**Simulation results for discussion with Takeshi 05/16/2019**

**General Comments**

**Problem with:**

* Convergence issues, mainly in case of estimation using the Clayton copula
* Percentage of coverage generally less than 80%
* Estimation with the clayton-copula, by integrating using the Monte-Carlo method with more than 100 replications
* Using 100 replications for the Monte-Carlo integration, we generally faced estimations issues on the standard errors of the parameters.
* The sensitivity to the number of replication for Monte-Carlo integration is not present when data are generated using the joint surrogate model. However, the estimations are not so good

**Less convergence issues in case of:**

* Low individual level association
* Default initial values (different from true simulation values), mainly with less individual level association (theta copula = 1).
* Estimation using Gumbel-Hougaard copula model
* Simulation with joint surrogate model, but less convergence properties for the parameters (bias and percentage of coverage)
* Monte-Carlo integration with 100 replications

**Questions / Discussions**

1. Did you experience this kind of issues in your previous simulation?
2. Is the generation algorithm correct?
3. If so,
   1. Can we use another parametrization of the Clayton copula function for data generation?
   2. Do you have any recommendation for the data generation process in case of bad generation with the proposed algorithm?
   3. Do you have any algorithm to use for data generation using Gumbel copula model?
4. Is there any knew relationship between the Clayton copula and the Gumbel copula? The idea is to be able to predict the Clayton copula parameter based on an estimation of the Gumbel copula parameter. In fact, when data are generated using the Clayton copula and estimated using the Gumbel copula, the true copula parameter is not equivalent to the estimated copula parameter.

For All simulations: nb.simul = 200 int.method = 0 kappa.use = 4 gamma.S = 1.3

Gamma.T = 1.1 rho.S = 0.0025 rho.T = 0.0025

**Description of the empirical parameters, from the data generation:**

Parameters True Mean Median SD

1 MuvS 0 0.009 0.012 0.148

2 sigmaS 0.7 0.690 0.679 0.195

3 MuvT 0 0.004 0.012 0.160

4 sigmaT 0.7 0.702 0.701 0.188

5 SigmaST 0.63 0.626 0.621 0.183

6 Muui 0 -0.041 -0.041 0.281

7 gamma 2.5 2.466 2.437 0.639

8 median.S - 109.465 104.601 26.737

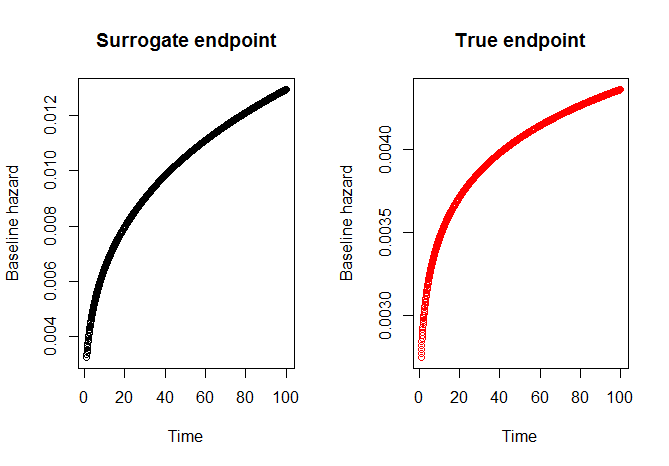
9 median.T - 262.687 252.912 61.809

10 prop.S - 0.666 0.668 0.045

11 propT - 0.558 0.562 0.057

12 prop.trt 0.5 0.500 0.500 0.021

**Baseline hazard functions for the surrogate and the true endpoints. Weibull parametrization:** lambda\_0(t) =rho \* gamma \* time\*\*(gamma -1)



1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 100 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(1)**

The program took 130.81 minutes n.iter = 14

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.055 0.335 0.309 94

3 gamma 2.5 2.675 0.772 0.437 74

4 alpha 1 0.999 0.051 0.041 90

5 sigma.S 0.7 0.613 0.342 0.164 58

6 sigma.T 0.7 0.724 0.424 0.193 62

7 sigma.ST 0.63 0.594 0.345 0.159 61

8 beta.S -1.25 -1.255 0.218 0.146 81

9 beta.T -1.25 -1.252 0.218 0.159 80

10 R2trial 0.81 0.786 0.189 0.079 61

11 K.tau 0.6 0.603 0.026 0.024 94

Rejected datasets : n(%) = 111(56)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 100 true.init.value = 0 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(14)**

