Bayesian Statistics
Time-to-Event Models

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Before We Begin...

Time-to-Event models applied in:

Reliability Theory
Survival Theory
Geoscientific Prediction

Focus on Parametric Approach

Lifetime Distributions

Notation

- T- lifetime, time-to-event. (naturally, $T \geq 0$)
- $F(t) = P(T \leq t)$: cdf
- $S(t) = 1 - F(t) = P(T > t)$: Survival function
- $f(t)$ - density of T, $f(t) = \frac{dF(t)}{dt} = -\frac{dS(t)}{dt}$
- $P(a \leq T \leq b) = F(b) - F(a) = S(a) - S(b)$
- $h(t)dt = P(t \leq T \leq t + dt | T \geq t) = \frac{S(t) - S(t+dt)}{S(t)}$
- $h(t) = \lim_{dt \to 0} \left(\frac{S(t) - S(t+dt)}{dt} \cdot \frac{1}{S(t)} \right) = -\frac{S(t)'}{S(t)} = -(\log S(t))'$
- $h(t)$ is called hazard function

Lifetime Distributions

- $h(t) = -\frac{S(t)'}{S(t)} = \frac{f(t)}{S(t)}$
- $f(t)dt = P(t \leq T \leq T + dt)$

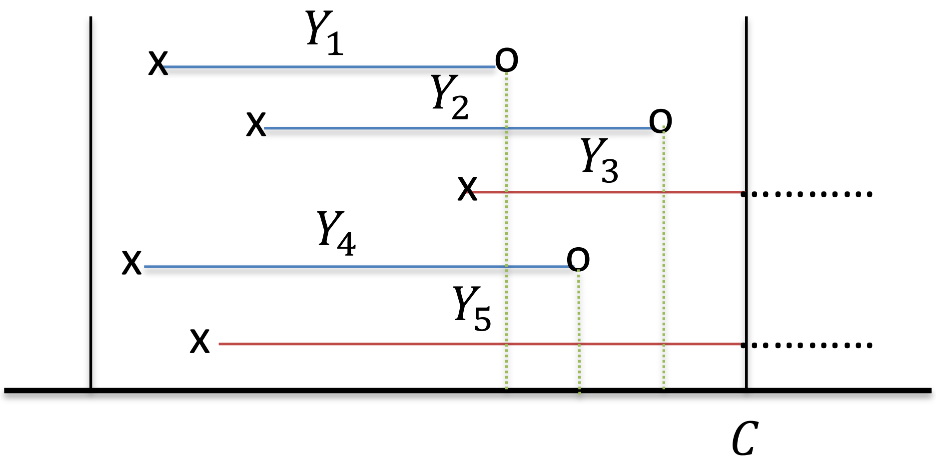
  $h(t)dt = P(t \leq T \leq T + dt \,| T \geq t)$
- Cumulative Hazard

$$H(t) = \int_0^t h(u)du = -\int_0^t (\log S(u))' du = -\log S(t) + 0$$

$$\Longrightarrow S(t) = e^{-H(t)}$$

$S(t)$, $h(t)$ most popular summaries in time-to-event modeling

Censoring



Y_1, Y_2, Y_4- fully observed

Y_3, Y_5- censored

Censoring indicator: $\delta = 0$ (observed), $\delta = 1$ (censored)

$Time$	Y_1	Y_2	Y_3	Y_4	Y_5
δ	0	0	1	0	1

- Typical – right-censored data
- Censoring types
  - I. - censoring time fixed, number of observed random
  - II. - censoring time random, number of observed fixed
- Most common: right-censoring of type I

Likelihood with Censored Observations

$Y_i \sim f(y_i|\theta), \quad i = 1, \dots, n$

$\delta_i = 0, \quad i = 1, \dots, k, \quad \delta_i = 1, \quad i = k+1, \dots, n$

$$L(\theta|y_1, \dots, y_n) = \prod_{i=1}^{n} (f(y_i|\theta))^{1-\delta_i} (S(y_i|\theta))^{\delta_i}$$

$$S(y_i|\theta) = P^{\theta}(Y_i > y_i)$$

- Bayesian inference about θ $\longrightarrow$ $L(\theta|y_1, \dots, y_n) + \pi(\theta)$

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Example 1:

$$Y_1, Y_2, \ldots, Y_n \sim \mathcal{E}(\lambda)$$

Let $\delta_i = 0, \quad i = 1, \ldots, k; \quad \delta_i = 1, \quad i = k+1, \ldots, n$

