each combination of covariates. Note that

1. There is one file per survivor/hazard function and per covariate combination. Indeces of these files (1, ..., 8) correspond to rows of `preddata`. Structure of these files is following

1st row	=	grid values
2nd row	=	post. predictive 0% quantile (minimum)
3rd row	=	post. predictive 2.5% quantile
4th row	=	post. predictive 50% quantile (median)
5th row	=	post. predictive 97.5% quantile
6th row	=	post. predictive 100% quantile (maximum)
last row	=	post. predictive mean

2. There is only one file for posterior predictive expected survivor times and all combinations of covariates (`quantET.sim`). Structure of this file is following:

1st row	=	character labels ET1 - ET8 indicating that each column corresponds to one covariate combination
remaining rows	=	same as for `quantS*.sim` or `quanthazard*.sim`

You might specify also other quantiles (parameter `quantile` in function `predictive`) to be computed. Posterior predictive mean is always computed and stored on the last row.

8 Drawing posterior predictive survivor/hazard curves

In this section we draw posterior predictive survivor and hazard curves for new patients with covariate combinations defined in the previous section.

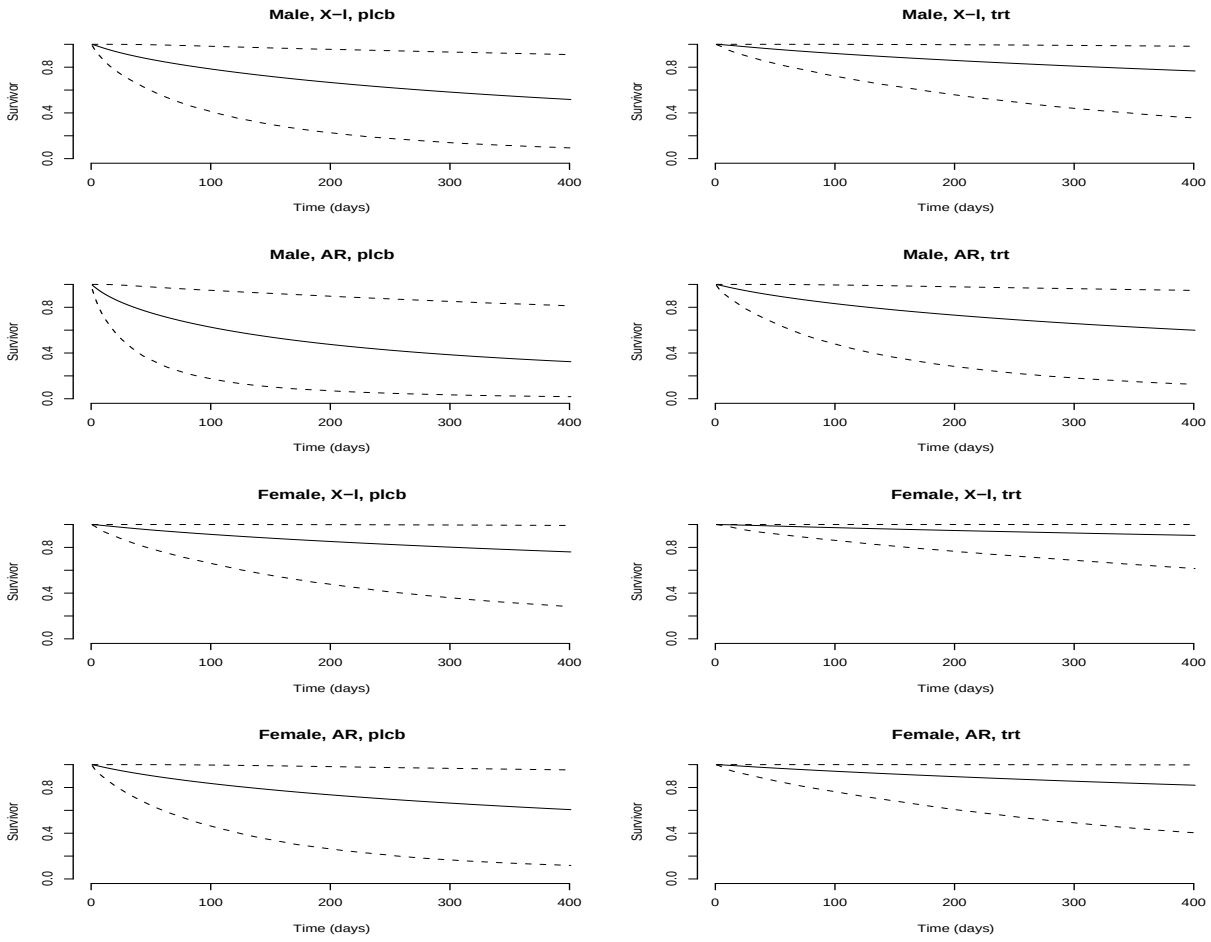
Posterior predictive survivor curve and its 95% pointwise CI (1 plot per covariate combination). The result is given in Figure 1.

```
> labels <- c("Male, X-l, plcb", "Male, X-l, trt", "Male, AR, plcb",
+     "Male, AR, trt", "Female, X-l, plcb", "Female, X-l, trt",
+     "Female, AR, plcb", "Female, AR, trt")
> par(mfrow = c(4, 2))
> for (i in 1:8) {
+     gridS <- scan(paste(dirsim1, "/quantS", i, ".sim", sep = ""),
+         nlines = 1)
+     Sfun <- read.table(paste(dirsim1, "/quantS", i, ".sim", sep = ""),
+         header = TRUE)
+     rownames(Sfun) <- c("0%", "2.5%", "50%", "97.5%", "100%",
+         "mean")
+     plot(gridS, Sfun["mean", ], type = "l", lty = 1, ylim = c(0,
+         1), xlab = "Time (days)", ylab = "Survivor", bty = "n")
+     lines(gridS, Sfun["2.5%", ], lty = 2)
+     lines(gridS, Sfun["97.5%", ], lty = 2)
+     title(main = labels[i])
+ }
```

Posterior predictive hazard curve and its 95% pointwise CI (1 plot per covariate combination). The result is given in Figure 2.

```
> labels <- c("Male, X-l, plcb", "Male, X-l, trt", "Male, AR, plcb",
+     "Male, AR, trt", "Female, X-l, plcb", "Female, X-l, trt",
+     "Female, AR, plcb", "Female, AR, trt")
> par(mfrow = c(4, 2))
> for (i in 1:8) {
+     gridhaz <- scan(paste(dirsim1, "/quanthazard", i, ".sim",
+         sep = ""), nlines = 1)
+     hfun <- read.table(paste(dirsim1, "/quanthazard", i, ".sim",
+         sep = ""), header = TRUE)
+     rownames(hfun) <- c("0%", "2.5%", "50%", "97.5%", "100%",
+         "mean")
+     plot(gridhaz, hfun["97.5%", ], type = "l", lty = 2, xlab = "Time (days)",
+         ylab = "Hazard", bty = "n")
+     lines(gridhaz, hfun["mean", ], lty = 1)
+     lines(gridhaz, hfun["2.5%", ], lty = 2)
+     title(main = labels[i])
+ }
```

Figure 1: Posterior predictive survivor curves and their 95% pointwise CI.



Posterior predictive survivor curves (1 plot per gender with 4 curves on it). The result is given in Figure 3.

```
> gg <- c("Male", "Female")
> par(mfrow = c(2, 1))
> for (j in 1:2) {
+     for (i in 1:4) {
+         gridS <- scan(paste(dirsim1, "/quantS", (j - 1) * 4 +
+             i, ".sim", sep = ""), nlines = 1)
+         Sfun <- read.table(paste(dirsim1, "/quantS", (j - 1) *
+             4 + i, ".sim", sep = ""), header = TRUE)
+         rownames(Sfun) <- c("0%", "2.5%", "50%", "97.5%", "100%",
+             "mean")
+         if (i == 1)
+             plot(gridS, Sfun["mean", ], type = "l", lty = 1,
+                 ylim = c(0, 1), xlab = "Time (days)", ylab = "Survivor",
+                 bty = "n")
+         else lines(gridS, Sfun["mean", ], lty = i)
+         legend(0, 0.6, legend = c("trtmt, X-l", "trtmt, AuRec",
+             "placebo, X-l", "placebo, AuRec"), lty = c(2, 4,
+             1, 3), bty = "n")
+     }
+     title(main = gg[j])
```