The program took 145.11 minutes n.iter = 15

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.066 0.359 0.31 92

3 gamma 2.5 2.55 0.631 0.417 80

4 alpha 1 1.001 0.049 0.04 91

5 sigma.S 0.7 0.567 0.285 0.158 65

6 sigma.T 0.7 0.695 0.38 0.186 65

7 sigma.ST 0.63 0.55 0.301 0.154 61

8 beta.S -1.25 -1.137 0.237 0.139 72

9 beta.T -1.25 -1.125 0.231 0.147 75

10 R2trial 0.81 0.768 0.217 0.078 61

11 K.tau 0.6 0.603 0.028 0.024 88

Rejected datasets : n(%) = 112(56)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 0 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(15)**

The program took 149.39 minutes n.iter = 14

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 2.976 0.271 0.301 100

3 gamma 2.5 1.568 0.31 0.234 20

4 alpha 1 1.013 0.043 0.04 92

5 sigma.S 0.7 0.705 0.423 0.205 65

6 sigma.T 0.7 0.945 0.583 0.277 72

7 sigma.ST 0.63 0.716 0.421 0.207 70

8 beta.S -1.25 -1.211 0.317 0.151 60

9 beta.T -1.25 -1.216 0.286 0.175 72

10 R2trial 0.81 0.79 0.132 0.083 82

11 K.tau 0.6 0.597 0.022 0.024 100

Rejected datasets : n(%) = 160(80)

1. **Nb.subjects = 1000 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(13)**

The program took 77.53 minutes n.iter = NA

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 NaN <NA> NaN <NA>

3 gamma 2.5 NaN <NA> NaN <NA>

4 alpha 1 NaN <NA> NaN <NA>

5 sigma.S 0.7 NaN <NA> NaN <NA>

6 sigma.T 0.7 NaN <NA> NaN <NA>

7 sigma.ST 0.63 NaN <NA> NaN <NA>

8 beta.S -1.25 NaN <NA> NaN <NA>

9 beta.T -1.25 NaN <NA> NaN <NA>

10 R2trial 0.81 NaN <NA> NaN <NA>

11 K.tau 0.6 NaN <NA> NaN <NA>

Rejected datasets : n(%) = 200(100)

1. **Nb.subjects = 1000 nb.trials = 30 nb.mc = 100 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(2)**

The program took 191.69 minutes n.iter = 14

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.059 0.218 0.239 96

3 gamma 2.5 2.7 0.688 0.341 60

4 alpha 1 1.002 0.032 0.031 94

5 sigma.S 0.7 0.673 0.269 0.136 67

6 sigma.T 0.7 0.85 0.391 0.165 59

7 sigma.ST 0.63 0.669 0.294 0.134 55

8 beta.S -1.25 -1.262 0.247 0.115 72

9 beta.T -1.25 -1.306 0.256 0.126 69

10 R2trial 0.81 0.789 0.137 0.058 58

11 K.tau 0.6 0.604 0.017 0.019 96

Rejected datasets : n(%) = 117(58)

1. **Nb.subjects = 1000 nb.trials = 30 nb.mc = 100 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(2)** nb.simul = 500

The program took 457.2 minutes n.iter = 14

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.041 0.257 0.236 93

3 gamma 2.5 2.71 0.707 0.335 60

4 alpha 1 1.004 0.034 0.031 92

5 sigma.S 0.7 0.665 0.277 0.133 62

6 sigma.T 0.7 0.782 0.385 0.155 55

7 sigma.ST 0.63 0.63 0.286 0.129 59

8 beta.S -1.25 -1.246 0.238 0.111 69

9 beta.T -1.25 -1.255 0.255 0.121 65

10 R2trial 0.81 0.781 0.152 0.06 59

11 K.tau 0.6 0.602 0.02 0.019 92

Rejected datasets : n(%) = 280(56)

1. **Nb.subjects = 1000 nb.trials = 50 nb.mc = 100 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(2)** nb.simul = 500