- What is (frequentist) estimator of λ?
  - If all are observed $\Longrightarrow \dfrac{n}{\sum_{i=1}^{n} Y_i} = \dfrac{1}{\bar{Y}}$
- Shall we ignore censored data? If so,

$$\Longrightarrow \hat{\lambda} = \frac{k}{\sum_{i=1}^{k} Y_i} \quad \text{[Wrong!]}$$

- Shall we consider censored as observed? If so,

$$\Longrightarrow \frac{n}{\sum_{i=1}^{n} Y_i} = \frac{1}{\bar{Y}} \quad \text{[Wrong!]}$$

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Example 1: (cont.)

$$Y_1, Y_2, \dots, Y_n \sim \mathcal{E}(\lambda)$$

Let $\delta_i = 0, \quad i = 1, \dots, k; \quad \delta_i = 1, \quad i = k+1, \dots, n$

- The likelihood is $L(\theta | y_1, \dots, y_n) = \lambda^k e^{-\left(\lambda \sum_{i=1}^{n} Y_i\right)}$, so

MLE $\Longrightarrow \hat{\lambda} = \dfrac{k}{\sum_{i=1}^{n} Y_i} = \dfrac{k}{n\bar{Y}}$ [Correct!, as an exercise show this]

Example 2:

Let: $Y_1 = 2, Y_2 = 3, Y_3 = 1^*, Y_4 = \frac{5}{2}, Y_5 = 3^*;$

Assume that: $Y_i \sim Wei(\nu, \lambda), \nu = \frac{3}{2}.$

- Using prior on $\lambda \sim \mathcal{G}a(2,3)$, estimate λ.
  - Note that $\begin{cases} f(y_i \mid \nu, \lambda) = \nu\lambda y_i^{\nu-1} e^{-\lambda y_i^{\nu}}, y_i \geq 0 \\ S(y_i \mid \nu, \lambda) = e^{-\lambda y_i^{\nu}}, y_i \geq 0 \end{cases}$
  - The likelihood is:

$$\underbrace{\prod_{i=1}^{k} \nu\lambda y_i^{\nu-1} e^{-\lambda y_i^{\nu}}}_{\text{observed}} \underbrace{\prod_{i=k+1}^{n} e^{-\lambda y_i^{\nu}}}_{\text{censored}} = \nu^k \lambda^k \left(\prod_{i=1}^{k} y_i\right)^{\nu-1} e^{-\lambda \sum_{i=1}^{n} y_i^{\nu}}$$

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Example 2: (cont.)

- The likelihood is: $\prod_{i=1}^{k} \nu\lambda y_i^{\nu-1} e^{-\lambda y_i^{\nu}} \prod_{i=k+1}^{n} e^{-\lambda y_i^{\nu}} = \nu^k \lambda^k \left(\prod_{i=1}^{k} y_i\right)^{\nu-1} e^{-\lambda \sum_{i=1}^{n} y_i^{\nu}}$

$\Longrightarrow L(\lambda\,|\nu, y_1, \dots, y_n) \propto \lambda^k e^{-\lambda \sum_{i=1}^{n} y_i^{\nu}}$

$\Longrightarrow \pi(\lambda\,|\alpha, \beta) \propto \lambda^{\alpha-1} e^{-\beta\nu}$

$$\Longrightarrow \pi(\lambda\,|\nu, y_1, \dots, y_n, \alpha, \beta) \propto \lambda^{k+\alpha-1} e^{-\lambda\left(\beta + \sum_{i=1}^{n} y_i^{\nu}\right)}$$

- For $k = 3, \nu = \frac{3}{2}, \alpha = 2, \beta = 3$, and $\sum_{i=1}^{5} y_i^{3/2} = 18.1736$:

$$\Longrightarrow \pi(\lambda\,|\nu, y_1, \dots, y_n, \alpha, \beta) \sim \mathcal{G}a(3 + 2\,, 18.1736 + 3)$$