Figure 2: Posterior predictive hazard curves and their 95% pointwise CI

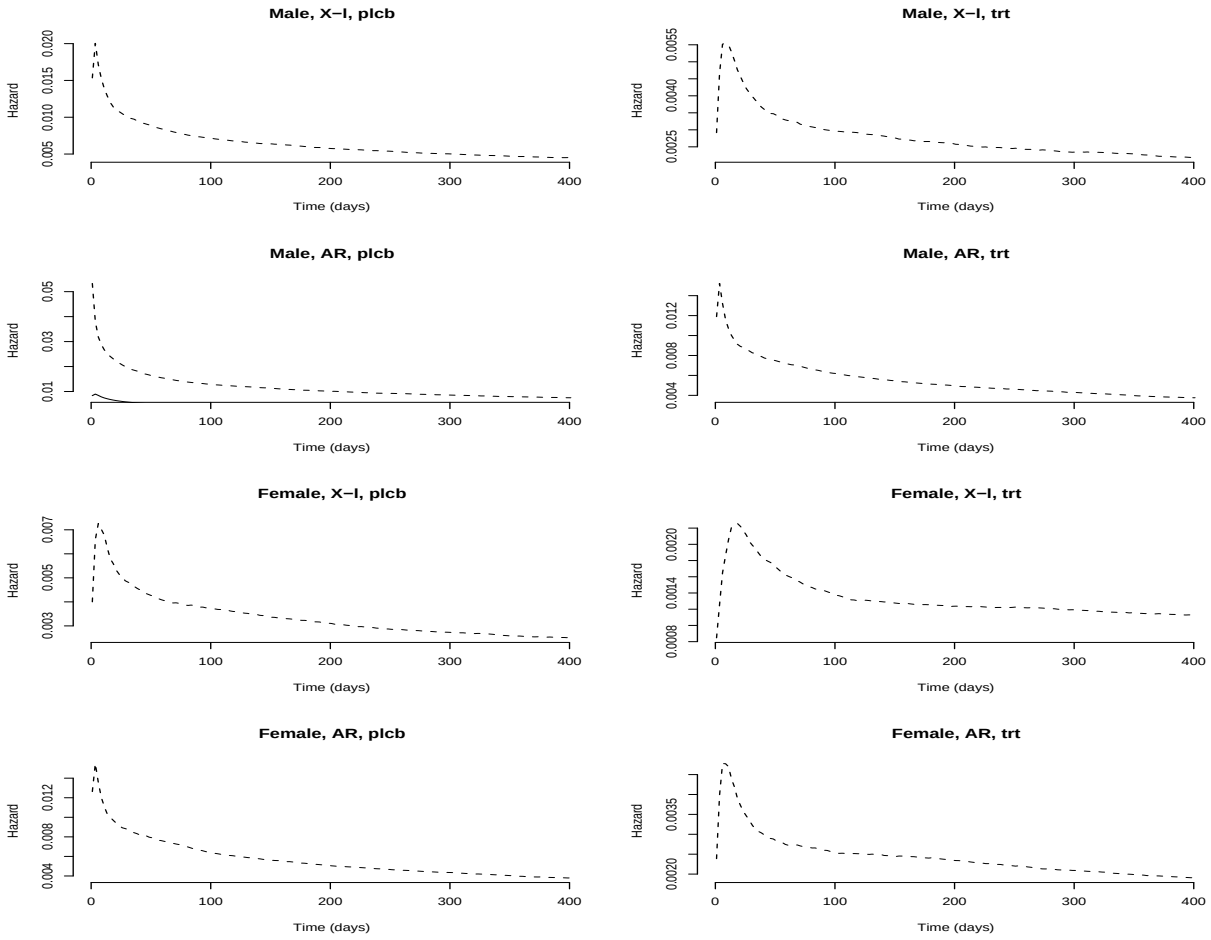
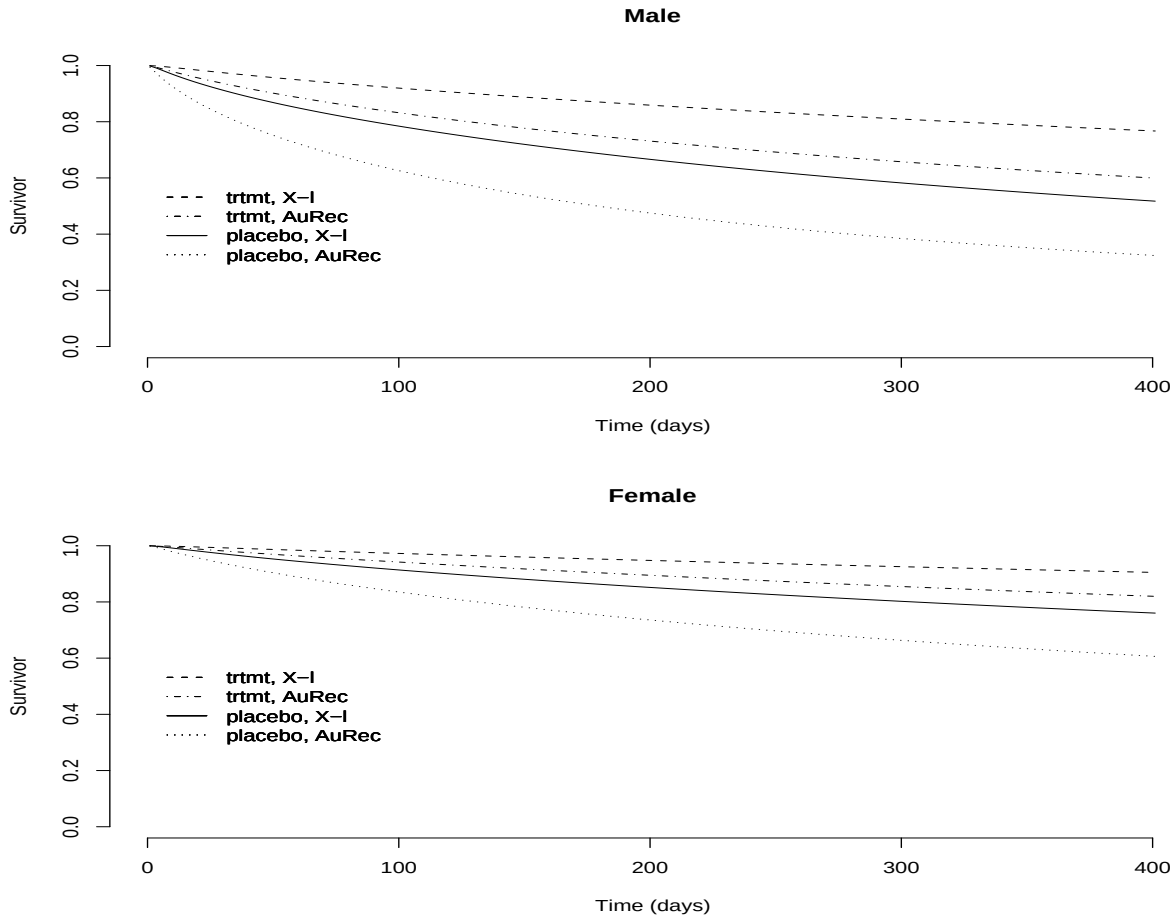


Figure 3: Posterior predictive survivor curves.

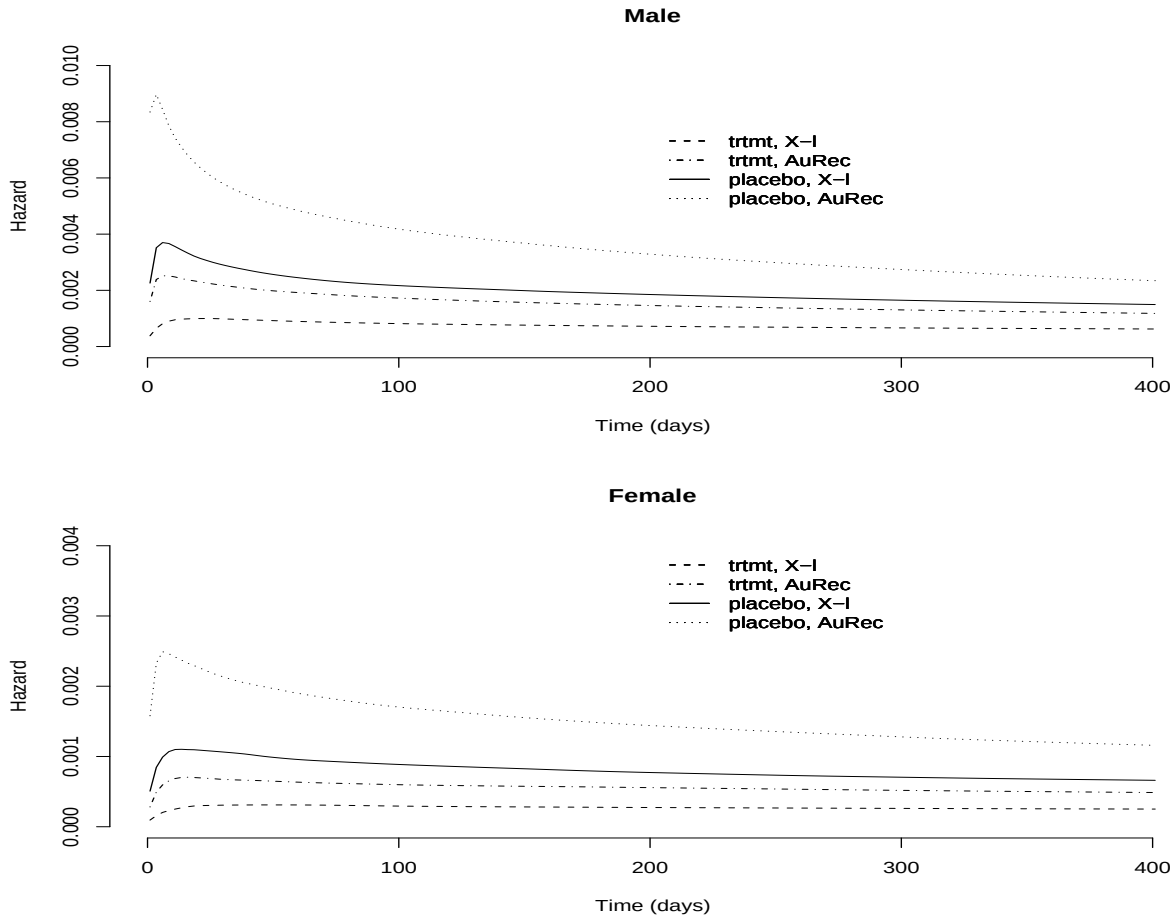



```
+ }
```

Posterior predictive hazard curves (1 plot per gender with 4 curves on it). The result is given in Figure 4.

```
> gg <- c("Male", "Female")
> par(mfrow = c(2, 1))
> leg <- c(0.008, 0.004)
> ylim <- c(0.01, 0.004)
> for (j in 1:2) {
+     for (i in 1:4) {
+         gridhaz <- scan(paste(dirsim1, "/quanthazard", (j - 1) *
+             4 + i, ".sim", sep = ""), nlines = 1)
+         hfun <- read.table(paste(dirsim1, "/quanthazard", (j -
+             1) * 4 + i, ".sim", sep = ""), header = TRUE)
+         rownames(hfun) <- c("0%", "2.5%", "50%", "97.5%", "100%",
+             "mean")
+         if (i == 1)
+             plot(gridhaz, hfun["mean", ], type = "l", lty = 1,
+                 ylim = c(0, ylim[j]), xlab = "Time (days)", ylab = "Hazard",
+                 bty = "n")
+         else lines(gridhaz, hfun["mean", ], lty = i)
+         legend(200, leg[j], legend = c("trtmt, X-l", "trtmt, AuRec",
+             "placebo, X-l", "placebo, AuRec"), lty = c(2, 4,
```

