**Table: A Parameter estimates and standard errors for the separate models of the Pr, Rr, and Wh**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | P-value | <.0001 | <.0001 | <.0001 | | 0.0019 | | <.0001 | <.0001 | | 0.0002 | | <.0001 | <.0001 | <.0001 | 0.0006 | 0.0308 | <.0001 | <.0001 | <.0001 | 0.0002 | 0.0001 |
| **Pulse Rate** | Estimate  (SE) | 1.8902  (0.02265 ) | -0.04484 (0.001815) | 0.000968 (0.000219) | | -0.02184 (0.007002) | | -0.1142  (0.02228) | -0.1341  (0.02140) | | -0.07104  (0.01911) | | 0.001020 (0.000114) | 0.000741  (0.000168) | 0.03382 (0.008587) | 0.02953 (0.008551) | 0.01636  (0.007562) | 0.002022  (0.000159) | 0.3453  (0.04972) | 0.004939  (0.001123) | -0.00159  (0.000427) | 0.000670 (0.000181) |
|  | Effects | Inter() | Ti() | Age() | | Sex() | | I() | II() | | III() | | Sys() | Dias() | I\*Ti() | II\*Ti() | III\*T() | Sigma1() |  |  |  |  |
| NYHAC | | | | |  | NYH\*Ti | | |
|  | P-value | <.0001 | <.0001 | 0.0069 | 0.0017 | | <.0001 | <.0001 | <.0001 | <.0001 | | | 0.0003 | 0.0073 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 |
| **Respiratory rate** | Estimate  (SE) | 1.4401  (0.03207) | -0.1161  (0.007169 ) | 0.000918 (0.000339) | -0.03344  (0.01062 ) | | -0.2038  (0.03356) | -0.2028  (0.03151) | -0.1785  (0.02646) | 0.000921  (0.000123) | | | 0.000647  (0.000179) | 0.03854  (0.01434) | 0.07713  (0.01149 ) | 0.06895  (0.01163 ) | 0.05666  (0.009849 ) | 0.002422  (0.000231) | 0.4217  (0.05425) | 0.01305 (0.002235) | -0.00418 (0.000832) | 0.001745 (0.000351) |
|  | Effects | Inter() | Ti() | Age() | Sex() | | I() | II() | III() | Sys() | | | Dias() | Vhds) | I\*Ti() | II\*Ti() | III\*Ti() | Sigma1() |  |  |  |  |
| NYHAC | | | | |  | | | NYHAC\*Ti | | |  |  |  |  |  |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Weight** | P-value | <.0001 | <.0001 | <.0001 | 0.0004 | 0.7206 | 0.0208 | 0.4478 | <.0001 | 0.0003 | 0.0022 | 0.0231 | 0.0999 | 0.0074 | <.0001 | <.0001 | <.0001 |
| Estimate  (SE) | 1.6873  (0.01726) | -0.00465 (0.001130) | 0.001406  (.000294) | 0.03561  (0.009957) | -0.00322  (0.008995) | -0.02164  (0.009347) | 0.004438 (0.005844) | 0.000191  (0.000034) | 0.000198 (0.000050) | 0.07656  (0.02494) | 0.002734 (0.001202) | 0.001959 (0.00119) | 0.003152 (0.001175) | 0.000329 (0.000036) | 0.6535  (0.03944) | 0.003383 (0.00041) |
| Effects | Inter() | Ti() | Age() | Sex() | I() | II() | III() | Sys() | Dias() | Smok() | Other\*Ti() | Sev.\*Ti() | CHD\*Ti() | Sigma1() |  |  |
| NYHAC | | | DIG HIS\*T | | |