$$\boxed{\Longrightarrow \hat{\lambda}_{bayes} = \frac{5}{21.1736} = 0.2361}$$

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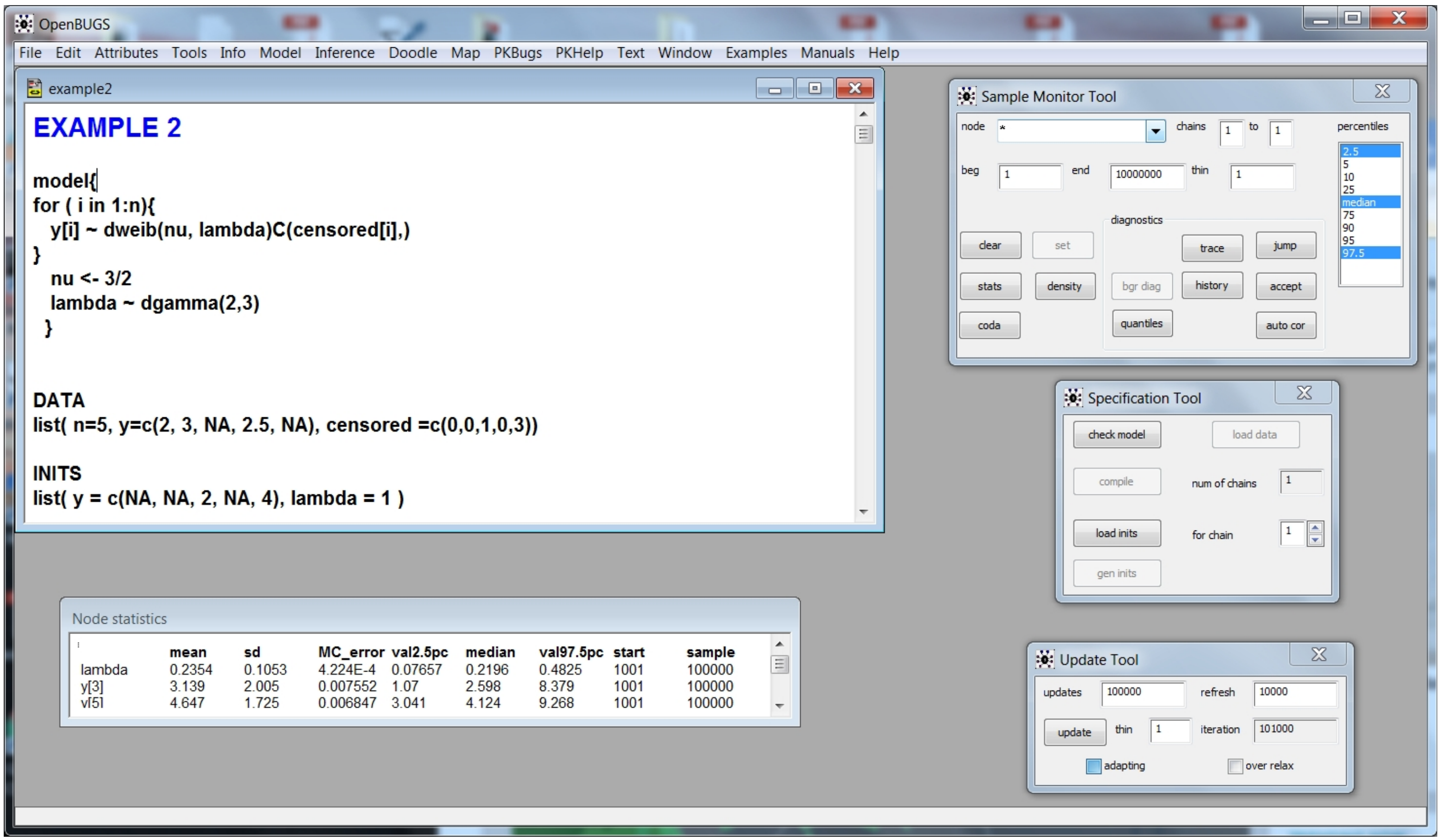
Example 2: (cont.)