Figure 4: Posterior predictive hazard curves.




```
+             1, 3), bty = "n")
+     }
+     title(main = gg[j])
+ }
```

9 Computing and drawing predictive error density

Here, we compute posterior standardized (zero mean, unit variance) and unstandardized predictive error densities, separately for each chain. Vector `dgrid` is a grid of values where the unstandardized density is to be evaluated, vector `dgrids` is a grid of values where the standardized density is to be evaluated.

```
> dgrid <- seq(-2, 9, length = 100)
> dgrids <- seq(-3, 3, length = 100)
> dens <- list()
> for (ch in 1:2) {
+     dens[[ch]] <- bayesDensity(dir = get(paste("dirsim", ch,
+         sep = "")), grid = dgrid, stgrid = dgrids)
+ }

Computing predictive densities.
Computing predictive densities.
```

Now, we plot first the unstandardized predictive error densities for each chain and then the standardized ones (conditional densities given k are plotted only for $k = 1, \ldots, 9$). The result is seen in Figure 5.

```
> par(bty = "n", mfrow = c(2, 2))
> for (ch in 1:2) {
+     xlim <- c(-2, 8)
+     xleg <- -2
+     yleg <- 0.3
+     ylim <- c(0, 0.3)
+     plot(dens[[ch]], k.cond = 0:9, standard = FALSE, dim.plot = FALSE,
+         xlim = xlim, ylim = ylim, xleg = xleg, yleg = yleg, main = "")
+     title(main = paste("Unstandardized, Chain ", ch, sep = ""))
+ }
> for (ch in 1:2) {
+     xlim <- c(-2.5, 2.5)
+     xleg <- -2.5
+     yleg <- 0.7
+     ylim <- c(0, 0.7)
+     plot(dens[[ch]], k.cond = 0:9, standard = TRUE, dim.plot = FALSE,
+         xlim = xlim, ylim = ylim, xleg = xleg, yleg = yleg, main = "")
+     title(main = paste("Standardized, Chain ", ch, sep = ""))
+ }
```

10 Predictive values of individual random effects b_i

Sampled individual random effects (from both chains):

```
> ids <- unique(data$ID)
> bb <- list()
> for (ch in 1:2) {
+     bb[[ch]] <- matrix(scan(paste(get(paste("dirsim", ch, sep = "")),
+         "/b.sim", sep = ""), skip = 1), ncol = 128, byrow = TRUE)
+     colnames(bb[[ch]]) <- ids
+ }
> bbs <- rbind(bb[[1]], bb[[2]])
```

Compute the posterior mean and some quantiles for each individual random effect:

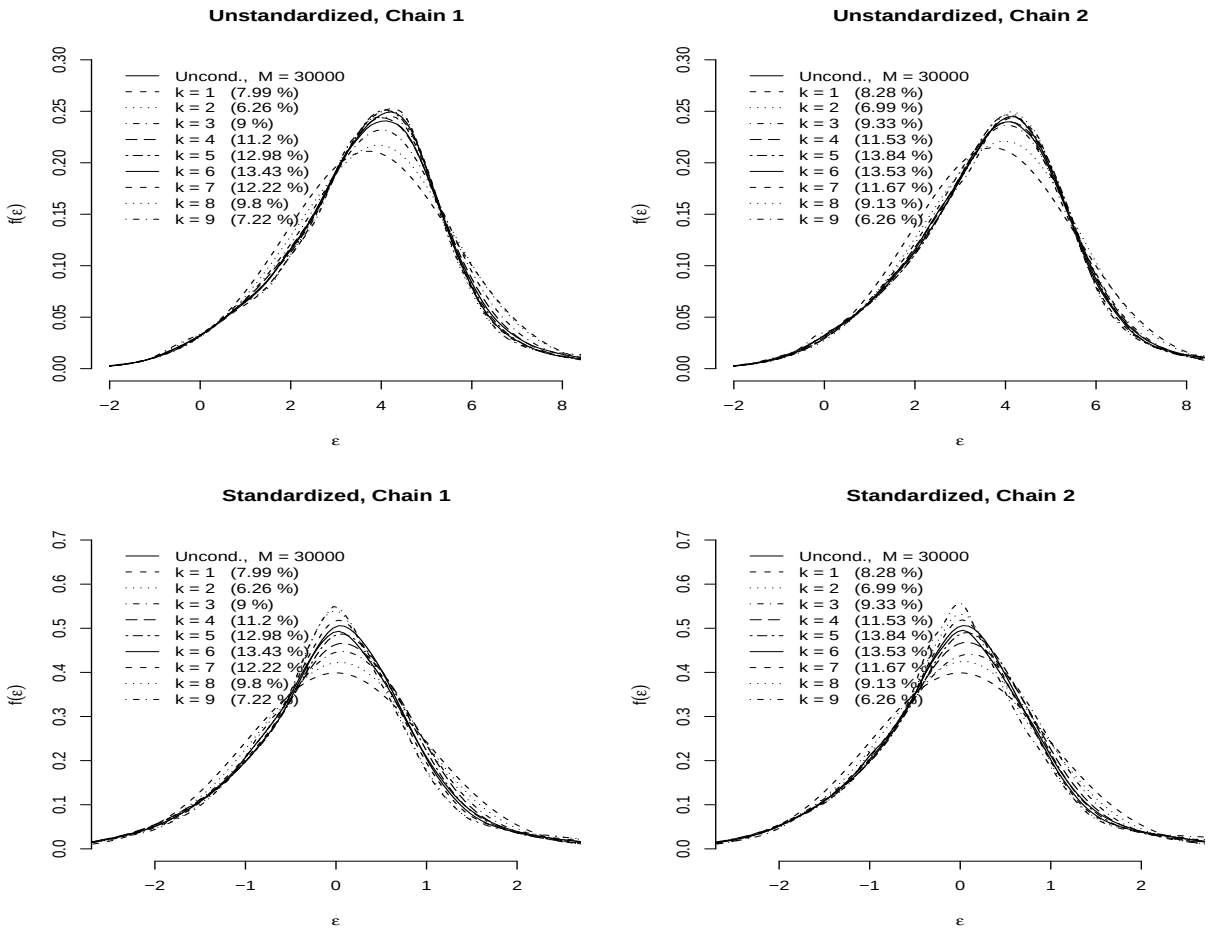
```
> b.mean <- apply(bbs, 2, mean)
> b.median <- apply(bbs, 2, quantile, 0.5)
> b.low <- apply(bbs, 2, quantile, 0.025)
> b.up <- apply(bbs, 2, quantile, 0.975)
```

Sort patients according to number of events:

```
> n <- dim(data)[1]
> id1 <- data$ID[1:(n - 1)]
> id2 <- data$ID[2:n]
> difid <- c(1, id2 - id1)
> first <- difid > 0
> frevent <- table(data$ID)
> freqv <- as.numeric(frevent)
> frval <- data.frame(ID = data$ID[first], trtmt = data$trtmt[first],
+     freq = as.numeric(frevent), b.mean, b.median, b.low, b.up,
+     nevent = freqv)
> frval <- frval[order(frval$trtmt), ]
> frval <- frval[order(frval$freq), ]
```

Figure 5: Predictive error densities.

.