**Table: B Parameter estimates and standard errors for the bivariate models of the Pr, Rr and Wh.**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Joint(Pr andRr) | | Pulse rate(Pr) | | Respiratory rate(Rr) | | | | | | | |
| Effects | | Estimate(SE) | P-value | effects | | | Estimate(SE) | | P-value | | |
| Inter() | | 1.9089( 0.02247) | <.0001 | Inter() | | | 1.4674(0.03046) | | <.0001 | | |
| Time() | | -0.05208(0.005436) | <.0001 | Time() | | | -0.1180(0.007196) | | <.0001 | | |
| Age() | | 0.000997(0.000221) | <.0001 | Age() | | | 0.001157(0.000336) | | 0.0006 | | |
| Sex() | | -0.02185(0.007057) | 0.0020 | Sex() | | | -0.03396(0.01078) | | 0.0017 | | |
| NYHAC | I() | -0.1239(0.02246) | <.0001 | NYHAC | | I() | -0.2351(0.03190) | | <.0001 | | |
| II() | -0.1409(0.02169) | <.0001 | II() | -0.2170(0.03060) | | <.0001 | | |
| III() | -0.08153(0.01887) | <.0001 | III() | -0.1845(0.02629) | | <.0001 | | |
| Sys() | | 0.000981(0.000110) | <.0001 | Sys() | | | 0.000911(0.000120) | | <.0001 | | |
| Dias() | | 0.000693(0.000163) | <.0001 | Dias() | | | 0.000645(0.000175) | | 0.0002 | | |
| NYHAC\*Ti | I\*T() | 0.03838(0.008594) | <.0001 |  | | |  | |  | | |
| II\*T() | 0.03451(0.008733) | <.0001 | NYHAC\*Ti | I\*T( | | | 0.08186(0.01151) | | <.0001 | |
| III\*T() | 0.02232(0.007433) | 0.0027 | II\*T() | | | 0.06576(0.01176) | | <.0001 | |
| Sigma1() | | 0.001911(0.000134) | <.0001 | III\*T() | | | 0.06012(0.009725) | | <.0001 | |
|  | | 0.3179(0.04645) | <.0001 | Sigma1() | | | | 0.002310(0.000200) | | | <.0001 |
|  | | 0.005767(0.001154) | <.0001 |  | | | | 0.4015(0.05129) | | | <.0001 |
|  | | -0.00198(0.000448) | <.0001 |  | | | | 0.01411(0.002278) | | | <.0001 |
|  | | 0.000872(0.000193) | <.0001 |  | | | | -0.00460(0.000850) | | | <.0001 |
|  | |  |  |  | | | | 0.001958(0.000360) | | | <.0001 |
|  | |  |  |
| Common parameters | |  |  |  | | | | 0.006891(0.001264) | | | <.0001 |
|  |  |  | | | | -0.00261(0.000499) | | | <.0001 |
|  |  |  | | | | -0.00237(0.000514) | | | <.0001 |
|  |  |  | | | | 0.001114(0.000210) | | | <.0001 |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Joint(Pr and Wh) | | | | | | | | | | | | | |
| Log of pulse rate | | | | | | |  | **Log of weight** | | | | | |
| Effects | | | Estimate(SE) | | P-value | |  | effects | | | Estimate(SE) | P-value | |
| Inter() | | | 1.8948(0.02259) | | <.0001 | |  | Inter() | | | 1.6789(0.01570) | <.0001 | |
| Time() | | | -0.04553(0.005390) | | <.0001 | |  | Time() | | | -0.00432(0.001127) | 0.0001 | |
| Age() | | | 0.000963(0.000218) | | <.0001 | |  | Age() | | | 0.001532(0.000285) | <.0001 | |
| Sex() | | | -0.02167(0.006980) | | 0.0019 | |  | Sex() | | | 0.03368(0.009926) | 0.0007 | |
| NYHAC | I() | | -0.1187(0.02241) | | <.0001 | |  | Sys() | | | 0.000188(0.000034) | <.0001 | |
| II() | | -0.1365(0.02141) | | <.0001 | |  | Dias() | | | 0.000191(0.000050) | 0.0001 | |
| III() | | -0.07217(0.01900) | | 0.0001 | |  | Smok() | | | 0.07510(0.02464) | 0.0023 | |
| Sys() | | | 0.001007(0.000113) | | <.0001 | |  | Diag\*Ti | | I\*T() | 0.002462(0.001199) | | 0.0403 |
| Dias() | | | 0.000723(0.000166) | | <.0001 | |  | II\*T() | 0.001522(0.001183) | | 0.1983 |
| NYHAC\*Ti NYHAC\*Ti | | I\*T() | 0.03553(0.008611) | | <.0001 | |  | III\*T() | 0.002798(0.001171) | | 0.0170 |
| II\*T() | 0.03055(0.008532) | | 0.0004 | |  | Sigma1() | | | 0.000331(0.000036) | | <.0001 |
| III\*T() | 0.01677(0.007523) | | 0.0259 | |  |  | | | 0.6533(0.03924) | | <.0001 |
| Sigma1() | | | 0.002030(0.000164) | | <.0001 | |  |  | | | 0.003389(0.000409) | | <.0001 |
|  | | | 0.3513(0.05056) | | <.0001 | |  |  | | |  | |  |
|  | | | 0.004952(0.001139) | | <.0001 | |  |  | | |  | |  |
|  | | | -0.00160(0.000434) | | 0.0002 | |  |  | | |  | |  |
|  | | | 0.000668(0.000185) | | 0.0001 | |  |  | | |  | |  |
|  | | | **Common parameters** |  | |  | | |  | | -0.00033(0.000471) | 0.4812 | |
|  | | |  | | 0.000173(0.000198) | 0.3826 | |