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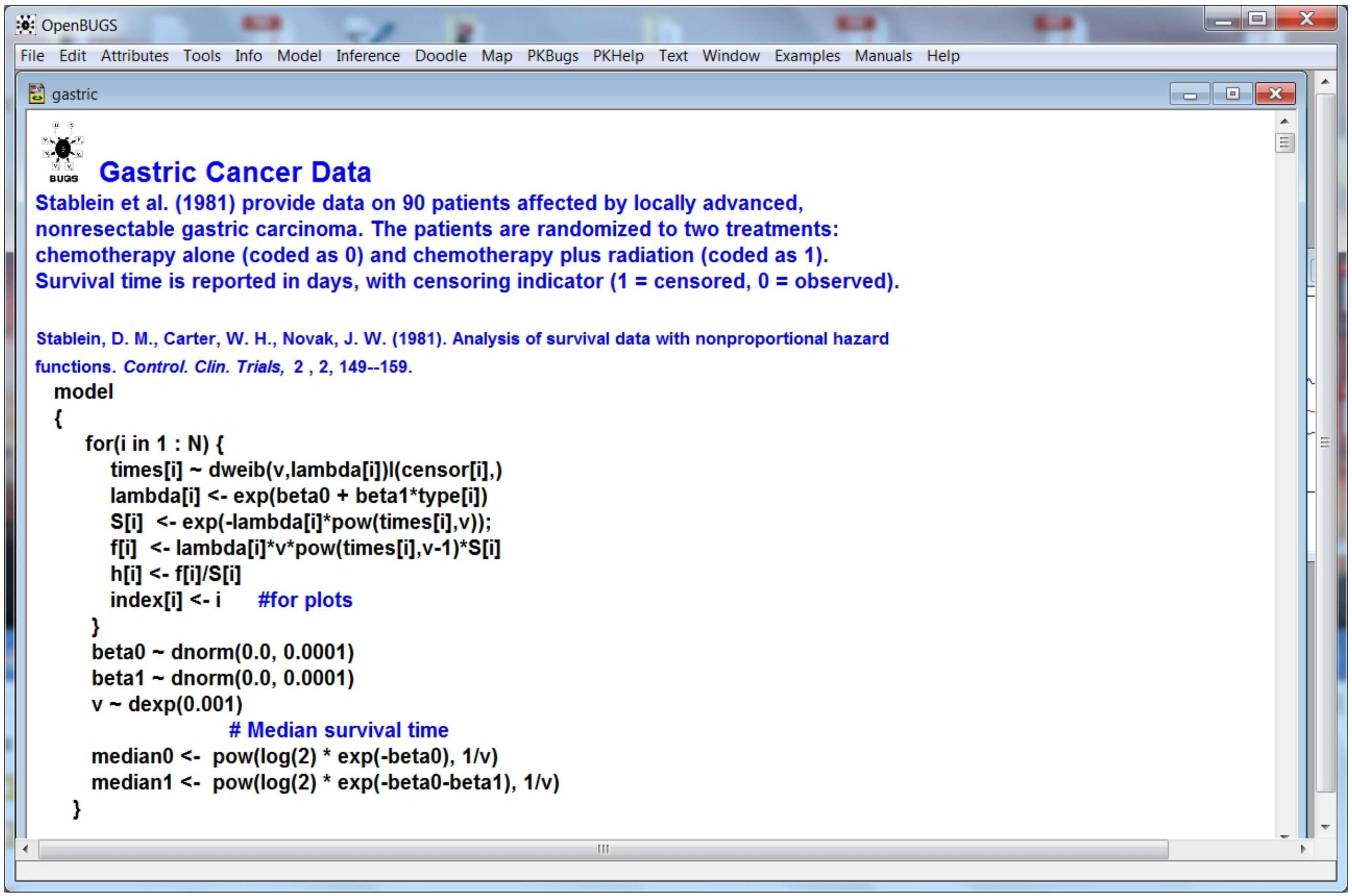
Example 3:



Gastric Cancer Data

Stablein et al. (1981) provide data on 90 patients affected by locally advanced, nonresectable gastric carcinoma. The patients are randomized to two treatments: chemotherapy alone (coded as 0) and chemotherapy plus radiation (coded as 1). Survival time is reported in days, with censoring indicator (1 = censored, 0 = observed).

Stablein, D. M., Carter, W. H., Novak, J. W. (1981). Analysis of survival data with nonproportional hazard functions. *Control. Clin. Trials,* 2 , 2, 149--159.

```
model
{
    for(i in 1 : N) {
        times[i] ~ dweib(v,lambda[i])I(censor[i],)
        lambda[i] <- exp(beta0 + beta1*type[i])
        S[i]  <- exp(-lambda[i]*pow(times[i],v));
        f[i]  <- lambda[i]*v*pow(times[i],v-1)*S[i]
        h[i] <- f[i]/S[i]
        index[i] <- i      #for plots
    }
    beta0 ~ dnorm(0.0, 0.0001)
    beta1 ~ dnorm(0.0, 0.0001)
    v ~ dexp(0.001)
                        # Median survival time
    median0 <-  pow(log(2) * exp(-beta0), 1/v)
    median1 <-  pow(log(2) * exp(-beta0-beta1), 1/v)
}
```

