

Supplementary Materials for Bayesian Shrinkage Approach for a Joint Model of Longitudinal and Survival Outcomes Assuming Different Association Structures

Eleni-Rosalina Andrinopoulou, Dimitris Rizopoulos

Department of Biostatistics, Erasmus MC, Rotterdam, The Netherlands

Corresponding author: Eleni-Rosalina Andrinopoulou, Department of Biostatistics, Erasmus

MC, PO Box 2040, 3000 CA Rotterdam, The Netherlands

email: e.andrinopoulou@erasmusmc.nl, Tel: +31/10/7043731, Fax: +31/10/7043014

1 Derivatives and integrals

- Derivatives:

For the serum bilirubin outcome, we approximate the derivative as

$$\begin{aligned} \frac{d\eta_{Bi}(t)}{dt} &= \sum_{v=1}^V \beta_{B(v+1)} dns(t) + \sum_{v=1}^V b_{Bvi} dns(t) \approx \\ & \frac{\sum_{v=1}^V \beta_{B(v+1)} ns(t + \lambda) - \sum_{v=1}^V \beta_{B(v+1)} ns(t - \lambda)}{t + \lambda - (t - \lambda)} + \\ & \frac{\sum_{v=1}^V b_{Bvi} ns(t + \lambda) - \sum_{v=1}^V b_{Bvi} ns(t - \lambda)}{t + \lambda - (t - \lambda)} = \\ & \frac{\sum_{v=1}^V \beta_{B(v+1)} \{ns(t + \lambda) - ns(t - \lambda)\} + \sum_{v=1}^V b_{Bvi} \{ns(t + \lambda) - ns(t - \lambda)\}}{2\lambda}, \end{aligned}$$

where $ns(\cdot)$ denotes the natural cubic spline matrix, $dns(\cdot)$ denotes the derivative of $ns(\cdot)$ and $\lambda = 0.001 * \max(|t|, 1)$. The same formula holds for the serum cholesterol

outcome, $\frac{d\eta_{Ci}(t)}{dt}$. For the dichotomous outcome hepatomegaly we have,

$$\frac{d\text{expit}\{\eta_{Hi}(t)\}}{dt} = \frac{\exp\{\eta_{Hi}(t)\}}{[1 + \exp\{\eta_{Hi}(t)\}]^2} \frac{d\eta_{Hi}(t)}{dt} = \frac{\exp(\beta_{H0} + \beta_{H1}\mathbf{Gender}_i + \beta_{H2}t + b_{H0i} + b_{H1i}t)}{\{1 + \exp(\beta_{H0} + \beta_{H1}\mathbf{Gender}_i + \beta_{H2}t + b_{H0i} + b_{H1i}t)\}^2} (\beta_{H2} + b_{H1i})$$

- Integrals:

The integral for the serum bilirubin outcome is

$$\int_0^t \eta_{Bi}(s) ds = \beta_{B0}t + \beta_{B1}\mathbf{Gender}_i t + \sum_{v=1}^V \beta_{B(v+1)} \text{ins}(t) + b_{B0i}t + \sum_{v=1}^V b_{Bvi} \text{ins}(t),$$

where $\text{ins}(\cdot)$ denotes the integral for $n_s(\cdot)$. Using a 15-point GaussKronrod rule we obtain the following approximation

$$\int_0^t \eta_{Bi}(s) ds \approx \beta_{B0}t + \beta_{B1}\mathbf{Gender}_i t + \sum_{v=1}^V \beta_{B(v+1)} \sum_{a=1}^{15} w_a n_s(st) + b_{B0i}t + \sum_{v=1}^V b_{Bvi} \sum_{a=1}^{15} w_a n_s(st),$$

where $st = [\{ \min(t, \rho_p) - \min(T_i, \rho_{p-1}) \} s_a + \min(t, \rho_p) + \min(t, \rho_{p-1})] / 2$, $\rho_1 \dots \rho_P$ denotes a split of the time scale and w_a, s_a denote prespecified weights and abscissas, respectively. The same formula holds for the serum cholesterol outcome, $\int_0^t \eta_{Ci}(s) ds$. For the dichotomous outcome hepatomegaly we have,

$$\int_0^t \eta_{Hi}(s) ds = \beta_{H0}t + \beta_{H1}\mathbf{Gender}_i t + \beta_{H2} \frac{t^2}{2} + b_{H0i}t + b_{H1i} \frac{t^2}{2}.$$