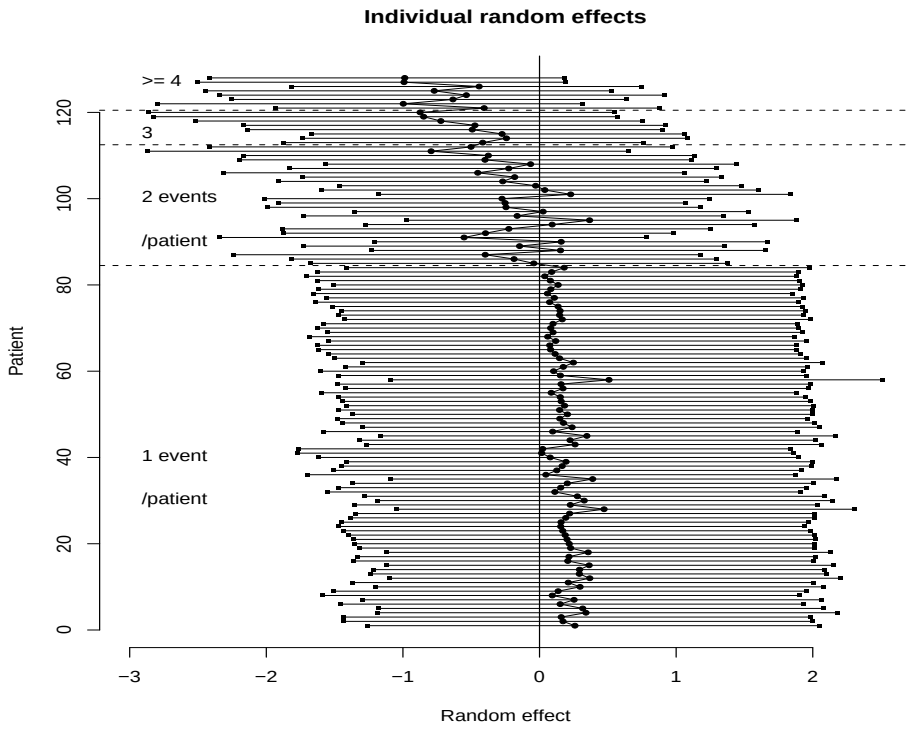


Plot means and 95% CI for each individual random effect b_i (see Figure 6 for the result).

```
> par(bty = "n")
> plot(frval$b.mean, 1:128, type = "p", pch = 20, xlim = c(-3,
+     2.5), bty = "n", ylab = "Patient", xlab = "Random effect")
> lines(frval$b.mean, 1:128)
> points(frval$b.low, 1:128, pch = 15, cex = 0.5)
> points(frval$b.up, 1:128, pch = 15, cex = 0.5)
> for (pat in 1:n) {
+     lines(c(frval$b.low[pat], frval$b.up[pat]), c(pat, pat),
+         lty = 1)
+ }
> title(main = "Individual random effects")
> abline(h = 84.5, lty = 2)
> abline(h = 112.5, lty = 2)
> abline(h = 120.5, lty = 2)
> abline(v = 0, lty = 1)
> text(-3, 40, "1 event", pos = 4)
> text(-3, 30, "/patient", pos = 4)
> text(-3, 100, "2 events", pos = 4)
> text(-3, 90, "/patient", pos = 4)
> text(-3, 115, "3", pos = 4)
```

Figure 6: Individual random effects b_i.

.




```
> text(-3, 127, ">= 4", pos = 4)
```

11 Summary statistics and convergence diagnostics

Now we compute some summary statistics and perform some convergence diagnostics using the R package `coda`.

First, we load the `coda` package and say how many chains we have:

```
> library(coda)
> nchains <- 2
```

Here we compute separately chains with the standard deviation $\sqrt{d}$ of the random intercept b_i (only the variance d is stored in the file `D.sim`). Further, we compute the log-scale of the mixture (only the variance of the whole mixture is stored in the file `mixmoment.sim`).

```
> sdb <- list()
> logscale <- list()
> for (ch in 1:nchains) {
+     sdb[[ch]] <- read.table(paste(get(paste("dirsim", ch, sep = "")),
+         "/D.sim", sep = ""), header = TRUE)
+     sdb[[ch]] <- data.frame(sdb = sqrt(sdb[[ch]][, 2]))
+     logscale[[ch]] <- read.table(paste(get(paste("dirsim", ch,
+         sep = "")), "/mixmoment.sim", sep = ""), header = TRUE)
+     logscale[[ch]] <- data.frame(logscale = sqrt(logscale[[ch]][,
+         2]))
+ }
```

Using the function `files2coda` we create the CODA `mcmc` objects for each parameter and each chain:

```
> pars <- list()
> for (ch in 1:nchains) {
+     pars[[ch]] <- files2coda(files = c("beta.sim", "mixmoment.sim"),
+         data.frames = c("sdb", "logscale"), thin = 1, dir = paste(get(paste("dirsim",
+             ch, sep = ""))), chain = ch)
+ }
```

We combine both chains into a CODA `mcmc.list`:

```
> parsls <- mcmc.list(pars[[1]], pars[[2]])
> rm(list = c("pars", "sdb", "logscale"))
```

Look what are the model parameters stored in this object:

```
> dimnames(parsls[[1]])[[2]]
```

```
 [1] "trtmt"        "inheritAuRec" "age"          "cortico"      "prophy"
 [6] "genderfemale" "hcatUS.other" "hcatEU.Am"    "hcatEU.other" "k"
[11] "Intercept"    "Scale"        "sdb"          "logscale"
```

11.1 Summary statistics

Summary statistics (separately for each chain):

```
> quant <- c(0, 0.025, 0.5, 0.75, 0.975, 1)
> means <- list()
> quantiles <- list()
> summ <- list()
> for (ch in 1:nchains) {
+     means[[ch]] <- apply(parsls[[ch]], 2, mean)
+     quantiles[[ch]] <- apply(parsls[[ch]], 2, quantile, quant)
+     summ[[ch]] <- rbind(means[[ch]], quantiles[[ch]])
+     rownames(summ[[ch]])[1] <- "mean"
+ }
> names(summ) <- paste("Chain ", 1:nchains, sep = "")
> print(summ)
```

```
$"Chain 1"
           trtmt inheritAuRec          age    cortico      prophy  genderfemale
mean   1.2952393  -0.88889973  0.047711099 -2.5305725  1.12710456  1.3426808385
0%    -0.4113581  -3.25038300 -0.044453680 -8.5209030 -1.22550700 -1.4097830000
2.5%   0.4871340  -1.81794835  0.005455738 -5.2309858  0.08478048 -0.0007541623
50%    1.2719995  -0.88578360  0.046848355 -2.4731380  1.10761450  1.3182455000
75%    1.5811632  -0.57989282  0.062110178 -1.6773263  1.47657200  1.8018465000
97.5%  2.2136023   0.03692818  0.093768835 -0.1364918  2.29062897  2.8135636250
100%   3.3180850   1.02502200  0.167860400  2.6627620  3.88840800  4.8311500000
      hcatUS.other  hcatEU.Am hcatEU.other         k Intercept     Scale
mean     0.4708446  1.5933397   1.22442635  5.757333 3.8333191 1.8571086
0%      -1.3670960 -1.6433490  -1.61149600  1.000000 0.5132017 0.9629224
2.5%    -0.4520949  0.1705688  -0.07181092  1.000000 2.1747884 1.2601308
50%      0.4598775  1.5470980   1.20281100  6.000000 3.8586200 1.7278890
75%      0.7767884  2.0873605   1.66435525  8.000000 4.3754333 2.0496230
97.5%    1.4965285  3.2851955   2.62552402 12.000000 5.4051495 3.1729197
100%     2.7890120  5.9596500   4.74614800 18.000000 6.9536050 5.8307780
             sdb logscale
```

```
mean  0.833728846 1.946205
0%    0.004319551 0.716381
2.5%  0.188781233 1.474716
50%   0.833260313 1.964337
75%   1.043242062 2.091754
97.5% 1.479499071 2.324898
100%  2.804735816 2.636969

$"Chain 2"
           trtmt inheritAuRec          age    cortico     prophy genderfemale
mean   1.3111115   -0.8809694  0.047097248 -2.5351073  1.0952944   1.39451035
0%    -0.3263018   -3.1168670 -0.051531330 -8.8917600 -1.3768960  -1.53255700
2.5%   0.5035612   -1.8043968  0.005417265 -5.3730490  0.0553078   0.06416812
50%    1.2923485   -0.8778754  0.046289855 -2.4714840  1.0748635   1.37927250
75%    1.5922275   -0.5704011  0.061379605 -1.6621527  1.4523812   1.86064125
97.5%  2.2135942    0.0338839  0.092566307 -0.0752535  2.2398131   2.82542137
100%   3.4475450    1.2762030  0.159643500  2.6708220  3.5902680   4.29455200
      hcatUS.other  hcatEU.Am hcatEU.other       k  Intercept     Scale
mean     0.4608834  1.5854185    1.2012839  5.6212 3.87034905 1.8842063
0%      -1.6901830 -1.8143200   -1.8439460  1.0000 0.01712473 0.9913276
2.5%    -0.4737526  0.1215553   -0.0693819  1.0000 2.26385775 1.2584596
50%      0.4551632  1.5531525    1.1781505  6.0000 3.86100400 1.7270735
75%      0.7772544  2.0898462    1.6224070  7.0000 4.40330250 2.0574698
97.5%    1.4478403  3.2455566    2.6241531 12.0000 5.52184587 3.4634859
100%     3.2358270  5.3361250    6.9541700 18.0000 7.49345500 6.0880480
             sdb  logscale
mean  0.81753077 1.9553976
0%    0.02315312 0.1308615
2.5%  0.20300459 1.5046122
50%   0.81327108 1.9649438
75%   1.02240110 2.0984048
97.5% 1.46854112 2.3498608
100%  2.19889268 2.7374176
```

11.2 Posterior densities

Histogram of sampled k (number of mixture components). The result is shown in Figure 7.

