**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($\hat{α}\_{10}$) | Ti($\hat{α}\_{11}$) | Age($\hat{α}\_{13}$) | Sex($\hat{α}\_{14}$) | I($\hat{α}\_{15}$) | II($\hat{α}\_{16}$) | III($\hat{α}\_{17}$) | Sys($\hat{α}\_{18}$) | Dias($\hat{α}\_{19}$) | I\*Ti($\hat{α}\_{110}$) | II\*Ti($\hat{α}\_{111}$) | III\*T($\hat{α}\_{112}$) | Sigma1($σ\_{1}$) | $$ε\_{1}$$ | $$\hat{σ}^{2}\_{b10}$$ | $$σ\_{b10,b11}$$ | $$\hat{σ}^{2}\_{b11}$$ |
| 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($\hat{α}\_{20}$) | Ti($\hat{α}\_{21}$) | Age($\hat{α}\_{23}$) | Sex($\hat{α}\_{24}$) | I($\hat{α}\_{25}$) | II($\hat{α}\_{26}$) | III($\hat{α}\_{27}$) | Sys($\hat{α}\_{28}$) | Dias($\hat{α}\_{29}$) | Vhds$( \hat{α}\_{210}$) | I\*Ti($\hat{α}\_{211}$) | II\*Ti($\hat{α}\_{212}$) | III\*Ti($\hat{α}\_{213}$) | Sigma1($σ\_{2}$) | $$ε\_{2}$$ | $$\hat{σ}^{2}\_{b20}$$ | $$σ\_{b20,b21}$$ | $$\hat{σ}^{2}\_{b21}$$ |
| 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($\hat{α}\_{30}$) | Ti($\hat{α}\_{31}$) | Age($\hat{α}\_{31}$) | Sex($\hat{α}\_{32}$) | I($\hat{α}\_{33}$) | II($\hat{α}\_{34}$) | III($\hat{α}\_{35}$) | Sys($\hat{α}\_{36}$) | Dias($\hat{α}\_{37}$) | Smok($\hat{α}\_{38}$) | Other\*Ti($\hat{α}\_{39}$) | Sev.\*Ti($\hat{α}\_{310}$) | CHD\*Ti($\hat{α}\_{311}$) | Sigma1($σ\_{3}$) | $$ε\_{3}$$ | $$\hat{σ}^{2}\_{b30}$$ |
| 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($\hat{α}\_{10}$) | 1.9089( 0.02247)  | <.0001 | Inter($\hat{α}\_{20}$) | 1.4674(0.03046)  | <.0001 |
| Time($\hat{α}\_{11}$) | -0.05208(0.005436)  | <.0001 | Time($\hat{α}\_{21}$) | -0.1180(0.007196)  | <.0001 |
| Age($\hat{α}\_{12}$) | 0.000997(0.000221)  | <.0001 | Age($\hat{α}\_{22}$) | 0.001157(0.000336)  | 0.0006 |
| Sex($\hat{α}\_{13}$) | -0.02185(0.007057)  | 0.0020 | Sex($\hat{α}\_{23}$) | -0.03396(0.01078)  | 0.0017 |
| NYHAC | I($\hat{α}\_{14}$) | -0.1239(0.02246)  | <.0001 | NYHAC | I($\hat{α}\_{24}$) | -0.2351(0.03190)  | <.0001 |
| II($\hat{α}\_{15}$) | -0.1409(0.02169)  | <.0001 | II($\hat{α}\_{25}$) | -0.2170(0.03060)  | <.0001 |
| III($\hat{α}\_{16}$) | -0.08153(0.01887)  | <.0001 | III($\hat{α}\_{26}$) | -0.1845(0.02629)  | <.0001 |
| Sys($\hat{α}\_{17}$) | 0.000981(0.000110)  | <.0001 | Sys($\hat{α}\_{27}$) | 0.000911(0.000120)  | <.0001 |
| Dias($\hat{α}\_{18}$) | 0.000693(0.000163)  | <.0001 | Dias($\hat{α}\_{28}$) | 0.000645(0.000175)  | 0.0002 |
| NYHAC\*Ti | I\*T($\hat{α}\_{19}$) | 0.03838(0.008594)  | <.0001 |  |  |  |
| II\*T($\hat{α}\_{110}$) | 0.03451(0.008733)  | <.0001 | NYHAC\*Ti | I\*T($\hat{α}\_{29}$ | 0.08186(0.01151)  | <.0001 |
