**Réunion du 24-03-2019 à 15h00**

**Discussion autour de la programmation et des résultats de simulation pour le modèle joint-frailty copula**

# censure a 349 jours. Description des pamareters empiriques: 300 dataset

lambda.S = 1.3, nu.S = 0.0025,lambda.T = 1.1, nu.T = 0.0025

Parameters True Mean Median SD

1 MuvS 0 0.000 -0.011 0.160

2 sigmaS 0.7 0.673 0.660 0.169

3 MuvT 0 0.001 0.004 0.154

4 sigmaT 0.7 0.691 0.672 0.165

5 SigmaST 0.626 0.547 0.533 0.151

6 Muui 0 0.035 0.038 0.279

7 gamma 2.5 2.464 2.375 0.637

8 median.S - 103.320 98.162 25.664

9 median.T - 248.031 243.286 62.176

10 prop.S - 0.668 0.670 0.046

11 propT - 0.572 0.574 0.057

12 prop.trt 0.5 0.500 0.500 0.020

# ==================5============================================

type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula=3 true.init.val 1 typecopula= 1 numsimul= 5

Simulation and estimation pamareters

nb.subject = 600 nb.trials = 30

nb.simul = 100

int.method = 0

nb.mc = 100

kappa.use = 4

n.knots = 6

n.iter = 14

Simulation results

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

2 theta 3 3.053 0.306 0.308 98

3 gamma 2.5 2.772 0.678 0.492 86

4 alpha 1 0.996 0.052 0.041 90

5 sigma.S 0.7 0.644 0.336 0.163 55

6 sigma.T 0.7 0.751 0.399 0.192 62

7 sigma.ST 0.63 0.621 0.332 0.16 55

8 beta.S -1.25 -1.259 0.212 0.148 79

9 beta.T -1.25 -1.257 0.196 0.162 81

10 R2trial 0.81 0.802 0.142 0.08 69

11 K.tau 0.75 0.752 0.019 0.005 38

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

The program took 62.44 minutes

Commentaires :

- problème estimation des des ecart-types des parametres de variances des effets aléatoire au niveau essai en interaction avec le traitement, et donc du R2

- problème de convergence

- problème tau de couverture Ktau

+ Moins de problème de biais----------------

Simulation and estimation pamareters

nb.subject = 600 nb.trials = 30

nb.simul = 10

int.method = 0

nb.mc = 100

kappa.use = 4

n.knots = 6

n.iter = 17

Simulation results

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

2 theta 3 3.151 0.267 0.314 100

3 gamma 2.5 2.537 0.555 0.542 100

4 alpha 1 1.022 0.041 0.041 100

5 sigma.S 0.7 0.677 0.63 0.162 25

6 sigma.T 0.7 0.839 0.586 0.212 50

7 sigma.ST 0.63 0.662 0.568 0.164 25

8 beta.S -1.25 -1.244 0.196 0.131 75

9 beta.T -1.25 -1.232 0.155 0.145 100

10 R2trial 0.81 0.755 0.143 0.087 75

11 K.tau 0.75 0.758 0.015 0.004 50

Rejected datasets : n(%) = 6(60)

The program took 4.7 minutes

#==================6 ou 11=======================================

type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula= 3 true.init.val 0 typecopula= 1 numsimul= 6 ou numsimul= 11

Simulation and estimation pamareters

nb.subject = 600 nb.trials = 30

nb.simul = 200

int.method = 0

nb.mc = 100

kappa.use = 4

n.knots = 6

n.iter = 15

Simulation results

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

2 theta 3 3.056 0.354 0.309 93

3 gamma 2.5 2.52 0.631 0.412 79

4 alpha 1 1 0.049 0.04 92

5 sigma.S 0.7 0.575 0.285 0.161 66

6 sigma.T 0.7 0.716 0.386 0.192 65

7 sigma.ST 0.63 0.565 0.303 0.158 62

8 beta.S -1.25 -1.135 0.237 0.14 71

9 beta.T -1.25 -1.128 0.237 0.149 73

10 R2trial 0.81 0.783 0.198 0.076 63

11 K.tau 0.75 0.752 0.022 0.005 36

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

The program took 146.58 minutes

-Leger problemes de biais comparé à l’initialisation avec les vrais paramètres.