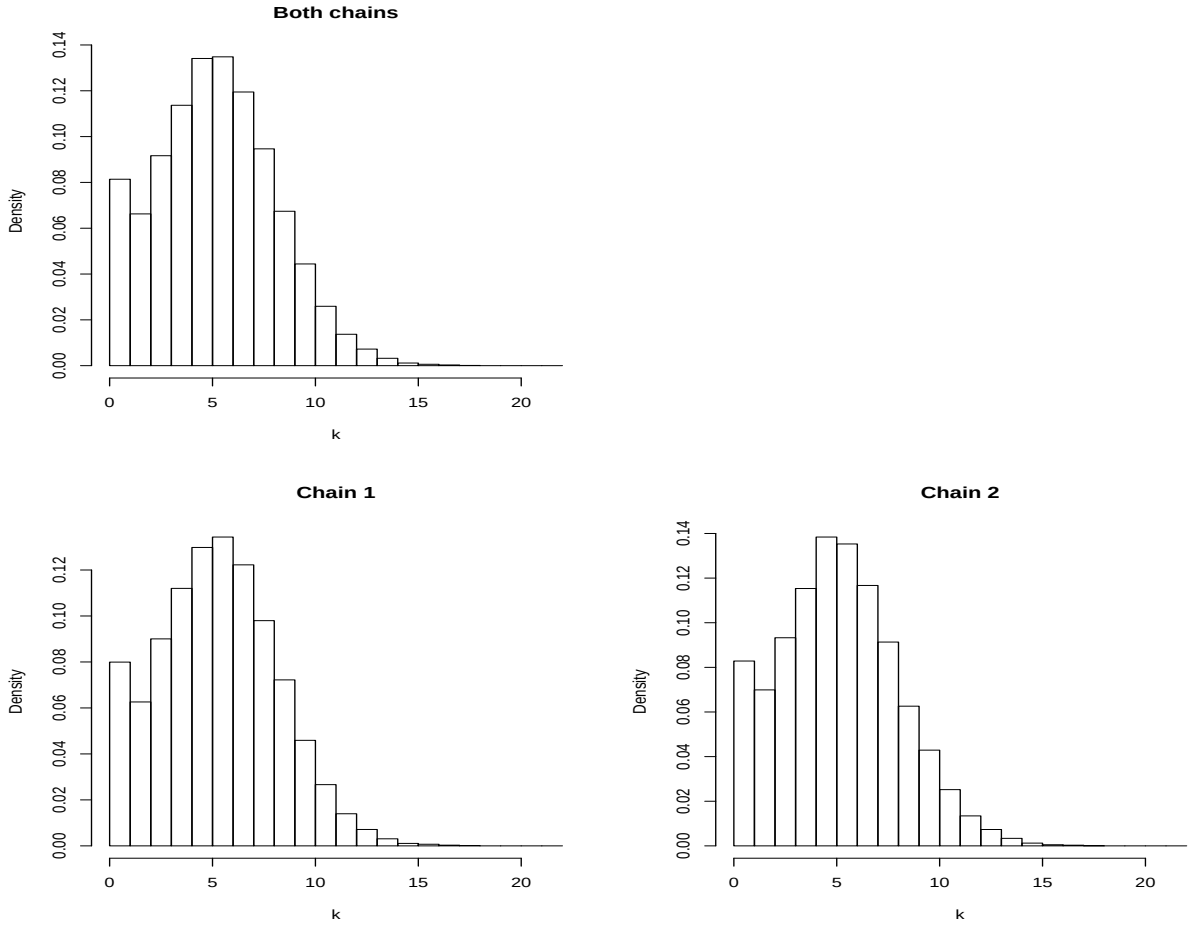
```
> par(bty = "n")
> par(mfrow = c(2, 2))
> kall <- c(parsls[[1]][, "k"], parsls[[2]][, "k"])
> hist(kall, xlab = "k", prob = TRUE, main = "Both chains", breaks = 0:22)
> plot.new()
> hist(parsls[[1]][, "k"], xlab = "k", prob = TRUE, main = "Chain 1",
+     breaks = 0:22)
> hist(parsls[[2]][, "k"], xlab = "k", prob = TRUE, main = "Chain 2",
+     breaks = 0:22)
```

Posterior densities of $\boldsymbol{\beta}$ parameters (based on the first chain only). The result is shown in Figure 8.

```
> ch <- 1
> par(bty = "n")
> par(mfrow = c(3, 3))
> for (i in 1:9) {
+     densplot(parsls[[ch]][, i], show.obs = FALSE, bty = "n")
+     title(main = paste(attr(parsls[[ch]], "dimnames")[[2]][i],
+         ", chain ", ch, sep = ""))
+ }
```

Figure 7: Histogram of sampled k.

.



Posterior densities of k, standard deviation $\sqrt{d}$ of the random intercept b_i, mixture overall mean (intercept) and mixture overall standard deviation (error scale) (based on the first chain). The result is shown in Figure 9.

```
> ch <- 1
> par(mfrow = c(2, 2))
> densplot(parsls[[ch]][, "k"], show.obs = FALSE, bty = "n")
> title(main = paste("k, chain", ch, sep = ""))
> densplot(parsls[[ch]][, "sdb"], show.obs = FALSE, bty = "n")
> title(main = paste("Std. Dev. of b, chain", ch, sep = ""))
> densplot(parsls[[ch]][, "Intercept"], show.obs = FALSE, bty = "n")
> title(main = paste("Intercept, chain ", ch, sep = ""))
> densplot(parsls[[ch]][, "Scale"], show.obs = FALSE, bty = "n")
> title(main = paste("Error Scale, chain ", ch, sep = ""))
```

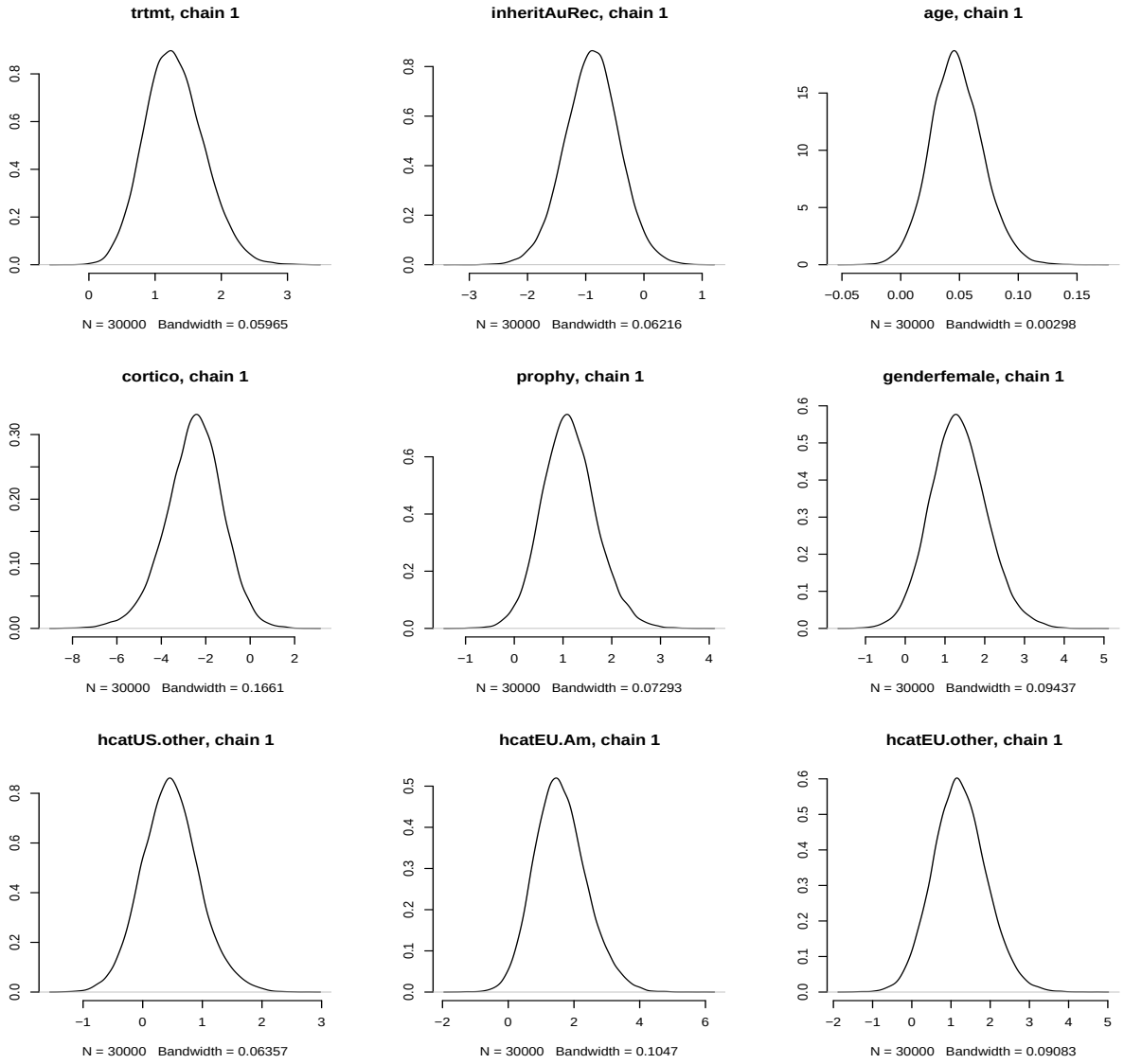
11.3 Autocorrelations

Autocorrelation plots for some parameters in the first chain (see Figure 10 and 11 for the results).

```
> ch <- 1
> par(bty = "n")
```

Figure 8: Posterior densities of $\boldsymbol{\beta}$ parameters.

.



