1. **Potential interaction between RSV and seasonal influenza**
2. **Methods:**
3. The population is divided into Susceptible (*S*), Infectious (*I*), Cross-protected (*C*) or Recovered (*R*) for each of RSV and seasonal influenza (INF: IAV/IBV for Flu A /Flu B) virus. Susceptible individuals with no immunity were infected at rates  and , and entered the corresponding *I* compartment. Following the infectious period (with mean duration 1/ ), individuals recover and move to the cross-protected compartment (*C*), where individuals were fully protected against homologous re-infection and had some cross-protection against another virus. Individuals then lost this cross-protection with rate but retain pathogen-specific immunity to move to the *R* compartment. If individuals experience an infection with the second virus, they move to the final model compartment R upon recovery, which corresponds to individuals with type-specific immunity to both viruses. Pathogen-specific immunity also wanes with rate .
4. We hypothesize that infections with another pathogen might be less likely in the *I* and *C* classes, so there is a reduced infection rate from infectious class (1 - (n the proportion of inhibition to be co-infected takes values between 0 (no inhibition of co-infection) to 1 (fully inhibited of co-infection). In the *C* compartment, there is a similar reduced infection rate to the second virus due to cross-protection (1 - , the strength of cross-protection takes a value between 0 (no-cross protection) to 1 (perfect cross-protection).

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| **Hypothesis** | **Model name** | **Parameters** |
| There is no interaction of RSV and seasonal influenza can be observed using an ecological model | Independent model |  |
| RSV and seasonal influenza can either by inhibit of co-infection or gain a short-term cross-immunity to another pathogen after infection | Interaction model |  |

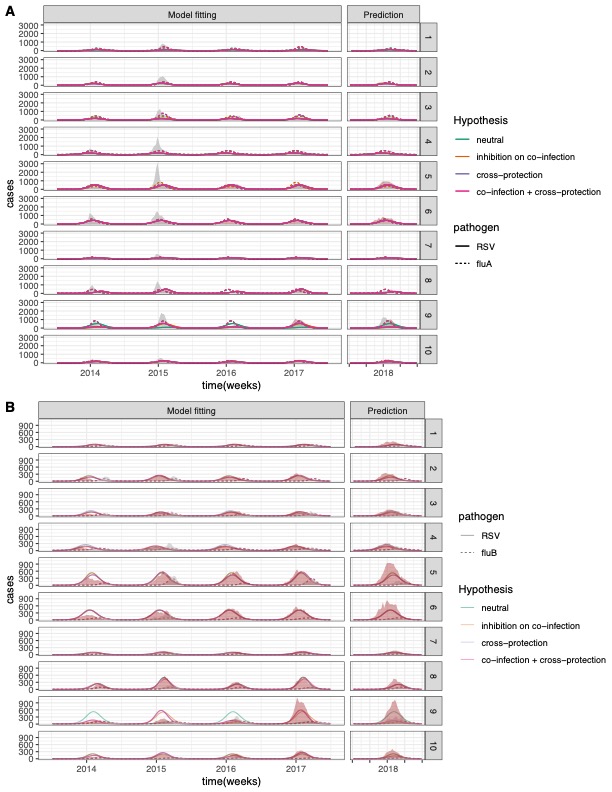
1. Parameters used in the analysis:

|  |  |  |
| --- | --- | --- |
| **Symbol** | **Value** | **Definition** |
| N | 3e7 | Total population |
|  | [0.5,10] | Reproductive number of RSV |
|  | [0.5,10] | Reproductive number of INF |
|  | 9 | Infectious period of RSV |
|  | 3 | Infectious period of INF |
|  | 1/30 | Cross protection period after RSV infection |
|  | 1/30 | Cross protection period after INF infection |
|  | 1y | Duration of RSV immunity |
|  | 1y | Duration of INF immunity |
|  | [0,1] | The amplitude of seasonality for RSV |
|  | [0,1] | The amplitude of seasonality for INF |
|  | [1/365.25,1] | Timing of seasonal peak for RSV |
|  | [1/365.25,1] | Timing of seasonal peak for INF |
|  | (0,1] | Case report rate for RSV |
|  | (0,1] | Case report rate for INF |
|  | [0,1] | The proportion of inhibition of co-infection |
|  | [0,1] | Strength of cross-protection |