| III\*T($\hat{α}\_{111}$) | 0.02232(0.007433)  | 0.0027 | II\*T($\hat{α}\_{210}$) | 0.06576(0.01176)  | <.0001 |
| Sigma1($σ\_{1}$) | 0.001911(0.000134)  | <.0001 | III\*T($\hat{α}\_{211}$) | 0.06012(0.009725)  | <.0001 |
| $$ε\_{1}$$ | 0.3179(0.04645)  | <.0001 | Sigma1($σ\_{2}$) | 0.002310(0.000200)  | <.0001 |
| $$\hat{σ}^{2}\_{b10}$$ | 0.005767(0.001154)  | <.0001 | $$ε\_{2}$$ | 0.4015(0.05129)  | <.0001 |
| $$σ\_{b10,b11}$$ | -0.00198(0.000448)  | <.0001 | $$\hat{σ}^{2}\_{b20}$$ | 0.01411(0.002278)  | <.0001 |
| $$\hat{σ}^{2}\_{b11}$$ | 0.000872(0.000193)  | <.0001 | $$σ\_{b20,b21}$$ | -0.00460(0.000850)  | <.0001 |
|  |   |  | $$\hat{σ}^{2}\_{b21}$$ | 0.001958(0.000360)  | <.0001 |
|  |  |  |
| Common parameters | $$σ\_{b10,b20}$$ |  |  | 0.006891(0.001264)  | <.0001 |
| $$σ\_{b10,b21}$$ |  |  | -0.00261(0.000499)  | <.0001 |
| $$σ\_{b20,b11}$$ |  |  | -0.00237(0.000514)  | <.0001 |
| $$ σ\_{b11,b21}$$ |  |  | 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($\hat{α}\_{10}$) | 1.8948(0.02259)  | <.0001 |  | Inter($\hat{α}\_{30}$) | 1.6789(0.01570)  | <.0001 |
| Time($\hat{α}\_{11}$) | -0.04553(0.005390)  | <.0001 |  | Time($\hat{α}\_{31}$) | -0.00432(0.001127)  | 0.0001 |
| Age($\hat{α}\_{12}$) | 0.000963(0.000218)  | <.0001 |  | Age($\hat{α}\_{32}$) | 0.001532(0.000285)  | <.0001 |
| Sex($\hat{α}\_{13}$) | -0.02167(0.006980)  | 0.0019 |  | Sex($\hat{α}\_{33}$) | 0.03368(0.009926)  | 0.0007 |
| NYHAC | I($\hat{α}\_{14}$) | -0.1187(0.02241)  | <.0001 |  | Sys($\hat{α}\_{34}$) | 0.000188(0.000034)  | <.0001 |
| II($\hat{α}\_{15}$) | -0.1365(0.02141)  | <.0001 |  | Dias($\hat{α}\_{35}$) | 0.000191(0.000050)  | 0.0001 |
| III($\hat{α}\_{16}$) | -0.07217(0.01900)  | 0.0001 |  | Smok($\hat{α}\_{36}$) | 0.07510(0.02464)  | 0.0023 |
| Sys($\hat{α}\_{17}$) | 0.001007(0.000113)  | <.0001 |  |  Diag\*Ti | I\*T($\hat{α}\_{37}$) | 0.002462(0.001199)  | 0.0403 |
| Dias($\hat{α}\_{18}$) | 0.000723(0.000166)  | <.0001 |  | II\*T($\hat{α}\_{38}$) | 0.001522(0.001183)  | 0.1983 |
| NYHAC\*Ti NYHAC\*Ti | I\*T($\hat{α}\_{19}$) | 0.03553(0.008611)  | <.0001 |  | III\*T($\hat{α}\_{39}$) | 0.002798(0.001171)  | 0.0170 |
| II\*T($\hat{α}\_{110}$) | 0.03055(0.008532)  | 0.0004 |  | Sigma1($σ\_{3}$) | 0.000331(0.000036)  | <.0001 |
| III\*T($\hat{α}\_{111}$) | 0.01677(0.007523)  | 0.0259 |  | $$ε\_{3}$$ | 0.6533(0.03924)  | <.0001 |
| Sigma1($σ\_{1}$) | 0.002030(0.000164)  | <.0001 |  | $$\hat{σ}^{2}\_{b30}$$ | 0.003389(0.000409)  | <.0001 |
| $$ε\_{1}$$ | 0.3513(0.05056)  | <.0001 |  |  |  |  |