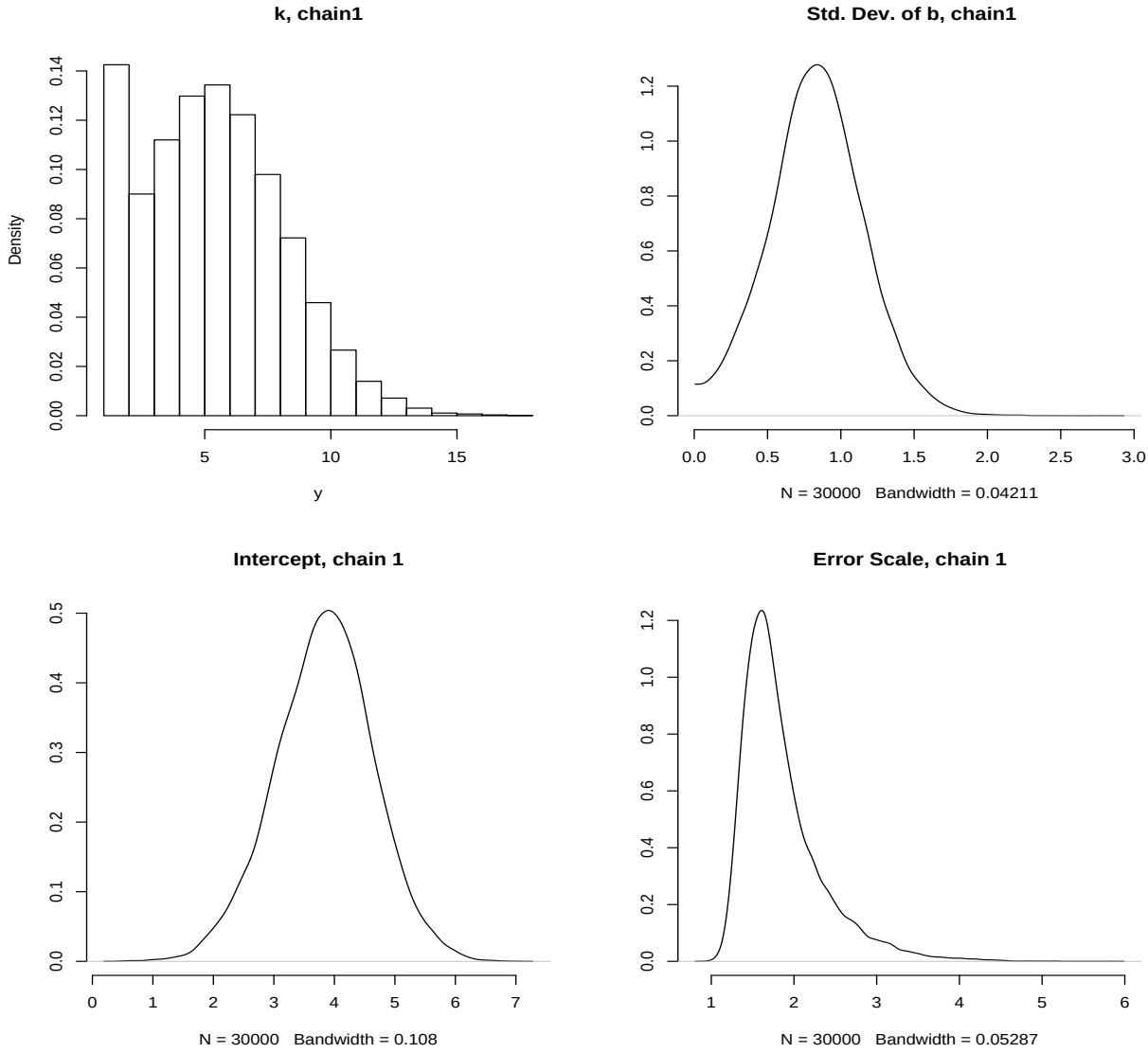

```
> par(mfrow = c(3, 3))
> autocorr.plot(parsls[[ch]][, 1:9], ask = FALSE, sub = paste("Chain ",
+     ch, sep = ""))

> par(bty = "n")
> par(mfrow = c(2, 2))
> plot.new()
> autocorr.plot(parsls[[ch]][, 13], auto.layout = FALSE, ask = FALSE,
+     sub = paste("Chain ", ch, sep = ""), main = "sdb")
> autocorr.plot(parsls[[ch]][, 11:12], auto.layout = FALSE, ask = FALSE,
+     sub = paste("Chain ", ch, sep = ""))
```

11.4 Crosscorrelations

Crosscorrelations (separately for each chain)

Figure 9: Posterior densities of some other parameters.

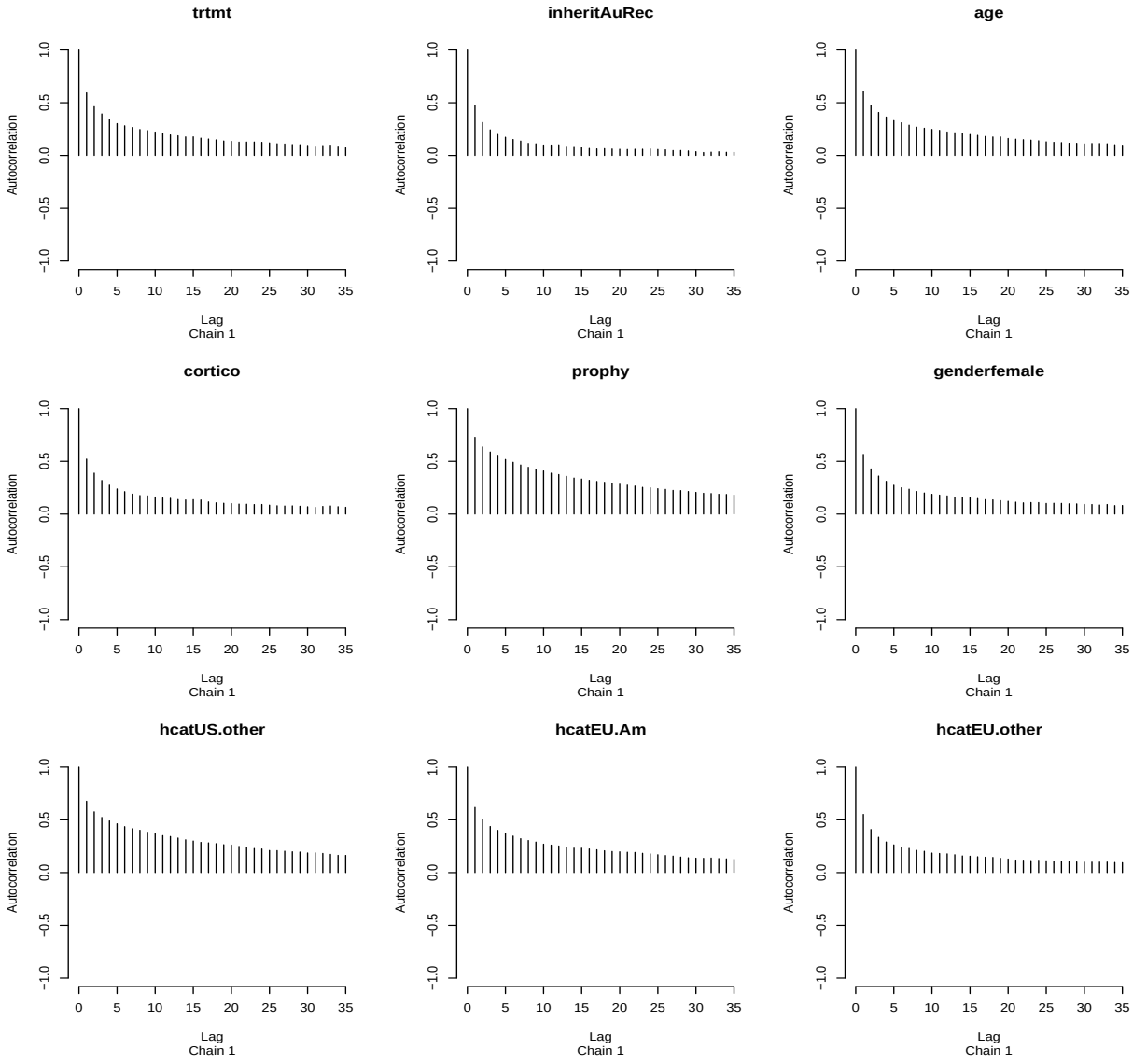
.




```
> croscor <- lapply(parsls, crosscorr)
> croscor <- lapply(croscor, round, digits = 2)
> names(croscor) <- paste("Chain ", 1:nchains, sep = "")
> print(croscor)

$"Chain 1"
              trtmt inheritAuRec   age cortico prophy genderfemale hcatUS.other
trtmt          1.00         0.06  0.04    0.05   0.03         0.09         0.17
inheritAuRec   0.06         1.00 -0.14    0.31  -0.21        -0.49        -0.01
age            0.04        -0.14  1.00   -0.15   0.16         0.00         0.29
cortico        0.05         0.31 -0.15    1.00  -0.10        -0.48        -0.08
prophy         0.03        -0.21  0.16   -0.10   1.00         0.21         0.23
genderfemale   0.09        -0.49  0.00   -0.48   0.21         1.00         0.06
hcatUS.other   0.17        -0.01  0.29   -0.08   0.23         0.06         1.00
hcatEU.Am      0.06        -0.23  0.08   -0.43   0.41         0.23         0.48
hcatEU.other   0.07        -0.09  0.11   -0.06   0.10         0.05         0.45
```

Figure 10: Autocorrelation plots.

.