Comparation of different hypothesis of RSV and seasonal influenza interaction in 10 HHS region with AIC

A, Different hypothesis of RSV and Flu A interaction. B, Different hypothesis of RSV and Flu B interaction



Model Fitting with 2014-2017 and prediction with 2018 using RSV and seasonal influenza surveillance data collected in 10 HHS regions

A, Different hypothesis of RSV and Flu A interaction. B, Different hypothesis of RSV and Flu B interaction

Brown area indicate the surveillance data of RSV, gray area indicates the surveillance data of seasonal influenza (flu A / fluB)



Confidence Interval of estimated parameter with interest under inhibition on co-infection and cross-protection hypothesis.

Psi, strength of inhibition to be co-infected

Chi, proportion of cross-protection

A, interaction of RSV and fluA B, interaction of RSV and flu B





Simulating cases in each state illustrated by an example in HHS region 5 for RSV and fluA

Upper: no interaction hypothesis

Lower: inhibition to be co-infected and cross protection hypothesis

Estimated parameters:

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 1 | R01 | 1.4871 | 1.4580 | 1.8444 | **1.8917** | 1.4871 | 1.4887 | **1.3358** | 1.3649 |
| R02 | 1.3654 | 1.0523 | 1.3138 | **1.2713** | 1.0000 | 1.0000 | **1.0000** | 1.0882 |
| amplitude1 | 0.2559 | 0.3335 | 0.1326 | **0.1451** | 0.2559 | 0.2563 | **0.2856** | 0.2994 |
| amplitude2 | 0.0959 | 0.2665 | 0.1727 | **0.2299** | 0.2810 | 0.3183 | **0.3779** | 0.3192 |
| tpeak1 | 0.9144 | 0.9269 | 0.9753 | **0.9887** | 0.9144 | 0.9158 | **0.8983** | 0.9028 |
| tpeak2 | 0.1000 | 0.0257 | 0.1173 | **0.1068** | 0.1428 | 0.1372 | **0.1630** | 0.1647 |
| rho1 | 0.0002 | 0.0002 | 0.0002 | **0.0002** | 0.0002 | 0.0002 | **0.0003** | 0.0003 |
| rho2 | 0.0006 | 0.0011 | 0.0009 | **0.0009** | 0.0003 | 0.0003 | **0.0003** | 0.0002 |
| psi | 0.0000 | 1.0000 | 0.0000 | **1.0000** | 0.0000 | 1.0000 | **0.0000** | 0.9839 |
| chi | 0.0000 | 0.0000 | 0.5342 | **0.4549** | 0.0000 | 0.0000 | **0.3625** | 0.3878 |
| loglik | -4946.3701 | -3966.7437 | -3673.1085 | **-3463.3388** | -1504.8500 | -1491.1587 | **-1353.9941** | -1376.5631 |
| AIC | 9908.7402 | 7949.4873 | 7362.2171 | **6946.6775** | 3025.7000 | 2998.3174 | **2723.9882** | 2773.1261 |
| R2 | 0.2374 | 0.2567 | 0.2567 | **0.2636** | 0.3795 | 0.3785 | **0.3792** | 0.3754 |
| RMSE | 155.9184 | 153.7830 | 153.5587 | **152.9489** | 83.9783 | 83.9792 | **83.9634** | 83.9645 |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 2 | R01 | 1.5382 | 1.5612 | **1.1897** | 1.1897 | 1.5382 | 1.5411 | **1.1864** | 1.1864 |
| R02 | 1.5987 | 1.6790 | **1.6384** | 1.6384 | 1.6793 | 1.6830 | **1.7412** | 1.7412 |
| amplitude1 | 0.2096 | 0.2051 | **0.2826** | 0.2825 | 0.2096 | 0.2071 | **0.3105** | 0.3105 |
| amplitude2 | 0.0803 | 0.1041 | **0.0937** | 0.0937 | 0.1049 | 0.0968 | **0.1161** | 0.1161 |
| tpeak1 | 0.8238 | 0.8326 | **0.8098** | 0.8098 | 0.8238 | 0.8241 | **0.7959** | 0.7959 |
| tpeak2 | 0.2495 | 0.2314 | **0.2504** | 0.2504 | 0.4370 | 0.4321 | **0.4291** | 0.4291 |
| rho1 | 0.0003 | 0.0003 | **0.0007** | 0.0007 | 0.0003 | 0.0003 | **0.0007** | 0.0007 |
| rho2 | 0.0003 | 0.0003 | **0.0003** | 0.0003 | 0.0001 | 0.0001 | **0.0001** | 0.0001 |
| psi | 0.0000 | 1.0000 | **0.0000** | 0.0000 | 0.0000 | 0.4908 | **0.0000** | 0.0000 |
| chi | 0.0000 | 0.0000 | **0.3140** | 0.3139 | 0.0000 | 0.0000 | **0.2834** | 0.2834 |
| loglik | -8231.8870 | -8163.6851 | **-8161.4153** | -8161.4153 | -3371.6504 | -3370.8556 | **-3217.9092** | -3217.9092 |
| AIC | 16479.7739 | 16343.3703 | **16338.8306** | 16342.8307 | 6759.3007 | 6757.7112 | **6451.8184** | 6455.8184 |
| R2 | 0.3141 | 0.3176 | **0.3244** | 0.3244 | 1.5382 | 1.5411 | **1.1864** | 1.1864 |
| RMSE | 141.8860 | 141.5252 | **140.8640** | 140.8637 | 1.6793 | 1.6830 | **1.7412** | 1.7412 |