The program took 500.55 minutes n.iter = 13

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.043 0.25 0.248 95

3 gamma 2.5 2.78 0.678 0.402 74

4 alpha 1 1.003 0.035 0.032 93

5 sigma.S 0.7 0.612 0.239 0.154 63

6 sigma.T 0.7 0.696 0.323 0.168 66

7 sigma.ST 0.63 0.576 0.241 0.146 66

8 beta.S -1.25 -1.18 0.183 0.125 75

9 beta.T -1.25 -1.205 0.194 0.124 78

10 R2trial 0.81 0.797 0.123 0.067 71

11 K.tau 0.6 0.602 0.02 0.02 94

Rejected datasets : n(%) = 260(52)

1. **Nb.subjects = 600 nb.trials = 10 nb.mc = 100 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(3)**

The program took 109.36 minutes n.iter = 15

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.057 0.354 0.304 92

3 gamma 2.5 2.555 0.788 0.344 63

4 alpha 1 0.998 0.062 0.045 89

5 sigma.S 0.7 0.722 0.39 0.201 73

6 sigma.T 0.7 0.851 0.504 0.257 77

7 sigma.ST 0.63 0.671 0.367 0.195 73

8 beta.S -1.25 -1.3 0.334 0.134 56

9 beta.T -1.25 -1.308 0.324 0.158 65

10 R2trial 0.81 0.772 0.212 0.085 55

11 K.tau 0.6 0.603 0.027 0.024 89

Rejected datasets : n(%) = 129(64)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(12)**

The program took 56.44 minutes n.iter = 19

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.283 0.417 0.33 100

3 gamma 2.5 1.399 0.052 0.201 <NA>

4 alpha 1 0.978 0.009 0.038 100

5 sigma.S 0.7 0.542 0.04 0.237 100

6 sigma.T 0.7 0.549 0.141 0.205 100

7 sigma.ST 0.63 0.45 0.066 0.202 100

8 beta.S -1.25 -1.276 0.042 0.148 100

9 beta.T -1.25 -1.277 0.074 0.159 100

10 R2trial 0.81 0.687 0.028 0.119 100

11 K.tau 0.6 0.62 0.03 0.024 100

Rejected datasets : n(%) = 198(99)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 300 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.81 n.knots = 6(4)**

The program took 93.66 minutes n.iter = 12

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 2.986 0.224 0.305 100

3 gamma 2.5 1.471 0.152 0.244 <NA>

4 alpha 1 1.003 0.046 0.038 100

5 sigma.S 0.7 0.734 0.308 0.206 80

6 sigma.T 0.7 0.981 0.343 0.283 100

7 sigma.ST 0.63 0.763 0.241 0.214 100

8 beta.S -1.25 -1.488 0.137 0.165 80

9 beta.T -1.25 -1.481 0.142 0.193 100

10 R2trial 0.81 0.835 0.109 0.064 80

11 K.tau 0.6 0.598 0.018 0.024 100

Rejected datasets : n(%) = 195(98)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 0 k.tau = 0.33 estim = clayton generation = clayton R2 = 0.81 n.knots = 6 (9)**

The program took 120.04 minutes n.iter = 13

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 1 0.999 0.157 0.154 92

3 gamma 2.5 3.245 1.041 0.561 68

4 alpha 1 1.001 0.071 0.063 92

5 sigma.S 0.7 0.597 0.339 0.181 59

6 sigma.T 0.7 0.679 0.406 0.219 69

7 sigma.ST 0.63 0.567 0.319 0.167 63

8 beta.S -1.25 -1.179 0.249 0.163 78

9 beta.T -1.25 -1.172 0.251 0.175 78

10 R2trial 0.81 0.828 0.152 0.105 72

11 K.tau 0.333 0.331 0.035 0.034 93

Rejected datasets : n(%) = 46(23)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 0 k.tau = 0.33 estim = clayton generation = clayton R2 = 0.81 n.knots = 4 (cartage)**

The program took 276.83 minutes n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 1 0.99807 0.17011 0.15567 92

3 gamma 2.5 1.98431 0.45715 0.35331 59

4 alpha 1 1.00549 0.07348 0.06301 89

5 sigma.S 0.7 0.63292 0.32364 0.23428 72

6 sigma.T 0.7 0.71788 0.40965 0.29143 74

7 sigma.ST 0.63 0.59373 0.3177 0.21996 70

8 beta.S -1.25 -1.23011 0.25104 0.17488 80

9 beta.T -1.25 -1.22685 0.26693 0.18955 81

10 R2trial 0.81 0.80177 0.19244 0.1281 76

11 K.tau 0.33333 0.33079 0.03762 0.03463 93

Rejected datasets : n(%) = 77(38)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 100 true.init.value = 1 k.tau = 0.33 estim = clayton generation = clayton R2 = 0.81 n.knots = 4 (cartage)**

n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 1 1.00535 0.18845 0.15481 91

