**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

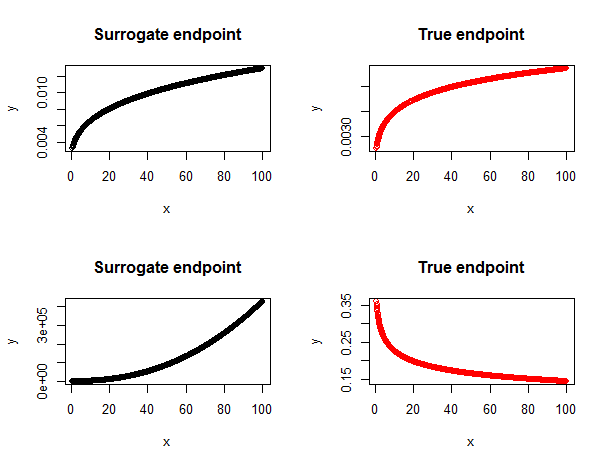
+ En considérant l’initialisation des paramètres avec ou pas les paramètres de simulation, l’on parvient à tomber sur des résultats comparables, même si l’initialisation à partir des valeurs par défaut demande légèrement plus de temps de calcul.

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 05/15/2019**

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

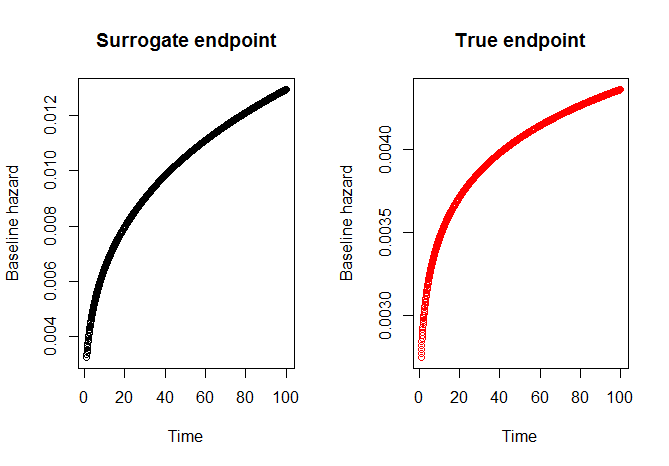
9 median.T - 262.687 252.912 61.809

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 simulation = 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 simulation = clayton R2 = 0.81 n.knots = 6(14)**
2. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 0 k.tau = 0.60 estim = clayton simulation = clayton R2 = 0.81 n.knots = 6(15)**
3. **Nb.subjects = 1000 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 simulation = 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 = 1 k.tau = 0.60 estim = Gumbel simulation = clayton R2 = 0.81 n.knots = 6(10)**
2. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton simulation = 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 simulation = joint surrogate R2 = 0.81 n.knots = 6(11)**
2. **Nb.subjects = 600 nb.trials = 30 nb.mc = 200 true.init.value = 1 k.tau = 0.60 estim = clayton simulation = 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 simulation = 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

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)

Questions