2 Results

Table 1: Results of proposed joint model assuming Bayesian lasso

	Mean	SE	2.5%	97.5%
<i>Serum bilirubin</i>				
$Intercept_B$	0.65	0.14	0.37	0.92
$\beta_B^{ns(year)1}$	0.99	0.15	0.69	1.26
$\beta_B^{ns(year)2}$	1.54	0.17	1.22	1.85
$\beta_B^{ns(year)3}$	1.46	0.24	1.00	1.90
β_B^{Gender}	-0.12	0.15	-0.40	0.18
<i>Serum cholesterol</i>				
$Intercept_C$	5.70	0.06	5.59	5.82
$\beta_C^{ns(year)1}$	-0.22	0.06	-0.34	-0.10
$\beta_C^{ns(year)2}$	-0.38	0.08	-0.54	-0.24
$\beta_C^{ns(year)3}$	-0.32	0.11	-0.56	-0.12
β_C^{Gender}	0.10	0.06	-0.02	0.21
<i>Hepatomegaly</i>				
$Intercept_H$	0.35	0.49	-0.57	1.34
β_H^{year}	0.15	0.08	0.002	0.31
β_C^{Gender}	-0.23	0.50	-1.24	0.75
<i>Survival</i>				
γ_{Age}	0.04	0.01	0.02	0.06
γ_{Gender}	-0.30	0.26	-0.81	0.22
α_{B1}	1.65	0.31	1.10	2.31
α_{B2}	0.05	0.11	-0.17	0.27
α_{B3}	-0.28	0.26	-0.84	0.16
α_{C1}	-0.29	0.15	-0.58	0.01
α_{C2}	0.10	0.06	-0.004	0.22
α_{C3}	0.11	0.42	-0.69	1.07
α_{H1}	0.10	0.15	-0.19	0.42
α_{H2}	-0.22	0.12	-0.48	-0.01

Table 2: Results of proposed joint model assuming Bayesian ridge

	Mean	SE	2.5%	97.5%
<i>Serum bilirubin</i>				
$Intercept_B$	0.60	0.16	0.29	0.90
$\beta_B^{ns(year)1}$	0.95	0.14	0.69	1.23
$\beta_B^{ns(year)2}$	1.56	0.20	1.18	1.93
$\beta_B^{ns(year)3}$	1.51	0.25	1.02	2.00
β_B^{Gender}	-0.08	0.16	-0.39	0.20
<i>Serum cholesterol</i>				
$Intercept_C$	5.70	0.06	5.58	5.83
$\beta_C^{ns(year)1}$	-0.21	0.06	-0.34	-0.10
$\beta_C^{ns(year)2}$	-0.37	0.08	-0.52	-0.22
$\beta_C^{ns(year)3}$	-0.31	0.11	-0.53	-0.10
β_C^{Gender}	0.10	0.06	-0.02	0.22
<i>Hepatomegaly</i>				
$Intercept_H$	0.31	0.48	-0.62	1.28
β_H^{year}	0.14	0.09	-0.03	0.30
β_C^{Gender}	-0.22	0.48	-1.21	0.70
<i>Survival</i>				
γ_{Age}	0.04	0.01	0.02	0.05
γ_{Gender}	-0.43	0.28	-0.96	0.11
α_{B1}	1.54	0.26	1.09	2.15
α_{B2}	0.06	0.09	-0.12	0.25
α_{B3}	-0.17	0.22	-0.71	0.13
α_{C1}	-0.19	0.14	-0.49	0.03
α_{C2}	0.09	0.05	-0.003	0.20
α_{C3}	0.02	0.25	-0.49	0.60
α_{H1}	0.07	0.13	-0.15	0.37
α_{H2}	-0.22	0.12	-0.48	0.002