| $$\hat{σ}^{2}\_{b10}$$ | 0.004952(0.001139)  | <.0001 |  |  |  |  |
| $$σ\_{b10,b11}$$ | -0.00160(0.000434)  | 0.0002 |  |  |  |  |
| $$\hat{σ}^{2}\_{b11}$$ | 0.000668(0.000185)  | 0.0001 |  |  |  |  |
|  | **Common parameters** |  | $$σ\_{b10,b30}$$ |  | -0.00033(0.000471)  | 0.4812 |
| $$σ\_{b30,b11}$$ |  | 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($\hat{α}\_{20}$) | 1.4424 (0.03154)  | <.0001 |  | Inter($\hat{α}\_{30}$) | 1.6790 (0.01549)  | <.0001 |
| Time($\hat{α}\_{21}$) | -0.1163 (0.007063)  | <.0001 |  | Time($\hat{α}\_{31}$) | -0.00208(0.000233)  | <.0001 |
| Age($\hat{α}\_{22}$) | 0.000900 (0.000328)  | 0.0062 |  | Age($\hat{α}\_{32}$) | 0.001505(0.000281)  | <.0001 |
| Sex($\hat{α}\_{23}$) | -0.03313 (0.01030)  | 0.0013 |  | Sex($\hat{α}\_{33}$) | 0.03485(0.009763)  | 0.0004 |
| NYHAC | I($\hat{α}\_{24}$) | -0.2056 (0.03335)  | <.0001 |  | Sys($\hat{α}\_{34}$) | 0.000189(0.000034)  | <.0001 |
| II($\hat{α}\_{25}$) | -0.2059 (0.03096)  | <.0001 |  | Dias($\hat{α}\_{35}$) | 0.000196(0.000050)  | <.0001 |
| III($\hat{α}\_{26}$) | -0.1804 (0.02571)  | <.0001 |  | Smok($\hat{α}\_{36}$) | 0.07155(0.02424)  | 0.0032 |
| Sys($\hat{α}\_{27}$) | 0.000913(0.000121)  | <.0001 |  | Sigma1($σ\_{3}$) | 0.000350(0.000040)  | <.0001 |
| Dias($\hat{α}\_{28}$) | 0.000644(0.000177)  | 0.0003 |  | $$ε\_{3}$$ | 0.6728(0.03860)  | <.0001 |
| Vhds($\hat{α}\_{29}$) | 0.03979(0.01444)  | 0.0059 |  | $$\hat{σ}^{2}\_{b30}$$ | 0.003277(0.000393)  | <.0001 |
|  |  | **Common parameters** |  |
| NYHAC\*Ti | I\*T($\hat{α}\_{210}$) | 0.07791(0.01139)  | <.0001 |  | $$σ\_{b20,b30}$$ | -0.00082(0.000646)  | 0.20600.3180 |
| II\*T($\hat{α}\_{211}$) | 0.06973 (0.01142)  | <.0001 |  |
| III\*T($\hat{α}\_{212}$) | 0.05675(0.009663)  | <.0001 |  | $$σ\_{b30,b31}$$ | 0.000258(0.000258) |
| Sigma1($σ\_{2}$) | 0.002456 (0.000245)  | <.0001 |  |
| $$ε\_{2}$$ | 0.4342 (0.05536)  | <.0001 |  |
| $$\hat{σ}^{2}\_{b20}$$ | 0.01237(0.002149)  | <.0001 |  |
| $$σ\_{b20,b21}$$ | -0.00397(0.000802)  | <.0001 |  |
| $$\hat{σ}^{2}\_{b21}$$ | 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($\hat{α}\_{10}$) | 1.9094(0.02248)  | <.0001 | Inter($\hat{α}\_{20}$) | 1.4438(0.03161)  | <.0001 | Inter($\hat{α}\_{30}$) | 1.6785(0.01565)  | <.0001  |
| T($\hat{α}\_{11}$) | -0.05257(0.005444)  | <.0001 | T($\hat{α}\_{21}$) | -0.1175(0.007202)  | <.0001 | T($\hat{α}\_{31}$) | -0.00209(0.000234)  | <.0001 |
| Age($\hat{α}\_{13}$) | 0.000998(0.000221)  | <.0001 | Age($\hat{α}\_{23}$) | 0.000982(0.000335)  | 0.0033 | Age($\hat{α}\_{31}$) | 0.001515(0.000283)  | <.0001 |