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Joint(Rr and Wh) | | | | | | | | |
| Log of respiratory rate | | | | |  | **Log of weight** | | |
| Effects | | | Estimate(SE) | P-value |  | effects | Estimate(SE) | P-value |
| Inter() | | | 1.4424 (0.03154) | <.0001 |  | Inter() | 1.6790 (0.01549) | <.0001 |
| Time() | | | -0.1163 (0.007063) | <.0001 |  | Time() | -0.00208(0.000233) | <.0001 |
| Age() | | | 0.000900 (0.000328) | 0.0062 |  | Age() | 0.001505(0.000281) | <.0001 |
| Sex() | | | -0.03313 (0.01030) | 0.0013 |  | Sex() | 0.03485(0.009763) | 0.0004 |
| NYHAC | | I() | -0.2056 (0.03335) | <.0001 |  | Sys() | 0.000189(0.000034) | <.0001 |
| II() | -0.2059 (0.03096) | <.0001 |  | Dias() | 0.000196(0.000050) | <.0001 |
| III() | -0.1804 (0.02571) | <.0001 |  | Smok() | 0.07155(0.02424) | 0.0032 |
| Sys() | | | 0.000913(0.000121) | <.0001 |  | Sigma1() | 0.000350(0.000040) | <.0001 |
| Dias() | | | 0.000644(0.000177) | 0.0003 |  |  | 0.6728(0.03860) | <.0001 |
| Vhds() | | | 0.03979(0.01444) | 0.0059 |  |  | 0.003277(0.000393) | <.0001 |
|  |  | **Common parameters** |  |
| NYHAC\*Ti | I\*T() | | 0.07791(0.01139) | <.0001 |  |  | -0.00082(0.000646) | 0.2060  0.3180 |
| II\*T() | | 0.06973 (0.01142) | <.0001 |  |
| III\*T() | | 0.05675(0.009663) | <.0001 |  |  | 0.000258(0.000258) |
| Sigma1() | | | 0.002456 (0.000245) | <.0001 |  |
|  | | | 0.4342 (0.05536) | <.0001 |  |
|  | | | 0.01237(0.002149) | <.0001 |  |
|  | | | -0.00397(0.000802) | <.0001 |  |
|  | | | 0.001647(0.000339) | <.0001 |  |