-Temps de calcul plus longs

Simulation and estimation pamareters

nb.subject = 600

nb.trials = 30

nb.simul = 100

int.method = 0

nb.mc = 100

kappa.use = 4

n.knots = 6

n.iter = 15

Simulation results

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

2 theta 3 3.041 0.342 0.306 95

3 gamma 2.5 2.565 0.598 0.414 82

4 alpha 1 1.004 0.051 0.041 93

5 sigma.S 0.7 0.618 0.329 0.162 61

6 sigma.T 0.7 0.765 0.498 0.188 61

7 sigma.ST 0.63 0.61 0.376 0.158 52

8 beta.S -1.25 -1.122 0.225 0.138 70

9 beta.T -1.25 -1.118 0.225 0.146 75

10 R2trial 0.81 0.792 0.189 0.07 64

11 K.tau 0.75 0.751 0.022 0.005 48

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

The program took 71.88 minutes

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Simulation and estimation pamareters

nb.subject = 600

nb.trials = 30

nb.simul = 10

int.method = 0

nb.mc = 100

kappa.use = 4

n.knots = 6

n.iter = 15

Simulation results

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

2 theta 3 3.017 0.217 0.299 100

3 gamma 2.5 2.601 0.426 0.417 100

4 alpha 1 1.027 0.046 0.038 100

5 sigma.S 0.7 0.482 0.094 0.131 60

6 sigma.T 0.7 0.73 0.213 0.184 100

7 sigma.ST 0.63 0.492 0.109 0.139 60

8 beta.S -1.25 -1.108 0.237 0.125 40

9 beta.T -1.25 -1.127 0.216 0.135 80

10 R2trial 0.81 0.721 0.213 0.073 40

11 K.tau 0.75 0.75 0.013 0.004 60

Rejected datasets : n(%) = 5(50)

The program took 5.47 minutes

# ==================7============================================

type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula= 3 true.init.val 1 typecopula= 2 numsimul= 7

Simulation and estimation pamareters

nb.subject = 600 nb.trials = 30

nb.simul = 100

int.method = 0

nb.mc = 200

kappa.use = 4

n.knots = 6

n.iter = 12

Simulation results

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

2 theta 3 0.92 0.117 0.102 <NA>

3 gamma 2.5 2.373 0.65 0.426 76

4 alpha 1 1.015 0.055 0.051 94

5 sigma.S 0.7 0.674 0.31 0.218 81

6 sigma.T 0.7 0.753 0.358 0.263 81

7 sigma.ST 0.63 0.632 0.298 0.209 85

8 beta.S -1.25 -1.265 0.256 0.171 83

9 beta.T -1.25 -1.275 0.213 0.19 98

10 R2trial 0.81 0.796 0.134 0.12 85

11 K.tau 0.6 0.314 0.027 0.024 <NA>

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

The program took 111.94 minutes

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Simulation and estimation pamareters

nb.subject = 600 nb.trials = 30

nb.simul = 10

int.method = 0

nb.mc = 200

kappa.use = 4

n.knots = 6

n.iter = 9

Simulation results

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

2 theta 3 0.883 0.052 0.098 <NA>

3 gamma 2.5 2.479 0.427 0.452 75

4 alpha 1 1.014 0.049 0.051 100

5 sigma.S 0.7 0.533 0.126 0.191 75

6 sigma.T 0.7 0.736 0.197 0.267 100

7 sigma.ST 0.63 0.543 0.181 0.194 75

8 beta.S -1.25 -1.146 0.187 0.161 100

9 beta.T -1.25 -1.218 0.15 0.185 100

10 R2trial 0.81 0.744 0.208 0.101 75

11 K.tau 0.6 0.306 0.012 0.024 <NA>

Rejected datasets : n(%) = 6(60)