3 gamma 2.5 2.00578 0.5375 0.3799 61

4 alpha 1 1.01218 0.08036 0.06597 91

5 sigma.S 0.7 0.66034 0.35805 0.21185 70

6 sigma.T 0.7 0.75297 0.44124 0.25857 71

7 sigma.ST 0.63 0.6248 0.35642 0.1964 67

8 beta.S -1.25 -1.25545 0.21469 0.1696 83

9 beta.T -1.25 -1.26255 0.24975 0.1862 82

10 R2trial 0.81 0.80446 0.19684 0.12455 76

11 K.tau 0.33333 0.33199 0.04114 0.03424 91

Rejected datasets : n(%) = 134(67)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 300 true.init.value = 1 k.tau = 0.33 estim = clayton generation = clayton R2 = 0.81 n.knots = 6 (cartage)**

The program took 125.76 minutes n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 1 1.00052 0.1623 0.15575 92

3 gamma 2.5 2.06168 0.42439 0.37885 69

4 alpha 1 1.00282 0.0727 0.06479 92

5 sigma.S 0.7 0.61442 0.32171 0.21963 73

6 sigma.T 0.7 0.76204 0.41872 0.27359 79

7 sigma.ST 0.63 0.6126 0.33059 0.20816 73

8 beta.S -1.25 -1.26766 0.22696 0.17055 83

9 beta.T -1.25 -1.26188 0.21807 0.1897 92

10 R2trial 0.81 0.81492 0.16429 0.13137 75

11 K.tau 0.33333 0.33155 0.0358 0.03459 94

Rejected datasets : n(%) = 148(74)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.33 estim = clayton generation = clayton R2 = 0.81 n.knots = 6 (cartage)**

The program took 95.39 minutes n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 1 1.00502 0.1885 0.15476 91

3 gamma 2.5 1.9907 0.55192 0.37762 59

4 alpha 1 1.01236 0.08054 0.066 91

5 sigma.S 0.7 0.65918 0.35938 0.2117 70

6 sigma.T 0.7 0.75282 0.44133 0.25859 71

7 sigma.ST 0.63 0.62282 0.35832 0.19606 67

8 beta.S -1.25 -1.25501 0.21564 0.16946 83

9 beta.T -1.25 -1.26472 0.24626 0.18621 83

10 R2trial 0.81 0.79875 0.20162 0.12467 74

11 K.tau 0.33333 0.33191 0.04115 0.03424 91

Rejected datasets : n(%) = 134(67)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 100 true.init.value = 1 k.tau = 0.60 estim = Gumbel generation = clayton R2 = 0.81 n.knots = 6(5)**

The program took 152.07 minutes n.iter = 12

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 0.956 0.127 0.105 <NA>

3 gamma 2.5 3.502 1.141 0.59 61

4 alpha 1 1.013 0.055 0.049 92

5 sigma.S 0.7 0.613 0.346 0.183 63

6 sigma.T 0.7 0.718 0.431 0.227 68

7 sigma.ST 0.63 0.596 0.359 0.178 61

8 beta.S -1.25 -1.221 0.247 0.162 79

9 beta.T -1.25 -1.233 0.252 0.178 85

10 R2trial 0.81 0.808 0.148 0.103 76

11 K.tau 0.75 0.487 0.033 0.027 <NA>

Rejected datasets : n(%) = 11(6)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 300 true.init.value = 0 k.tau = 0.60 estim = Gumbel generation = clayton R2 = 0.81 n.knots = 6(16)**

The program took 366.27 minutes n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 0.948 0.128 0.104 <NA>

3 gamma 2.5 2.227 0.547 0.397 70

4 alpha 1 1.016 0.058 0.05 90

5 sigma.S 0.7 0.658 0.373 0.219 70

6 sigma.T 0.7 0.762 0.443 0.268 80

7 sigma.ST 0.63 0.63 0.382 0.211 71

8 beta.S -1.25 -1.226 0.22 0.169 81

9 beta.T -1.25 -1.233 0.228 0.187 89

10 R2trial 0.81 0.785 0.167 0.118 81

11 K.tau 0.75 0.484 0.032 0.028 <NA>

Rejected datasets : n(%) = 64(32)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 300 true.init.value = 1 k.tau = 0.60 estim = Gumbel generation = clayton R2 = 0.81 n.knots = 6(10)**