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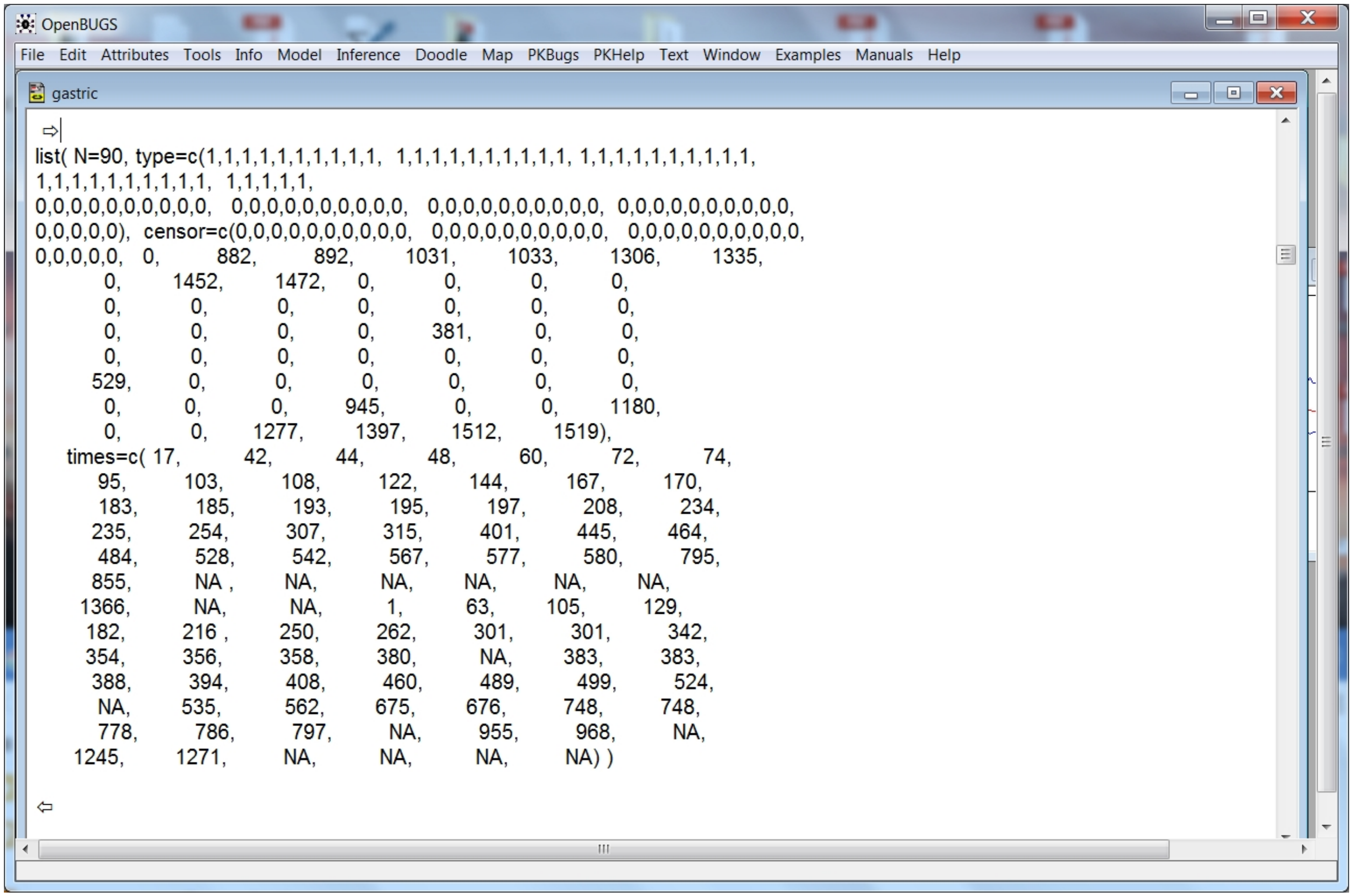
Example 3: (cont.)




```
⇨
list( N=90, type=c(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,
1,1,1,1,1,1,1,1,1,1,  1,1,1,1,1,
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,  0,0,0,0,0,0,0,0,0,0,
0,0,0,0,0),  censor=c(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,      882,      892,     1031,      1033,      1306,      1335,
      0,     1452,     1472,    0,         0,         0,        0,
      0,        0,        0,    0,         0,         0,        0,
      0,        0,        0,    0,       381,         0,        0,
      0,        0,        0,    0,         0,         0,        0,
    529,        0,        0,    0,         0,         0,        0,
      0,        0,        0,  945,         0,         0,     1180,
      0,        0,     1277, 1397,      1512,      1519),
   times=c( 17,       42,       44,       48,       60,       72,       74,
     95,      103,      108,      122,      144,      167,      170,
    183,      185,      193,      195,      197,      208,      234,
    235,      254,      307,      315,      401,      445,      464,
    484,      528,      542,      567,      577,      580,      795,
    855,      NA ,      NA,       NA,       NA,       NA,       NA,
   1366,      NA,       NA,        1,       63,      105,      129,
    182,      216 ,     250,      262,      301,      301,      342,
    354,      356,      358,      380,       NA,      383,      383,
    388,      394,      408,      460,      489,      499,      524,
     NA,      535,      562,      675,      676,      748,      748,
    778,      786,      797,       NA,      955,      968,       NA,
   1245,     1271,       NA,       NA,       NA,       NA) )

⇦
```