The program took 8.42 minutes

# ==================8============================================

type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula= 3 true.init.val 0 typecopula= 2 numsimul= 8

Simulation and estimation pamareters

nb.subject = 600

nb.trials = 30

nb.simul = 100

int.method = 0

nb.mc = 300

kappa.use = 4

n.knots = 8

n.iter = 13

Simulation results

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

2 theta 3 0.952 0.137 0.106 <NA>

3 gamma 2.5 2.34 0.492 0.407 86

4 alpha 1 1.016 0.051 0.05 92

5 sigma.S 0.7 0.614 0.413 0.206 69

6 sigma.T 0.7 0.721 0.609 0.249 67

7 sigma.ST 0.63 0.592 0.486 0.199 69

8 beta.S -1.25 -1.175 0.22 0.163 80

9 beta.T -1.25 -1.175 0.198 0.178 90

10 R2trial 0.81 0.774 0.169 0.133 82

11 K.tau 0.6 0.321 0.031 0.024 <NA>

Rejected datasets : n(%) = 49(49)

The program took 208.26 minutes

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Simulation and estimation pamareters

nb.subject = 600

nb.trials = 30

nb.simul = 10

int.method = 0

nb.mc = 200

kappa.use = 4

n.knots = 6

n.iter = 12

Simulation results

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

2 theta 3 1.041 <NA> 0.112 <NA>

3 gamma 2.5 1.988 <NA> 0.255 <NA>

4 alpha 1 0.978 <NA> 0.042 100

5 sigma.S 0.7 0.535 <NA> 0.212 100

6 sigma.T 0.7 0.862 <NA> 0.375 100

7 sigma.ST 0.63 0.571 <NA> 0.249 100

8 beta.S -1.25 -1.168 <NA> 0.144 100

9 beta.T -1.25 -1.141 <NA> 0.178 100

10 R2trial 0.81 0.705 <NA> 0.112 100

11 K.tau 0.6 0.342 <NA> 0.024 <NA>

Rejected datasets : n(%) = 9(90)

The program took 10.35 minutes

# ==================10===========================================

# censure a 5 ans. Description des pamareters empiriques: 300 dataset

lambda.S = 3.3, nu.S = 3.25,lambda.T = 0.8, nu.T = 0.45

Parameters True Mean Median SD

1 MuvS 0 0.000 -0.011 0.160

2 sigmaS 0.7 0.673 0.660 0.169

3 MuvT 0 0.001 0.004 0.154

4 sigmaT 0.7 0.691 0.672 0.165

5 SigmaST 0.626 0.547 0.533 0.151

6 Muui 0 0.035 0.038 0.279

7 gamma 2.5 2.464 2.375 0.637

8 median.S - 0.694 0.688 0.072

9 median.T - 3.037 2.886 1.068

10 prop.S - 0.746 0.743 0.045

11 propT - 0.580 0.582 0.057

12 prop.trt 0.5 0.500 0.500 0.020

type.joint.estim 3 type.joint.simul= 3 time.cens 5 theta.copula 3

true.init.val 1 typecopula= 2 numsimul= 10

Simulation and estimation pamareters

nb.subject = 600

nb.trials = 30

nb.simul = 50

int.method = 1

nb.gh = 9

nb.gh2 = 12

kappa.use = 4

n.knots = 8

n.iter = 17

Simulation results

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

2 theta 3 1.303 0.2 0.169 <NA>

3 gamma 2.5 1.679 0.566 0.467 33

4 alpha 1 1.13 0.111 0.062 40

5 sigma.S 0.7 0.556 0.228 0.204 67

6 sigma.T 0.7 0.685 0.315 0.28 80

7 sigma.ST 0.63 0.532 0.255 0.215 80

8 beta.S -1.25 -1.189 0.179 0.161 93

9 beta.T -1.25 -1.198 0.164 0.186 93

10 R2trial 0.81 0.741 0.151 0.149 87

11 K.tau 0.6 0.392 0.037 0.031 <NA>

Rejected datasets : n(%) = 35(70)