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|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 3 | R01 | 1.5391 | 1.9768 | 1.2776 | **1.2616** | 1.5391 | 1.5438 | **1.1747** | 1.1747 |
| R02 | 1.2257 | 1.2671 | 1.1473 | **1.1470** | 1.0000 | 1.0000 | **1.0804** | 1.0804 |
| amplitude1 | 0.2116 | 0.1114 | 0.2502 | **0.2512** | 0.2116 | 0.2100 | **0.3171** | 0.3171 |
| amplitude2 | 0.1003 | 0.1302 | 0.1934 | **0.2042** | 0.2064 | 0.2348 | **0.2075** | 0.2075 |
| tpeak1 | 0.8517 | 0.9499 | 0.8092 | **0.8156** | 0.8517 | 0.8526 | **0.8323** | 0.8323 |
| tpeak2 | 0.9739 | 0.0104 | 0.0027 | **0.0027** | 0.0904 | 0.0841 | **0.0989** | 0.0989 |
| rho1 | 0.0002 | 0.0002 | 0.0004 | **0.0004** | 0.0002 | 0.0002 | **0.0005** | 0.0005 |
| rho2 | 0.0007 | 0.0007 | 0.0010 | **0.0010** | 0.0003 | 0.0003 | **0.0002** | 0.0002 |
| psi | 0.0000 | 1.0000 | 0.0000 | **1.0000** | 0.0000 | 1.0000 | **0.0000** | 1.0000 |
| chi | 0.0000 | 0.0000 | 0.6299 | **0.5859** | 0.0000 | 0.0000 | **0.2041** | 0.2041 |
| loglik | -8531.4395 | -8302.7473 | -7106.1919 | **-6929.5145** | -2449.7294 | -2434.7553 | **-2292.0237** | -2292.0237 |
| AIC | 17078.8789 | 16621.4947 | 14228.3838 | **13879.0289** | 4915.4588 | 4885.5106 | **4600.0473** | 4604.0473 |
| R2 | 0.3008 | 0.3104 | 0.3449 | **0.3513** | 0.4651 | 0.4648 | **0.4941** | 0.4941 |
| RMSE | 144.0778 | 142.9996 | 140.7236 | **139.8470** | 71.3195 | 71.3158 | **68.0249** | 69.9885 |