Table 3: Results of proposed joint model assuming Bayesian elastic net

	Mean	SE	2.5%	97.5%
<i>Serum bilirubin</i>				
$Intercept_B$	0.66	0.15	0.38	0.96
$\beta_B^{ns(year)1}$	1.01	0.16	0.73	1.39
$\beta_B^{ns(year)2}$	1.55	0.16	1.26	1.88
$\beta_B^{ns(year)3}$	1.47	0.19	1.08	1.84
β_B^{Gender}	-0.13	0.15	-0.44	0.17
<i>Serum cholesterol</i>				
$Intercept_C$	5.71	0.06	5.60	5.82
$\beta_C^{ns(year)1}$	-0.22	0.07	-0.35	-0.09
$\beta_C^{ns(year)2}$	-0.39	0.08	-0.54	-0.25
$\beta_C^{ns(year)3}$	-0.34	0.11	-0.56	-0.13
β_C^{Gender}	0.10	0.06	-0.02	0.21
<i>Hepatomegaly</i>				
$Intercept_H$	0.39	0.50	-0.54	1.45
β_H^{year}	0.14	0.08	-0.02	0.31
β_C^{Gender}	-0.27	0.53	-1.37	0.69
<i>Survival</i>				
γ_{Age}	0.04	0.01	0.02	0.05
γ_{Gender}	-0.43	0.26	-0.94	0.10
α_{B1}	1.39	0.29	0.84	1.99
α_{B2}	0.11	0.12	-0.10	0.36
α_{B3}	-0.11	0.22	-0.59	0.30
α_{C1}	-0.22	0.14	-0.50	0.05
α_{C2}	0.08	0.06	-0.03	0.19
α_{C3}	0.09	0.36	-0.61	0.92
α_{H1}	0.13	0.15	-0.15	0.45
α_{H2}	-0.25	0.12	-0.51	-0.04

Table 4: Results of proposed joint model assuming Bayesian horseshoe

	Mean	SE	2.5%	97.5%
<i>Serum bilirubin</i>				
$Intercept_B$	0.59	0.15	0.30	0.93
$\beta_B^{ns(year)1}$	0.99	0.13	0.74	1.24
$\beta_B^{ns(year)2}$	1.54	0.21	1.17	2.04
$\beta_B^{ns(year)3}$	1.45	0.26	1.00	2.05
β_B^{Gender}	-0.06	0.16	-0.38	0.24
<i>Serum cholesterol</i>				
$Intercept_C$	5.70	0.06	5.58	5.82
$\beta_C^{ns(year)1}$	-0.21	0.06	-0.33	-0.10
$\beta_C^{ns(year)2}$	-0.41	0.09	-0.67	-0.26
$\beta_C^{ns(year)3}$	-0.38	0.13	-0.74	-0.17
β_C^{Gender}	0.10	0.06	-0.01	0.22
<i>Hepatomegaly</i>				
$Intercept_H$	0.31	0.55	-0.72	1.49
β_H^{year}	0.14	0.08	-0.01	0.31
β_C^{Gender}	-0.18	0.55	-1.32	0.83
<i>Survival</i>				
γ_{Age}	0.04	0.01	0.02	0.06
γ_{Gender}	-0.40	0.26	-0.91	0.13
α_{B1}	1.65	0.31	1.12	2.33
α_{B2}	0.06	0.11	-0.14	0.30
α_{B3}	-0.26	0.27	-0.85	0.13
α_{C1}	-0.24	0.15	-0.53	0.02
α_{C2}	0.09	0.06	-0.01	0.21
α_{C3}	0.07	0.38	-0.72	0.98
α_{H1}	0.07	0.14	-0.20	0.38
α_{H2}	-0.24	0.14	-0.58	-0.01

3 Simulations

Table 5: Simulation Scenarios

Scenario	β	σ_y	$diag\{\sigma_b\}$	γ	α
(7)	GenderMales = 0.77 GenderFemales = 0.51 Time1 = 0.82 Time2 = 1.07 Time3 = 0.76	0.25	0.99 1.3 1.15 0.94	(Intercept) = -3.94 GenderFemales = -0.44	1.1
(8)	GenderMales = 0.77 GenderFemales = 0.51 Time1 = 0.82 Time2 = 1.07 Time3 = 0.76	0.25	0.99 1.3 1.15 0.94	(Intercept) = -3.94 GenderFemales = -0.44	-2.58
(9)	GenderMales = 0.77 GenderFemales = 0.51 Time1 = 0.82 Time2 = 1.07 Time3 = 0.76	0.25	0.99 1.3 1.15 0.94	(Intercept) = -3.94 GenderFemales = -0.44	0.14
(10)	GenderMales = 0.77 GenderFemales = 0.51 Time1 = 0.82 Time2 = 1.07 Time3 = 0.76	0.25	0.99 1.3 1.15 0.94	(Intercept) = -3.94 GenderFemales = -0.44	1.07 -2.21