The program took 412.99 minutes

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Simulation and estimation pamareters

nb.subject = 600

nb.trials = 30

nb.simul = 1

int.method = 1

nb.gh = 9

nb.gh2 = 12

kappa.use = 4

n.knots = 8

n.iter = 18

Simulation results

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

2 theta 3 1.313 <NA> 0.16 <NA>

3 gamma 2.5 1.481 <NA> 0.439 <NA>

4 alpha 1 1.034 <NA> 0.056 100

5 sigma.S 0.7 0.426 <NA> 0.179 100

6 sigma.T 0.7 0.577 <NA> 0.248 100

7 sigma.ST 0.63 0.432 <NA> 0.191 100

8 beta.S -1.25 -1.378 <NA> 0.161 100

9 beta.T -1.25 -1.376 <NA> 0.185 100

10 R2trial 0.81 0.758 <NA> 0.14 100

11 K.tau 0.6 0.396 <NA> 0.029 <NA>

Rejected datasets : n(%) = 0(0)

The program took 10.12 minutes

Commentaires :

1. Cas copule de Clayton

* Problèmes d’estimation des écarts-type des paramètres de variances des effets aléatoires au niveau essai en interaction avec le traitement lorsque l’on estime à l’aide des copules de Clayton, comparer à l’estimation en considérant les copules de Gumbel
* Toutefois, ceci peut être résolu en augmentant je l’espère le nombre de simulation pour l’intégration par Monte-Carlo.
* Sur 10 jeux de données, réels problèmes de convergence lorsque l’on augmente le nombre de simulation pour le MC (100 à 200 ou 300) ;
* idem lorsque l’on considère plus de 5 points de quadrature pour une intégration par la quadrature de gauss-Hermite, pseudo-adaptative ou classique
* problème d’estimation des écart-types du taux de Kendal, pourtant l’on a une bonne estimation du paramètre de copule
* Réel problème de convergence avec plus de 50% des cas de non convergence
* En jouant sur les paramètres de la Weibull, ainsi que sur la censure, on parvient à améliorer les soucis de convergence, **mais comment choisir les bons paramètres** ?

+ Globalement l’on a moins de problème de biais sur les paramètres du model

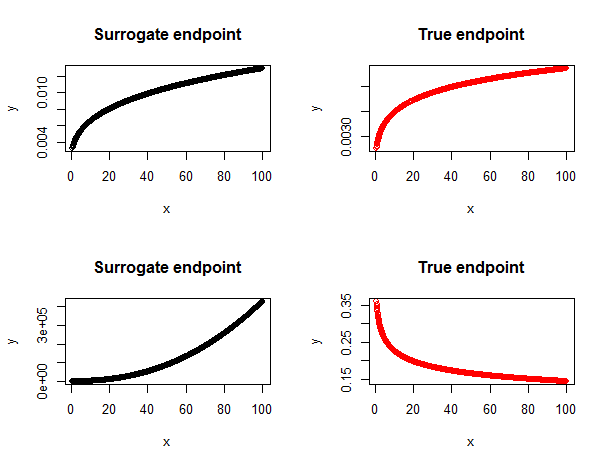
+ En considérant l’initialisation des paramètres avec ou pas les paramètres de simulation, l’on parvient à tomber sur des résultats comparables, même si l’initialisation à partir des valeurs par défaut demande légèrement plus de temps de calcul.