| Sex($\hat{α}\_{14}$) | -0.02216(0.007066)  | 0.0017 | Sex($\hat{α}\_{24}$) | -0.03449(0.01056)  | 0.0011 | Sex($\hat{α}\_{32}$) | 0.03430(0.009868)  | 0.0005 |
| NYHAC | I($\hat{α}\_{15}$) | -0.1245(0.02244)  | <.0001 | NYHAC | I($\hat{α}\_{25}$) | -0.2099(0.03350)  | <.0001 | Sys($\hat{α}\_{38}$) | 0.000189(0.000034)  | <.0001 |
| II($\hat{α}\_{16}$) | -0.1430(0.02167)  | <.0001 | II($\hat{α}\_{26}$) | -0.2008(0.03134)  | <.0001 | Dias($\hat{α}\_{37}$) | 0.000196(0.000050)  | <.0001 |
| III($\hat{α}\_{17}$) | -0.08198(0.01885)  | <.0001 | III($\hat{α}\_{27}$) | -0.1821(0.02606)  | <.0001 | Smok($\hat{α}\_{38}$) | 0.07749(0.02445)  | 0.0015 |
| Sys($\hat{α}\_{18}$) | 0.000984(0.000110)  | <.0001 | Sys($\hat{α}\_{28}$) | 0.000906(0.000120)  | <.0001 | Sigma1($σ\_{3}$) | 0.000352(0.000040)  | <.0001 |
| Dias($\hat{α}\_{19}$) | 0.000693(0.000163)  | <.0001 | Dias($\hat{α}\_{29}$) | 0.000659(0.000175)  | 0.0002 | $$ε\_{3}$$ | 0.6743(0.03869)  | <.0001 |
| NYHAC\*T | I\*T($\hat{α}\_{110}$) | 0.03897(0.008600)  | <.0001 | Vhds ($\hat{α}\_{210}$) | 0.03390 (0.01280)  |  | $$\hat{σ}^{2}\_{b30}$$ | 0.003368(0.000408)  | <.0001 |
| II\*T($\hat{α}\_{111}$) | 0.03545(0.008736)  | <.0001 |  |  |  |  Common parameters |
| III\*T($\hat{α}\_{112}$) | 0.02255(0.007431)  | 0.0024 |  | I\*T($\hat{α}\_{211}$) | 0.08043 (0.01153)  | <.0001 | Effects | Estimate(s.e) | P\_value |
| Sigma1($σ\_{1}$) | 0.001901(0.000132)  | <.0001 | **NYHAC** \*T | II\*T($\hat{α}\_{212}$) | 0.06630 (0.01173)  | <.0001 | $$σ\_{b10,b20}$$ | 0.006873(0.001260) | <.0001 |
| $$ε\_{1}$$ | 0.3135(0.04615)  | <.0001 | III\*T($\hat{α}\_{213}$) | 0.05916(0.009703)  | <.0001 | $$σ\_{b10,b30}$$ | -0.00039(0.000481) | 0.4123 |
| $$\hat{σ}^{2}\_{b10}$$ | 0.005817(0.001153)  | <.0001 | Sigma1($σ\_{2}$) | 0.002288(0.000194)  | <.0001 | $$σ\_{b10,b21}$$ | -0.00263(0.000500) | <.0001 |
| $$σ\_{b10,b11}$$ | -0.00201(0.000450)  | <.0001 | $$ε\_{2}$$ | 0.3956(0.05097)  | <.0001 | $$σ\_{b20,b30}$$ | -0.00092(0.000679) | 0.1765 |
| $$\hat{σ}^{2}\_{b11}$$ | 0.000889(0.000195)  | <.0001 | $$\hat{σ}^{2}\_{b20}$$ | 0.01402(0.002260)  | <.0001 | $$σ\_{b20,b11}$$ | -0.00237(0.000515) | <.0001 |
|  |  |  | $$σ\_{b20,b21}$$ | -0.00464(0.000851)  | <.0001 | $$σ\_{b30,b11}$$ | 0.000215(0.000205)  | 0.2952 |
|  |  |  | $$\hat{σ}^{2}\_{b21}$$ | 0.001984(0.000361)  | <.0001 | $$σ\_{b30,b21}$$ | 0.000336(0.000274)  | 0.2195 |
|  | $$σ\_{b11,b21}$$ | 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**