**Table: C Parameter estimates and standard errors for multivariate linear mixed effects model**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Multivariate | | | LogPr | | LogRr | | | | | | | | LogWh | | | | | | |
| Effect | | | Estimate(s.e) | p-value | Effects | | | | Estimate(s.e) | | p-value | | Effects | | | | Estimate(s.e) | | p-value |
| Inter() | | | 1.9094(0.02248) | <.0001 | Inter() | | | | 1.4438(0.03161) | | <.0001 | | Inter() | | | | 1.6785(0.01565) | | <.0001 |
| T() | | | -0.05257(0.005444) | <.0001 | T() | | | | -0.1175(0.007202) | | <.0001 | | T() | | | | -0.00209(0.000234) | | <.0001 |
| Age() | | | 0.000998(0.000221) | <.0001 | Age() | | | | 0.000982(0.000335) | | 0.0033 | | Age() | | | | 0.001515(0.000283) | | <.0001 |
| Sex() | | | -0.02216(0.007066) | 0.0017 | Sex() | | | | -0.03449(0.01056) | | 0.0011 | | Sex() | | | | 0.03430(0.009868) | | 0.0005 |
| NYHAC | I() | | -0.1245(0.02244) | <.0001 | NYHAC | | I() | | -0.2099(0.03350) | | <.0001 | | Sys() | | | | 0.000189(0.000034) | | <.0001 |
| II() | | -0.1430(0.02167) | <.0001 | II() | | -0.2008(0.03134) | | <.0001 | | Dias() | | | | 0.000196(0.000050) | | <.0001 |
| III() | | -0.08198(0.01885) | <.0001 | III() | | -0.1821(0.02606) | | <.0001 | | Smok() | | | | 0.07749(0.02445) | | 0.0015 |
| Sys() | | | 0.000984(0.000110) | <.0001 | Sys() | | | | 0.000906(0.000120) | | <.0001 | | Sigma1() | | | | 0.000352(0.000040) | | <.0001 |
| Dias() | | | 0.000693(0.000163) | <.0001 | Dias() | | | | 0.000659(0.000175) | | 0.0002 | |  | | | | 0.6743(0.03869) | | <.0001 |
| NYHAC\*T | | I\*T() | 0.03897(0.008600) | <.0001 | | Vhds () | | | | 0.03390 (0.01280) | |  | |  | | | | 0.003368(0.000408) | <.0001 |
| II\*T() | 0.03545(0.008736) | <.0001 | |  | | | |  | |  | | Common parameters | | | | | |
| III\*T() | 0.02255(0.007431) | 0.0024 | |  | | I\*T() | | 0.08043 (0.01153) | | <.0001 | | Effects | | Estimate(s.e) | | | P\_value |
| Sigma1() | | | 0.001901(0.000132) | <.0001 | **NYHAC** \*T | | | II\*T() | 0.06630 (0.01173) | | <.0001 | |  | | 0.006873(0.001260) | | | | <.0001 |
|  | | | 0.3135(0.04615) | <.0001 | III\*T() | 0.05916(0.009703) | | <.0001 | |  | | -0.00039(0.000481) | | | | 0.4123 |
|  | | | 0.005817(0.001153) | <.0001 | Sigma1() | | | | 0.002288(0.000194) | | <.0001 | |  | | -0.00263(0.000500) | | | | <.0001 | |
|  | | | -0.00201(0.000450) | <.0001 |  | | | | 0.3956(0.05097) | | <.0001 | |  | | -0.00092(0.000679) | | | | 0.1765 | |
|  | | | 0.000889(0.000195) | <.0001 |  | | | | 0.01402(0.002260) | | <.0001 | |  | | -0.00237(0.000515) | | | | <.0001 | |
|  | | |  |  |  | | | | -0.00464(0.000851) | | <.0001 | |  | | 0.000215(0.000205) | | | | 0.2952 | |
|  | | |  |  |  | | | | 0.001984(0.000361) | | <.0001 | |  | | 0.000336(0.000274) | | | | 0.2195 | |
|  | | | | | | | | | | | | |  | | 0.001120(0.000212) | | | | <.0001 |

*Where, inter=intercept, T=Time, Sys=systolic blood pressure, Dys= diastolic blood pressure and smok=smoking status*

**A**) **B)**

 

**C)** **D)**



**Figure 1: Model checking for log of pulse rate**

**A**) **B)**



**D) C)**



**Figure 2: Model checking for log of respiratory rate**

**A**) **B)**

**** 

**C)**



**Figure 3: Model checking for log of weight**