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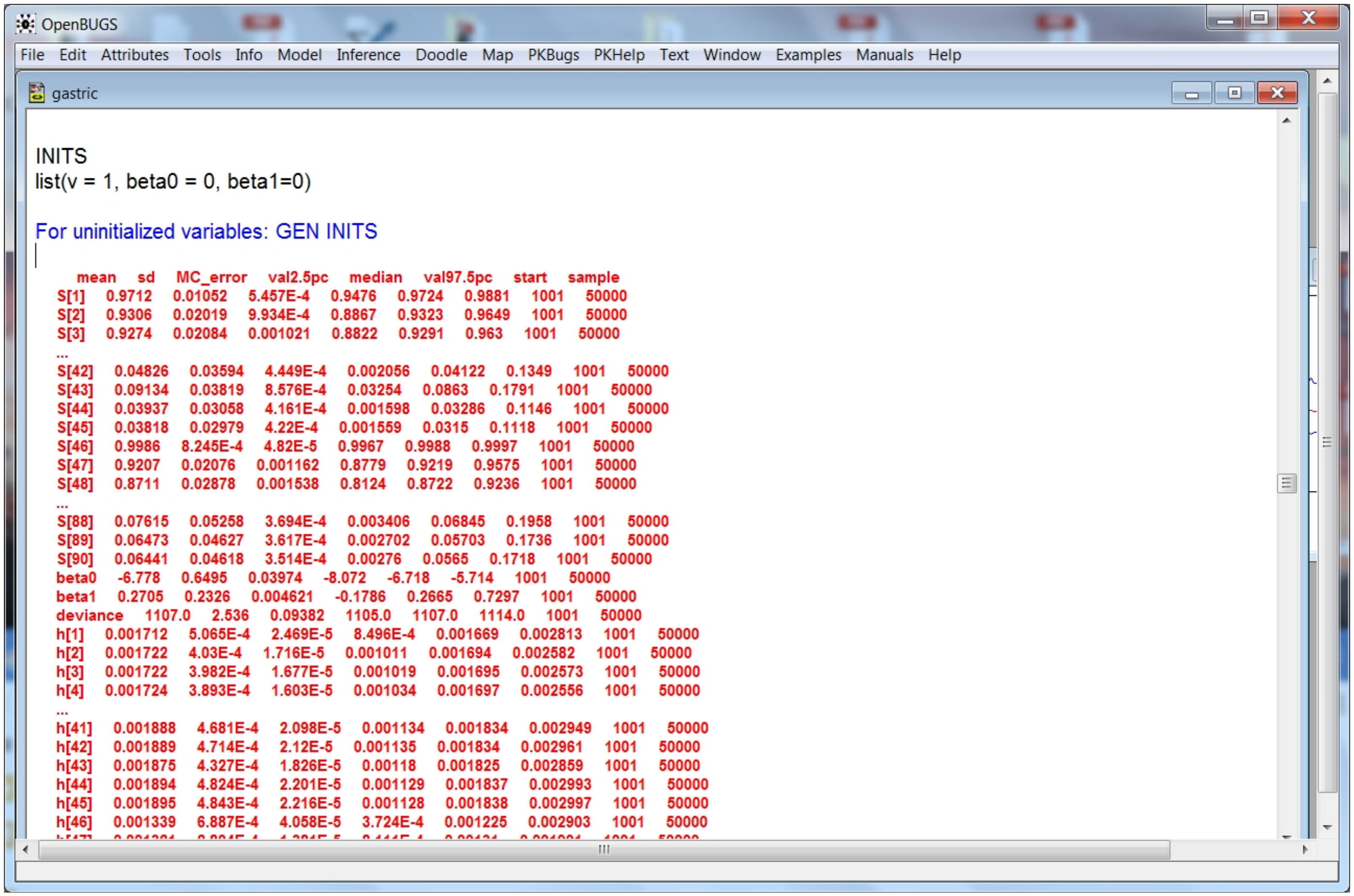
Example 3: (cont.)