1. Cas Copule de Gumbel

* Meilleure estimation des écart-types des paramètres du modèle avec de meilleurs taux de couverture
* Moins de problèmes de convergence comparés au cas Copule de Clayton, amis proportion de rejet reste élevée
* Temps de calcul un peu plus élevés
* Problème de biais sur le paramètre de copule et par conséquent sur le taux de Kendall, bien qu’on a l’impression que les écart-type sont assez bien estimés.
* Les mêmes observations sont faites lorsque l’on estime le modèle en approchant les intégrales pas la quadrature de Gauss-Hermite pseudo-adaptative. Toutefois, dans ce dernier cas, les temps de calcul deviennent très longs.

1. Globalement

* Lorsque les données ont été générées à partir du modèle **joint surrogate**, sur 10 jeux de données, **il n’y a pas eu de problème de convergence**, toutefois, les estimations étaient moins bonnes que lorsque la génération est faite par le modèle de copule.



Resultats du 30/04/2019

adaptatif 0 type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula 3 true.init.val 1 typecopula= 1 numsimul= 38

The program took 500.55 minutes

Simulation and estimation pamareters

nb.subject = 1000 nb.trials = 50 nb.simul = 500 int.method = 0

nb.mc = 100 kappa.use = 4 n.knots = 6 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)

adaptatif 0 type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula 3 true.init.val 1 typecopula= 1 numsimul= 13

The program took 457.2 minutes

Simulation and estimation pamareters

nb.subject = 1000 nb.trials = 30 nb.simul = 500 int.method = 0

nb.mc = 100 kappa.use = 4 n.knots = 6 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)

adaptatif 0 type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula 3 true.init.val 1 typecopula= 1 numsimul= 31

The program took 754.16 minutes

Simulation and estimation pamareters

nb.subject = 1000 nb.trials = 10 nb.simul = 500 int.method = 0 nb.mc = 100

kappa.use = 4 n.knots = 6 n.iter = 16

Simulation results

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

2 theta 3 3.156 0.641 0.639 94

3 gamma 2.5 1.574 1.163 0.53 48

4 alpha 1 1.008 0.25 13.618 96

5 sigma.S 0.7 0.549 0.58 0.349 55

6 sigma.T 0.7 0.848 1.6 1.029 71

7 sigma.ST 0.63 0.48 0.579 0.394 61

8 beta.S -1.25 -1.452 0.432 0.268 73

9 beta.T -1.25 -1.45 0.675 0.469 86

10 R2trial 0.81 0.787 0.289 543.556 65

11 K.tau 0.6 0.606 0.047 0.047 94

Rejected datasets : n(%) = 341(68)

10 simul : je joue sur les kappas

adaptatif 0 type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula 3 true.init.val 1 typecopula= 1 numsimul= 38100 ckappa= 0 0

The program took 12.12 minutes

Simulation and estimation pamareters

nb.subject = 1000 nb.trials = 50 nb.simul = 10 int.method = 0 nb.mc = 100

kappa.use = 4 n.knots = 6 n.iter = 12

Simulation results

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

2 theta 3 3.27 0.206 0.255 100

3 gamma 2.5 2.501 0.531 0.34 60

4 alpha 1 0.979 0.031 0.033 80

5 sigma.S 0.7 0.778 0.275 0.165 80

6 sigma.T 0.7 0.782 0.383 0.158 80

7 sigma.ST 0.63 0.69 0.351 0.146 80

8 beta.S -1.25 -1.27 0.172 0.129 60

9 beta.T -1.25 -1.274 0.162 0.124 100

10 R2trial 0.81 0.762 0.131 0.062 60

11 K.tau 0.6 0.62 0.015 0.018 80

Rejected datasets : n(%) = 5(50)

adaptatif 0 type.joint.estim 3 type.joint.simul= 3 time.cens 349 theta.copula 3 true.init.val 1 typecopula= 1 numsimul= 3810 ckappa= 1000 1000