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|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 4 | R01 | 1.4490 | **1.4570** | 1.1739 | 1.1720 | 1.4490 | 1.6273 | 1.1725 | **1.1725** |
| R02 | 1.4244 | **1.4838** | 1.4485 | 1.4638 | 1.6037 | 1.6756 | 1.7853 | **1.7853** |
| amplitude1 | 0.1632 | **0.1642** | 0.2185 | 0.2204 | 0.1632 | 0.1198 | 0.2270 | **0.2270** |
| amplitude2 | 0.0265 | **0.0434** | 0.0334 | 0.0385 | 0.0527 | 0.0510 | 0.0755 | **0.0755** |
| tpeak1 | 0.7588 | **0.7644** | 0.7462 | 0.7492 | 0.7588 | 0.7817 | 0.7400 | **0.7400** |
| tpeak2 | 0.1256 | **0.1203** | 0.1417 | 0.1312 | 0.3796 | 0.3624 | 0.3769 | **0.3769** |
| rho1 | 0.0002 | **0.0002** | 0.0004 | 0.0004 | 0.0002 | 0.0001 | 0.0004 | **0.0004** |
| rho2 | 0.0003 | **0.0003** | 0.0003 | 0.0003 | 0.0001 | 0.0001 | 0.0001 | **0.0001** |
| psi | 0.0000 | **1.0000** | 0.0000 | 1.0000 | 0.0000 | 1.0000 | 0.0000 | **1.0000** |
| chi | 0.0000 | **0.0000** | 0.2198 | 0.1946 | 0.0000 | 0.0000 | 0.1317 | **0.1317** |
| loglik | -12684.8778 | **-12621.9137** | -12703.0484 | -12691.4219 | -4621.0404 | -4599.6580 | -4587.5843 | **-4587.5843** |
| AIC | 25385.7556 | **25259.8275** | 25422.0968 | 25402.8438 | 9258.0808 | 9215.3159 | 9191.1686 | **9195.1686** |
| R2 | 0.2869 | **0.2855** | 0.2918 | 0.2899 | 0.3056 | 0.3035 | 0.2014 | **0.3455** |
| RMSE | 146.2556 | **146.4386** | 145.6421 | 145.8859 | 77.3038 | 77.4124 | 83.6966 | **75.2036** |

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|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 5 | R01 | 1.5564 | 1.5847 | 1.0534 | **1.1065** | 1.5564 | 1.6905 | **1.1133** | 1.1133 |
| R02 | 1.3099 | 1.0919 | 1.3099 | **1.3088** | 1.0000 | 1.0026 | **1.0000** | 1.0000 |
| amplitude1 | 0.2072 | 0.2092 | 0.3701 | **0.3581** | 0.2072 | 0.1690 | **0.3487** | 0.3487 |
| amplitude2 | 0.0481 | 0.1550 | 0.0481 | **0.0525** | 0.3029 | 0.3313 | **0.3050** | 0.3050 |
| tpeak1 | 0.8648 | 0.8679 | 0.8473 | **0.8458** | 0.8648 | 0.8808 | **0.8442** | 0.8442 |
| tpeak2 | 0.9366 | 0.9160 | 0.9366 | **0.9498** | 0.1069 | 0.1028 | **0.1072** | 0.1072 |
| rho1 | 0.0004 | 0.0004 | 0.0016 | **0.0011** | 0.0004 | 0.0003 | **0.0011** | 0.0011 |
| rho2 | 0.0005 | 0.0008 | 0.0005 | **0.0005** | 0.0002 | 0.0002 | **0.0002** | 0.0002 |
| psi | 0.0000 | 1.0000 | 0.0000 | **1.0000** | 0.0000 | 1.0000 | **0.0000** | 0.0000 |
| chi | 0.0000 | 0.0000 | 0.0000 | **0.0000** | 0.0000 | 0.0000 | **0.0068** | 0.0068 |
| loglik | -17674.4874 | -15063.1602 | -17517.3678 | **-17433.6870** | -4449.5667 | -4417.6697 | **-4107.3584** | -4107.3584 |
| AIC | 35364.9748 | 30142.3203 | 35050.7357 | **34887.3740** | 8915.1334 | 8851.3394 | **8230.7169** | 8234.7169 |
| R2 | 0.3372 | 0.3782 | 0.3383 | **0.3388** | 0.4841 | 0.4801 | **0.5152** | 0.5152 |
| RMSE | 160.6283 | 161.7047 | 160.1873 | **160.3212** | 105.0975 | 106.5966 | **102.7462** | 102.7469 |