The program took 343.4 minutes n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 0.949 0.121 0.104 <NA>

3 gamma 2.5 2.341 0.557 0.452 80

4 alpha 1 1.016 0.059 0.051 92

5 sigma.S 0.7 0.664 0.334 0.219 78

6 sigma.T 0.7 0.728 0.385 0.256 84

7 sigma.ST 0.63 0.619 0.332 0.207 81

8 beta.S -1.25 -1.25 0.22 0.17 84

9 beta.T -1.25 -1.25 0.211 0.184 91

10 R2trial 0.81 0.787 0.166 0.123 83

11 K.tau 0.75 0.485 0.031 0.028 <NA>

Rejected datasets : n(%) = 114(57)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton generation = joint surrogate R2 = 0.81 n.knots = 6(6)**

The program took 74.81 minutes n.iter = 11

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3.5 1.961 0.353 0.35 4

3 gamma 2.5 1.168 0.539 0.361 20

4 alpha 1 0.904 0.091 0.094 75

5 sigma.S 0.7 0.271 0.24 0.185 32

6 sigma.T 0.7 0.225 0.204 0.139 25

7 sigma.ST 0.63 0.209 0.185 0.137 26

8 beta.S -1.25 -0.75 0.222 0.196 34

9 beta.T -1.25 -0.676 0.173 0.161 8

10 R2trial 0.81 0.767 0.244 0.462 80

11 K.tau 0.595 0.491 0.045 0.045 35

Rejected datasets : n(%) = 21(10)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 300 true.init.value = 1 k.tau = 0.60 estim = clayton generation = joint surrogate R2 = 0.81 n.knots = 6(11)**

The program took 128.77 minutes n.iter = 10

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3.5 1.963 0.357 0.35 3

3 gamma 2.5 1.101 0.446 0.328 12

4 alpha 1 0.905 0.089 0.092 74

5 sigma.S 0.7 0.32 0.266 0.224 46

6 sigma.T 0.7 0.261 0.208 0.167 30

7 sigma.ST 0.63 0.25 0.201 0.169 38

8 beta.S -1.25 -0.763 0.212 0.195 30

9 beta.T -1.25 -0.682 0.167 0.16 8

10 R2trial 0.81 0.836 0.211 0.593 71

11 K.tau 0.595 0.491 0.046 0.045 39

Rejected datasets : n(%) = 21(10)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.36 n.knots = 6(7)**

The program took 126.75 minutes n.iter = 15

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.036 0.338 0.31 93

3 gamma 2.5 2.668 0.643 0.435 78

4 alpha 1 1.003 0.05 0.042 93

5 sigma.S 0.7 0.608 0.362 0.163 53

6 sigma.T 0.7 0.887 0.553 0.207 66

7 sigma.ST 0.42 0.39 0.361 0.13 49

8 beta.S -1.25 -1.22 0.272 0.137 67

9 beta.T -1.25 -1.244 0.272 0.149 71

10 R2trial 0.36 0.357 0.245 0.088 39

11 K.tau 0.6 0.601 0.027 0.024 90

Rejected datasets : n(%) = 106(53)

1. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton generation = clayton R2 = 0.36 n.knots = 4(8)**

The program took 101.15 minutes n.iter = 13

Simulation results

Parameters True value Mean Empirical SE Mean SE CP(%)

2 theta 3 3.06 0.327 0.312 95

3 gamma 2.5 2.801 0.796 0.478 77

4 alpha 1 0.993 0.046 0.04 93

5 sigma.S 0.7 0.553 0.301 0.148 55

6 sigma.T 0.7 0.629 0.323 0.17 65

7 sigma.ST 0.63 0.503 0.276 0.14 61

8 beta.S -1.25 -1.27 0.251 0.145 71

9 beta.T -1.25 -1.268 0.248 0.156 78

10 R2trial 0.81 0.74 0.224 0.088 68

11 K.tau 0.6 0.603 0.026 0.024 93

Rejected datasets : n(%) = 106(53)