The program took 12.15 minutes

Simulation and estimation pamareters

nb.subject = 1000 nb.trials = 50 nb.simul = 10 int.method = 0 nb.mc = 100

kappa.use = 4 n.knots = 6 n.iter = 12

Simulation results

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

2 theta 3 3.27 0.206 0.255 100

3 gamma 2.5 2.501 0.531 0.34 60

4 alpha 1 0.979 0.031 0.033 80

5 sigma.S 0.7 0.778 0.275 0.165 80

6 sigma.T 0.7 0.782 0.383 0.158 80

7 sigma.ST 0.63 0.69 0.351 0.146 80

8 beta.S -1.25 -1.27 0.172 0.129 60

9 beta.T -1.25 -1.274 0.162 0.124 100

10 R2trial 0.81 0.762 0.131 0.062 60

11 K.tau 0.6 0.62 0.015 0.018 80

Rejected datasets : n(%) = 5(50)

# ========== Test simulation par une exponentielle=========================

lambdas = 1, nus = 1, lambdat = 1, nut = 0.5

adaptatif 0 type.joint.estim 3 type.joint.simul= 3 time.cens 8 theta.copula 3 true.init.val 1 typecopula= 1 numsimul= 38100 ckappa= 0 0

Simulation and estimation pamareters

nb.subject = 1000 nb.trials = 50 nb.simul = 10 int.method = 0 nb.mc = 100

kappa.use = 4 n.knots = 6 n.iter = 12

Simulation results

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

2 theta 3 3.011 0.219 0.212 100

3 gamma 2.5 2.674 1.071 0.397 40

4 alpha 1 0.969 0.041 0.027 60

5 sigma.S 0.7 0.939 0.353 0.198 60

6 sigma.T 0.7 0.839 0.474 0.182 40

7 sigma.ST 0.63 0.835 0.416 0.185 60

8 beta.S -1.25 -1.311 0.305 0.119 80

9 beta.T -1.25 -1.313 0.276 0.111 60

10 R2trial 0.81 0.874 0.085 0.05 40

11 K.tau 0.6 0.6 0.017 0.017 100

Rejected datasets : n(%) = 5(50)

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

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 simulation:**

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

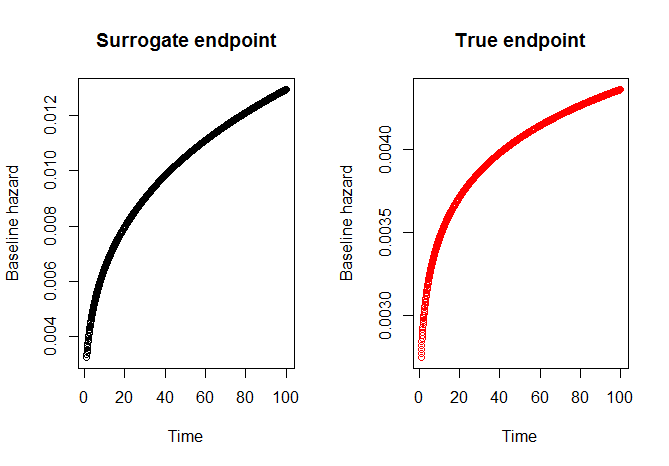
9 median.T - 262.687 252.912 61.809

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

Simulation and estimation pamareters

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 = 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)**
2. **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)

**Comments**

**Problem with :**

* Convergence issues, mainly in case of estiamtion using the Clayton copula
* Percentage of coverage generally less than 80%
* Estimation with the clayton-copula, by integratting using the Monte-Catlo method with more than 100 replications
* The sensitivity to the number of replication for Monte-carlo integration is not present when data are generated using the joint surrogate model.

**Less convergence issues in case of :**

* Low individual level association
* Default initial values (different from true simulation values)
* Estimation using Gumbel-Hougaard copula model
* Simulation with joint surrogate model, but less convergence properties for the parameters (biase 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 fonction for data generation ?
   2. Do you have any recommandation for the data generation process in case of bad generation with the proposed algorithm ?
   3. Do you have the algorithm to use for the 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 claton 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.