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|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 6 | R01 | 1.0636 | 1.5275 | 1.0636 | **1.1135** | 1.4589 | 1.4654 | **1.2192** | 1.0000 |
| R02 | 1.4350 | 1.4416 | 1.4351 | **1.4383** | 1.4149 | 1.4041 | **1.4718** | 1.4124 |
| amplitude1 | 0.3276 | 0.1982 | 0.3276 | **0.3176** | 0.2035 | 0.2115 | **0.2544** | 0.3615 |
| amplitude2 | 0.0551 | 0.0765 | 0.0551 | **0.0619** | 0.0880 | 0.1062 | **0.0883** | 0.0918 |
| tpeak1 | 0.8086 | 0.8297 | 0.8086 | **0.8094** | 0.8787 | 0.8817 | **0.8890** | 0.8857 |
| tpeak2 | 0.0458 | 0.0453 | 0.0458 | **0.0470** | 0.0687 | 0.0672 | **0.1058** | 0.0683 |
| rho1 | 0.0017 | 0.0004 | 0.0017 | **0.0013** | 0.0004 | 0.0004 | **0.0007** | 0.0015 |
| rho2 | 0.0004 | 0.0004 | 0.0004 | **0.0004** | 0.0004 | 0.0004 | **0.0004** | 0.0004 |
| psi | 0.0000 | 1.0000 | 0.0000 | **1.0000** | 0.0000 | 1.0000 | **0.0000** | 1.0000 |
| chi | 0.0000 | 0.0000 | 0.0000 | **0.0000** | 0.0000 | 0.0000 | **0.2594** | 0.0000 |
| loglik | -14089.4583 | -14041.5305 | -14089.4583 | **-14034.9147** | -4497.1095 | -4456.5523 | **-4344.1935** | -4439.7399 |
| AIC | 28194.9165 | 28099.0610 | 28194.9165 | **28089.8295** | 9010.2190 | 8929.1047 | **8704.3870** | 8899.4798 |
| R2 | 0.3288 | 0.3247 | 0.3288 | **0.3280** | 0.3523 | 0.3533 | **0.3594** | 0.3517 |
| RMSE | 151.2794 | 152.2394 | 151.2795 | **151.4891** | 156.7817 | 156.6734 | **156.3475** | 156.8066 |

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|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 7 | R01 | 1.4589 | 1.4654 | **1.2192** | 1.0000 | 1.0000 | 1.4589 | 1.0000 | **1.2386** |
| R02 | 1.4149 | 1.4041 | **1.4718** | 1.4124 | 1.0000 | 1.0000 | 1.0000 | **1.6295** |
| amplitude1 | 0.2035 | 0.2115 | **0.2544** | 0.3615 | 0.3528 | 0.2035 | 0.3466 | **0.2424** |
| amplitude2 | 0.0880 | 0.1062 | **0.0883** | 0.0918 | 0.2197 | 0.2197 | 0.2399 | **0.1157** |
| tpeak1 | 0.8787 | 0.8817 | **0.8890** | 0.8857 | 0.8828 | 0.8787 | 0.8931 | **0.8639** |
| tpeak2 | 0.0687 | 0.0672 | **0.1058** | 0.0683 | 0.0797 | 0.0797 | 0.0907 | **0.3219** |
| rho1 | 0.0004 | 0.0004 | **0.0007** | 0.0015 | 0.0015 | 0.0004 | 0.0022 | **0.0007** |
| rho2 | 0.0004 | 0.0004 | **0.0004** | 0.0004 | 0.0002 | 0.0002 | 0.0002 | **0.0001** |
| psi | 0.0000 | 1.0000 | **0.0000** | 1.0000 | 0.0000 | 0.0000 | 0.0000 | **0.0497** |
| chi | 0.0000 | 0.0000 | **0.2594** | 0.0000 | 0.0000 | 0.0000 | 0.8310 | **0.3564** |
| loglik | -4497.1095 | -4456.5523 | **-4344.1935** | -4439.7399 | -2374.2680 | -2424.0162 | -2372.0412 | **-2256.3799** |
| AIC | 9010.2190 | 8929.1047 | **8704.3870** | 8899.4798 | 4764.5361 | 4864.0324 | 4760.0824 | **4532.7598** |
| R2 | 0.3523 | 0.3533 | **0.3594** | 0.3517 | 0.4706 | 0.4736 | 0.4680 | **0.5115** |
| RMSE | 156.7817 | 156.6734 | **156.3475** | 156.8066 | 80.1828 | 80.0916 | 80.2306 | **78.7599** |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 8 | R01 | **1.3084** | 1.3081 | 1.3085 | 1.3085 | **1.3083** | 1.3084 | 1.3086 | 1.2619 |
| R02 | **1.4852** | 1.4847 | 1.4848 | 1.4845 | **1.2100** | 1.2084 | 1.2099 | 1.6701 |
| amplitude1 | **0.4187** | 0.4187 | 0.4187 | 0.4187 | **0.4188** | 0.4187 | 0.4188 | 0.3309 |
| amplitude2 | **0.0995** | 0.0995 | 0.0996 | 0.0995 | **0.0986** | 0.0990 | 0.0986 | 0.1286 |
| tpeak1 | **0.9448** | 0.9447 | 0.9448 | 0.9448 | **0.9448** | 0.9448 | 0.9448 | 0.9200 |
| tpeak2 | **0.1062** | 0.1059 | 0.1059 | 0.1058 | **0.1366** | 0.1360 | 0.1366 | 0.3412 |
| rho1 | **0.0011** | 0.0011 | 0.0011 | 0.0011 | **0.0011** | 0.0011 | 0.0011 | 0.0018 |
| rho2 | **0.0011** | 0.0011 | 0.0011 | 0.0011 | **0.0004** | 0.0004 | 0.0004 | 0.0003 |
| psi | **0.0000** | 0.0000 | 0.0000 | 0.0000 | **0.0000** | 0.0000 | 0.0000 | 0.0069 |
| chi | **0.0000** | 0.0000 | 0.0000 | 0.0000 | **0.0000** | 0.0000 | 0.0000 | 0.5366 |
| loglik | **-8367.0216** | -8367.0238 | -8367.0231 | -8367.0278 | **-2676.3421** | -2676.3437 | -2676.3433 | -3304.9287 |
| AIC | **16750.0433** | 16750.0476 | 16750.0463 | 16754.0555 | **5368.6843** | 5368.6875 | 5368.6867 | 6629.8573 |
| R2 | **0.3240** | 0.3241 | 0.3240 | 0.3241 | **0.4375** | 0.4374 | 0.4374 | 0.4367 |
| RMSE | **143.6361** | 143.6305 | 143.6370 | 143.6287 | **78.2220** | 78.2162 | 78.2234 | 75.1255 |