INITS
list(v = 1, beta0 = 0, beta1=0)

For uninitialized variables: GEN INITS

	mean	sd	MC_error	val2.5pc	median	val97.5pc	start	sample
S[1]	0.9712	0.01052	5.457E-4	0.9476	0.9724	0.9881	1001	50000
S[2]	0.9306	0.02019	9.934E-4	0.8867	0.9323	0.9649	1001	50000
S[3]	0.9274	0.02084	0.001021	0.8822	0.9291	0.963	1001	50000
...								
S[42]	0.04826	0.03594	4.449E-4	0.002056	0.04122	0.1349	1001	50000
S[43]	0.09134	0.03819	8.576E-4	0.03254	0.0863	0.1791	1001	50000
S[44]	0.03937	0.03058	4.161E-4	0.001598	0.03286	0.1146	1001	50000
S[45]	0.03818	0.02979	4.22E-4	0.001559	0.0315	0.1118	1001	50000
S[46]	0.9986	8.245E-4	4.82E-5	0.9967	0.9988	0.9997	1001	50000
S[47]	0.9207	0.02076	0.001162	0.8779	0.9219	0.9575	1001	50000
S[48]	0.8711	0.02878	0.001538	0.8124	0.8722	0.9236	1001	50000
...								
S[88]	0.07615	0.05258	3.694E-4	0.003406	0.06845	0.1958	1001	50000
S[89]	0.06473	0.04627	3.617E-4	0.002702	0.05703	0.1736	1001	50000
S[90]	0.06441	0.04618	3.514E-4	0.00276	0.0565	0.1718	1001	50000
beta0	-6.778	0.6495	0.03974	-8.072	-6.718	-5.714	1001	50000
beta1	0.2705	0.2326	0.004621	-0.1786	0.2665	0.7297	1001	50000
deviance	1107.0	2.536	0.09382	1105.0	1107.0	1114.0	1001	50000
h[1]	0.001712	5.065E-4	2.469E-5	8.496E-4	0.001669	0.002813	1001	50000
h[2]	0.001722	4.03E-4	1.716E-5	0.001011	0.001694	0.002582	1001	50000
h[3]	0.001722	3.982E-4	1.677E-5	0.001019	0.001695	0.002573	1001	50000
h[4]	0.001724	3.893E-4	1.603E-5	0.001034	0.001697	0.002556	1001	50000
...								
h[41]	0.001888	4.681E-4	2.098E-5	0.001134	0.001834	0.002949	1001	50000
h[42]	0.001889	4.714E-4	2.12E-5	0.001135	0.001834	0.002961	1001	50000
h[43]	0.001875	4.327E-4	1.826E-5	0.00118	0.001825	0.002859	1001	50000
h[44]	0.001894	4.824E-4	2.201E-5	0.001129	0.001837	0.002993	1001	50000
h[45]	0.001895	4.843E-4	2.216E-5	0.001128	0.001838	0.002997	1001	50000
h[46]	0.001339	6.887E-4	4.058E-5	3.724E-4	0.001225	0.002903	1001	50000

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Example 3: (cont.)

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h[4]	0.001724	3.893E-4	1.603E-5	0.001034	0.001697	0.002556	1001	50000
...								
h[41]	0.001888	4.681E-4	2.098E-5	0.001134	0.001834	0.002949	1001	50000
h[42]	0.001889	4.714E-4	2.12E-5	0.001135	0.001834	0.002961	1001	50000
h[43]	0.001875	4.327E-4	1.826E-5	0.00118	0.001825	0.002859	1001	50000
h[44]	0.001894	4.824E-4	2.201E-5	0.001129	0.001837	0.002993	1001	50000
h[45]	0.001895	4.843E-4	2.216E-5	0.001128	0.001838	0.002997	1001	50000
h[46]	0.001339	6.887E-4	4.058E-5	3.724E-4	0.001225	0.002903	1001	50000
h[47]	0.001321	2.804E-4	1.381E-5	8.111E-4	0.00131	0.001901	1001	50000
h[48]	0.001331	2.498E-4	1.056E-5	8.732E-4	0.001321	0.001846	1001	50000
h[49]	0.001336	2.402E-4	9.249E-6	8.933E-4	0.001325	0.001832	1001	50000
...								
h[88]	0.001445	3.603E-4	1.262E-5	8.484E-4	0.001408	0.002249	1001	50000
h[89]	0.001449	3.673E-4	1.315E-5	8.452E-4	0.001411	0.002265	1001	50000
h[90]	0.001449	3.677E-4	1.32E-5	8.448E-4	0.001409	0.002268	1001	50000
lambda[1]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
lambda[2]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
...								
lambda[44]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
lambda[45]	0.001798	0.001096	5.896E-5	3.946E-4	0.00157	0.004469	1001	50000
lambda[46]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
lambda[47]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
lambda[48]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
...								
lambda[89]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
lambda[90]	0.001373	8.26E-4	4.828E-5	3.12E-4	0.001209	0.003299	1001	50000
median0	525.8	89.16	2.452	377.9	516.5	725.5	1001	50000
median1	403.4	69.0	1.368	284.2	397.8	553.5	1001	50000
v	1.025	0.09478	0.00562	0.8642	1.017	1.222	1001	50000