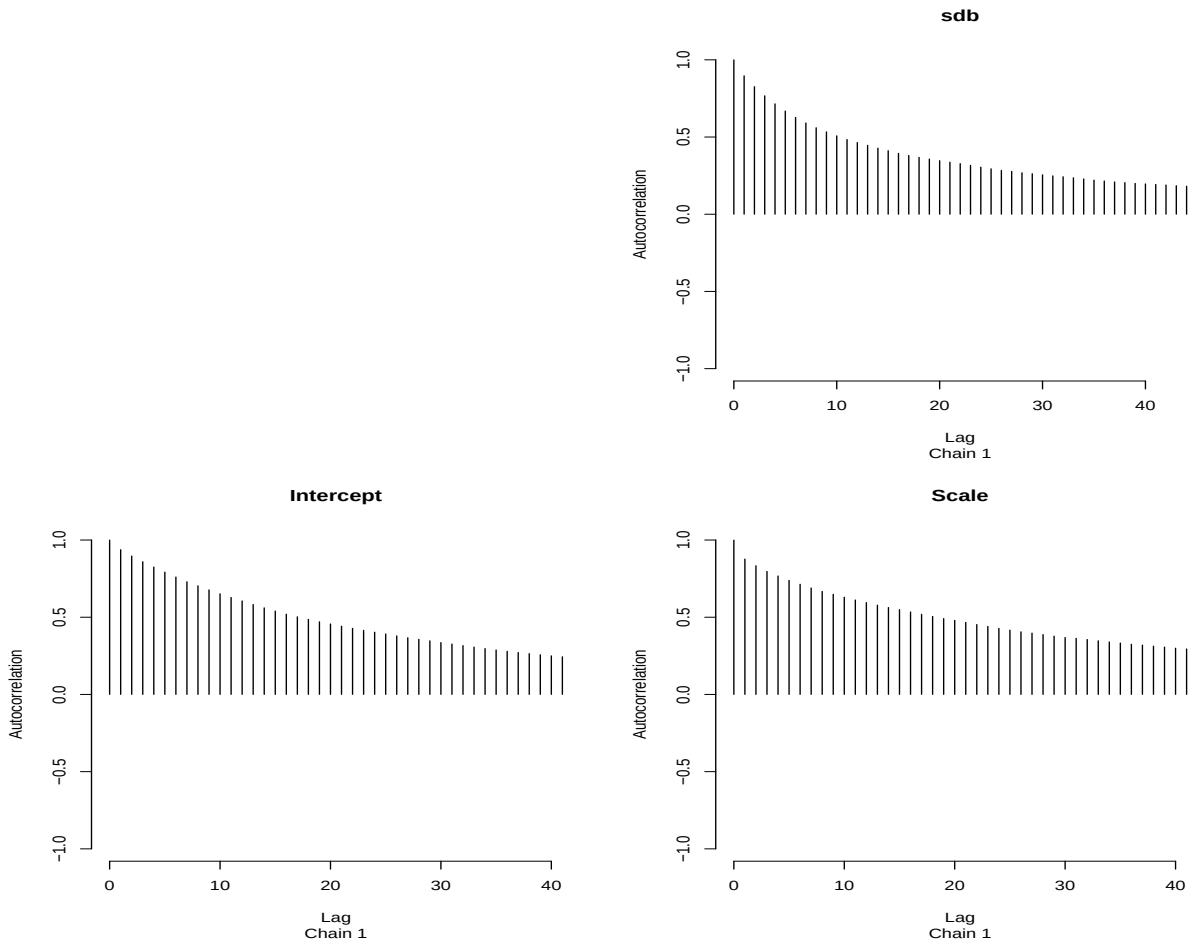


k	-0.08	0.00	-0.01	-0.10	-0.05	-0.01	0.02
Intercept	-0.26	0.03	-0.47	0.07	-0.70	-0.15	-0.63
Scale	0.07	-0.04	0.12	-0.19	0.08	0.13	0.07
sdb	0.07	-0.01	0.09	0.01	0.11	-0.02	0.19
logscale	-0.26	0.03	-0.48	0.08	-0.70	-0.15	-0.63

	hcatEU.Am	hcatEU.other	k	Intercept	Scale	sdb	logscale
trtmt	0.06	0.07	-0.08	-0.26	0.07	0.07	-0.26
inheritAuRec	-0.23	-0.09	0.00	0.03	-0.04	-0.01	0.03
age	0.08	0.11	-0.01	-0.47	0.12	0.09	-0.48
cortico	-0.43	-0.06	-0.10	0.07	-0.19	0.01	0.08
prophy	0.41	0.10	-0.05	-0.70	0.08	0.11	-0.70
genderfemale	0.23	0.05	-0.01	-0.15	0.13	-0.02	-0.15
hcatUS.other	0.48	0.45	0.02	-0.63	0.07	0.19	-0.63
hcatEU.Am	1.00	0.30	0.04	-0.47	0.17	0.06	-0.47
hcatEU.other	0.30	1.00	0.05	-0.33	0.04	0.12	-0.33
k	0.04	0.05	1.00	0.09	0.25	-0.03	0.09

Figure 11: Autocorrelation plots.

.




```
Intercept        -0.47        -0.33  0.09      1.00  0.13  0.00     1.00
Scale             0.17         0.04  0.25      0.13  1.00 -0.09     0.12
sdb               0.06         0.12 -0.03      0.00 -0.09  1.00    -0.01
logscale         -0.47        -0.33  0.09      1.00  0.12 -0.01     1.00

$"Chain 2"
             trtmt inheritAuRec   age cortico prophy genderfemale hcatUS.other
trtmt         1.00         0.05  0.04    0.10   0.05         0.04         0.16
inheritAuRec  0.05         1.00 -0.13    0.28  -0.22        -0.45        -0.01
age           0.04        -0.13  1.00   -0.15   0.18        -0.01         0.28
cortico       0.10         0.28 -0.15    1.00  -0.08        -0.47        -0.04
prophy        0.05        -0.22  0.18   -0.08   1.00         0.20         0.24
genderfemale  0.04        -0.45 -0.01   -0.47   0.20         1.00         0.05
hcatUS.other  0.16        -0.01  0.28   -0.04   0.24         0.05         1.00
hcatEU.Am     0.05        -0.23  0.08   -0.42   0.39         0.22         0.48
hcatEU.other  0.09        -0.06  0.11   -0.01   0.12         0.03         0.47
k            -0.01         0.03 -0.01   -0.09  -0.06         0.05         0.00
Intercept    -0.27         0.05 -0.48    0.03  -0.70        -0.13        -0.62
Scale         0.02         0.00  0.11   -0.24   0.05         0.14         0.04
sdb           0.07         0.02  0.06    0.03   0.10        -0.03         0.21
logscale     -0.27         0.05 -0.48    0.03  -0.70        -0.13        -0.62
             hcatEU.Am hcatEU.other     k Intercept Scale   sdb logscale
```

```
trtmt             0.05         0.09 -0.01     -0.27  0.02  0.07    -0.27
inheritAuRec     -0.23        -0.06  0.03      0.05  0.00  0.02     0.05
age               0.08         0.11 -0.01     -0.48  0.11  0.06    -0.48
cortico          -0.42        -0.01 -0.09      0.03 -0.24  0.03     0.03
prophy            0.39         0.12 -0.06     -0.70  0.05  0.10    -0.70
genderfemale      0.22         0.03  0.05     -0.13  0.14 -0.03    -0.13
hcatUS.other      0.48         0.47  0.00     -0.62  0.04  0.21    -0.62
hcatEU.Am         1.00         0.32  0.04     -0.45  0.15  0.05    -0.46
hcatEU.other      0.32         1.00  0.02     -0.35  0.04  0.13    -0.35
k                 0.04         0.02  1.00      0.09  0.28 -0.04     0.08
Intercept        -0.45        -0.35  0.09      1.00  0.18  0.00     0.99
Scale             0.15         0.04  0.28      0.18  1.00 -0.11     0.17
sdb               0.05         0.13 -0.04      0.00 -0.11  1.00    -0.01
logscale         -0.46        -0.35  0.08      0.99  0.17 -0.01     1.00
```

11.5 Gelman-Rubin convergence diagnostics

Gelman-Rubin convergence diagnostics:

```
> gelm <- gelman.diag(parsls)
> rownames(gelm$psrf) <- dimnames(parsls[[1]])[[2]]
> print(gelm)

Potential scale reduction factors:

             Point est. 97.5% quantile
trtmt              1.00           1.00
inheritAuRec       1.00           1.00
age                1.00           1.00
cortico            1.00           1.00
prophy             1.00           1.01
genderfemale       1.00           1.01
hcatUS.other       1.00           1.00
hcatEU.Am          1.00           1.00
hcatEU.other       1.00           1.00
k                  1.00           1.00
Intercept          1.00           1.00
Scale              1.01           1.01
sdb                1.00           1.00
logscale           1.00           1.00

Multivariate psrf

1.01+0i
```

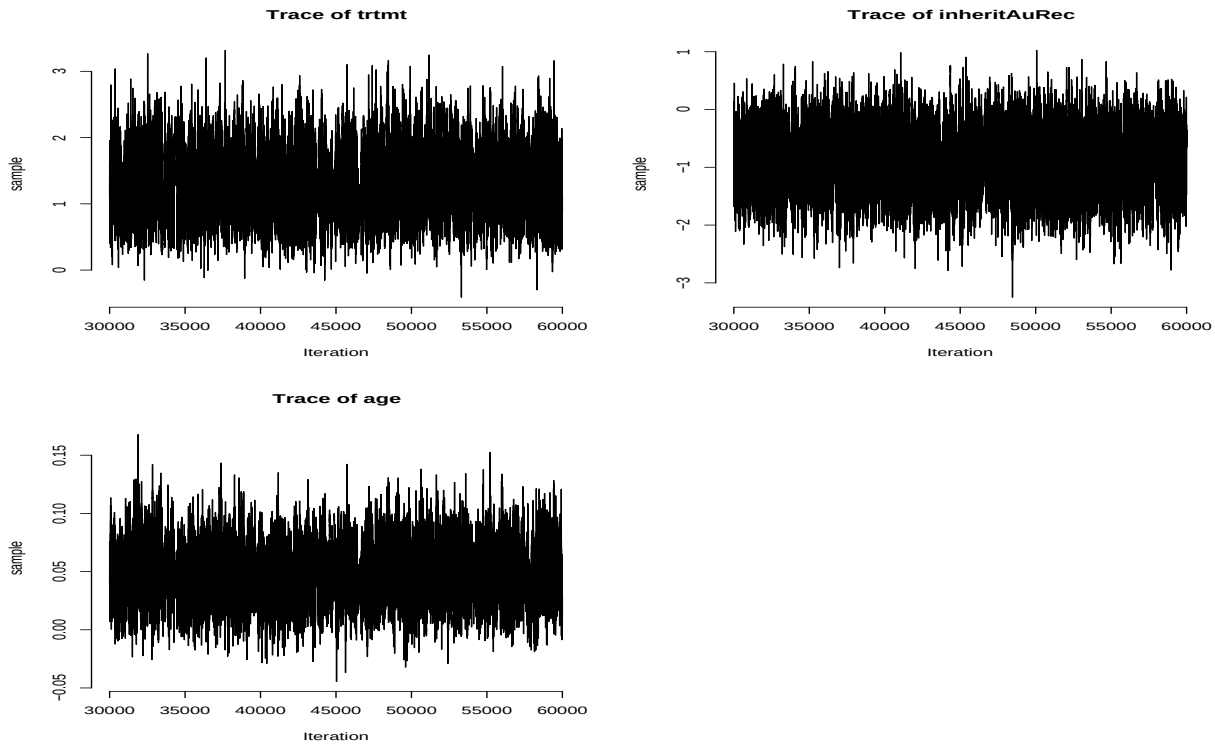
11.6 Traceplots

Traceplots for the first chain (see Figures 12, 13, 14 and 15 for the result). Observe that the function `densplot2` of the package `bayesSurv` is used.

```
> ch <- 1
> par(bty = "n")
> par(mfrow = c(2, 2))
> traceplot2(parsls[[ch]], chains = 1:3, sub = paste("Chain ",
+     ch, sep = ""))

> par(bty = "n")
> par(mfrow = c(2, 2))
```

Figure 12: Traceplots.

.




```
> traceplot2(parsls[[ch]], chains = 4:6, sub = paste("Chain ",
+     ch, sep = ""))

> par(bty = "n")
> par(mfrow = c(2, 2))
> traceplot2(parsls[[ch]], chains = 7:9, sub = paste("Chain ",
+     ch, sep = ""))

> par(bty = "n")
> par(mfrow = c(2, 2))
> traceplot2(parsls[[ch]], chains = 10, sub = paste("Chain ", ch,
+     sep = ""))
> traceplot2(parsls[[ch]], chains = 13, sub = paste("Chain ", ch,
+     sep = ""))
> traceplot2(parsls[[ch]], chains = 11:12, sub = paste("Chain ",
+     ch, sep = ""))
```

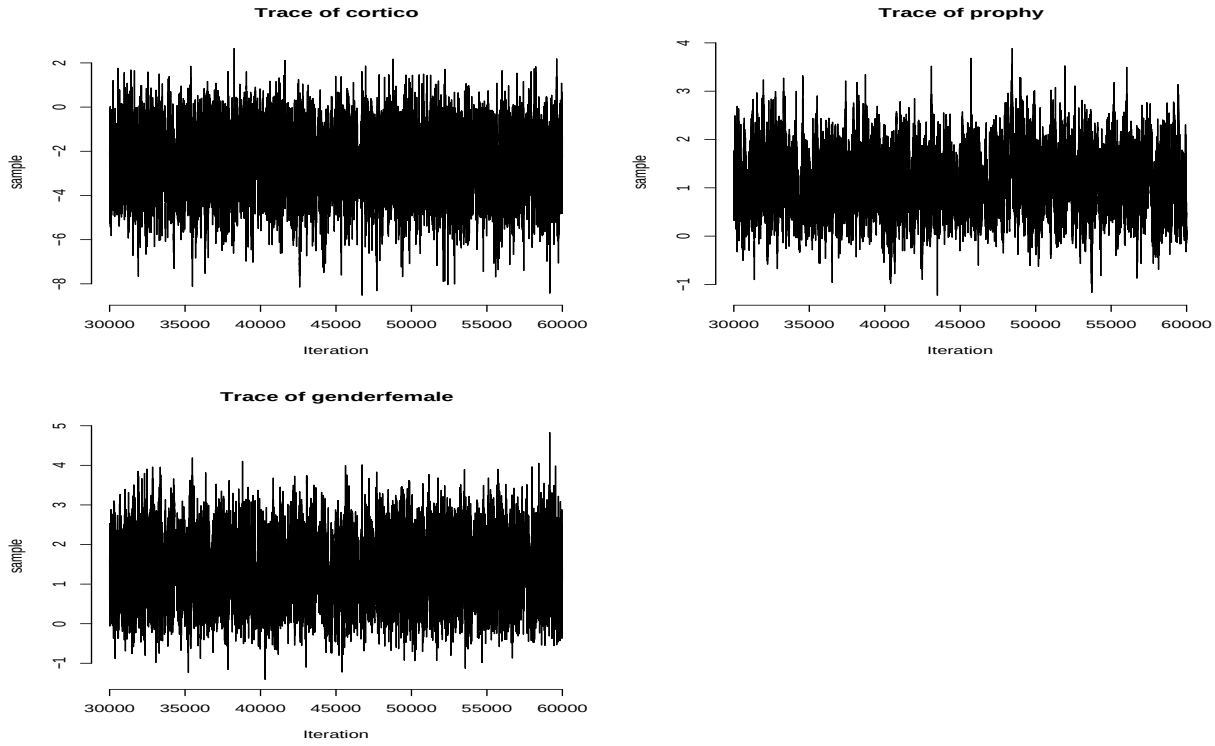
11.7 Performance of reversible jumps

Check the performance of reversible jumps (acceptance probabilities in split-combine move and in birth-death move):

```
> mh <- list()
> averMH <- list()
> for (ch in 1:nchains) {
+     mh[[ch]] <- files2coda(files = c("MHinfo.sim"), start = 1,
```

Figure 13: Traceplots.

.



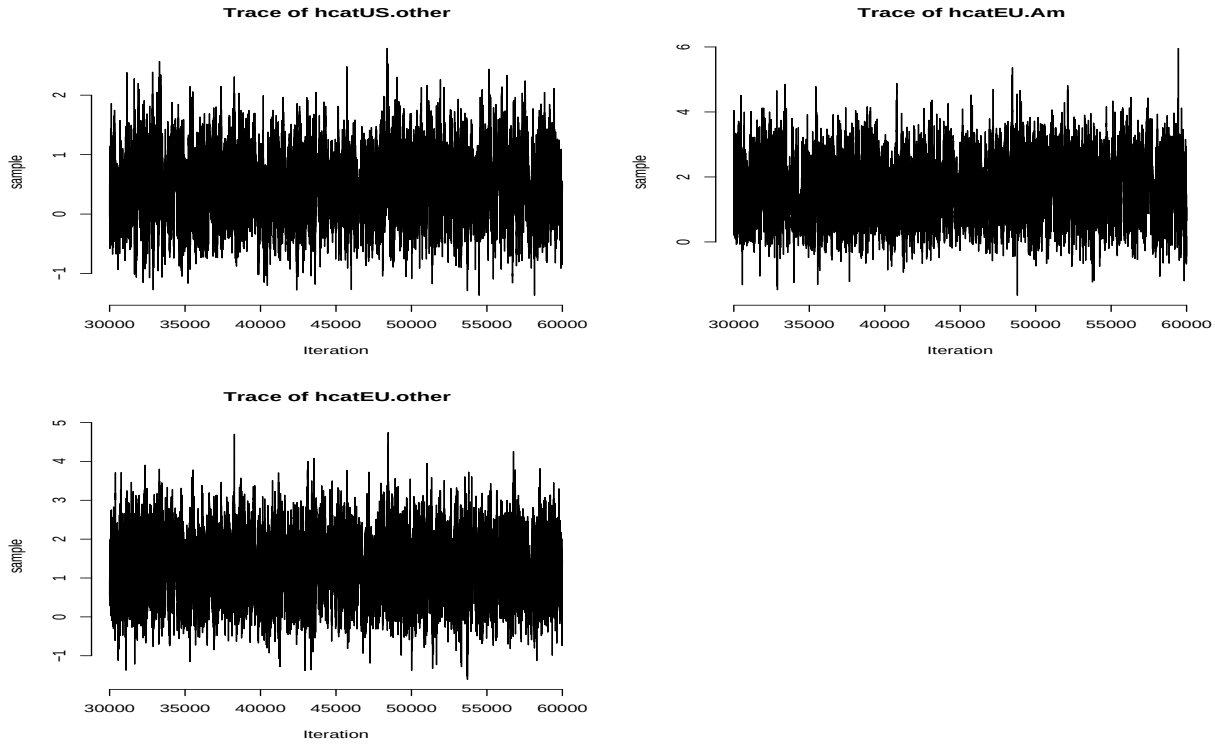

```
+         thin = 1, dir = get(paste("dirsim", ch, sep = "")))
+     averMH[[ch]] <- apply(mh[[ch]][, c(1, 3)], 2, mean)
+ }
> for (ch in 1:nchains) {
+     cat("Chain ", ch, ":\n", sep = "")
+     print(averMH[[ch]])
+ }

Chain 1:
   accept.spl.comb accept.birth.death
        0.19944146         0.07615784
Chain 2:
   accept.spl.comb accept.birth.death
        0.19883586         0.07468886
```

Finally, we perform cleaning of generated files:

```
> files1 <- dir("./cgdchain1")
> files2 <- dir("./cgdchain2")
> file.remove(paste("./cgdchain1/", files1, sep = ""))

 [1] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
[16] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
[31] TRUE

> file.remove(paste("./cgdchain2/", files2, sep = ""))

 [1] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
```

Figure 14: Traceplots.

.




```
> file.remove("cgdchain1")

[1] TRUE

> file.remove("cgdchain2")

[1] TRUE
```

Figure 15: Traceplots.

.