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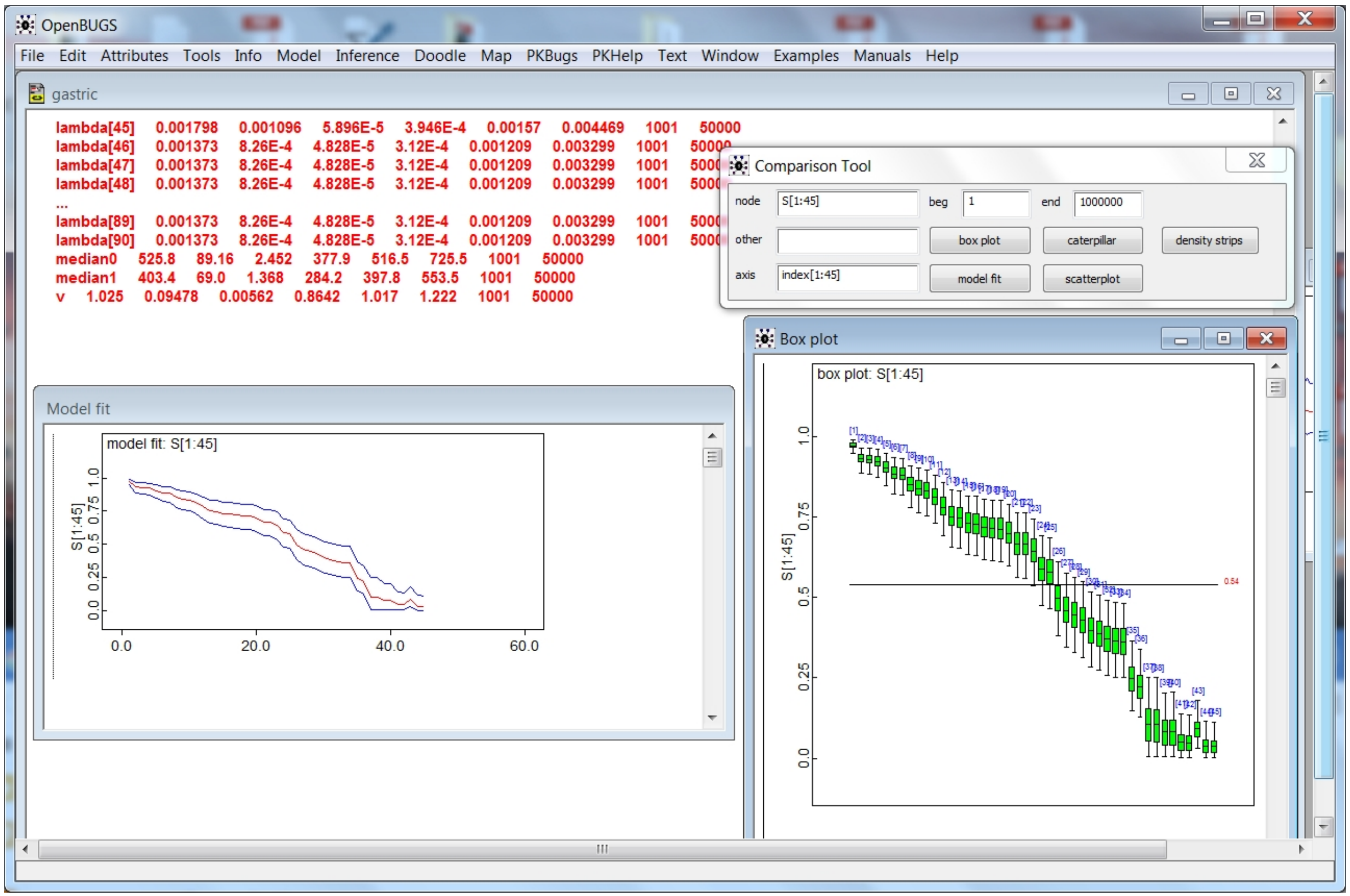
Example 3: (cont.)



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