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|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 9 | R01 | 1.1616 | 1.1606 | **1.1836** | 1.1834 | 1.1617 | 1.1619 | 1.1953 | **1.1879** |
| R02 | 1.7049 | 1.7312 | **1.7421** | 1.7444 | 1.1901 | 1.3133 | 1.4240 | **1.4502** |
| amplitude1 | 0.2424 | 0.2509 | **0.3175** | 0.3165 | 0.2423 | 0.2462 | 0.3609 | **0.3652** |
| amplitude2 | 0.1085 | 0.1175 | **0.1205** | 0.1213 | 0.0368 | 0.0240 | 0.0393 | **0.0385** |
| tpeak1 | 0.8778 | 0.8771 | **0.8502** | 0.8491 | 0.8778 | 0.8765 | 0.8378 | **0.8382** |
| tpeak2 | 0.2672 | 0.2641 | **0.2687** | 0.2689 | 0.0483 | 0.1311 | 0.2681 | **0.2747** |
| rho1 | 0.0006 | 0.0006 | **0.0007** | 0.0007 | 0.0006 | 0.0006 | 0.0006 | **0.0007** |
| rho2 | 0.0004 | 0.0004 | **0.0004** | 0.0004 | 0.0002 | 0.0002 | 0.0001 | **0.0001** |
| psi | 0.0000 | 0.6903 | **0.0000** | 0.0003 | 0.0000 | 1.0000 | 0.0000 | **0.8055** |
| chi | 0.0000 | 0.0000 | **0.2136** | 0.2137 | 0.0000 | 0.0000 | 0.4438 | **0.4019** |
| loglik | -11570.4285 | -11608.3676 | **-10589.1921** | -10596.1540 | -8045.1447 | -7894.6028 | -6490.8206 | **-6486.6379** |
| AIC | 23156.8571 | 23232.7352 | **21194.3842** | 21212.3080 | 16106.2894 | 15805.2056 | 12997.6411 | **12993.2759** |
| R2 | 0.2303 | 0.3063 | **0.3194** | 0.3185 | 0.1533 | 0.4309 | 0.4746 | **0.4750** |
| RMSE | 189.1086 | 176.1203 | **175.1328** | 175.5033 | 109.6651 | 83.7194 | 83.9901 | **83.5955** |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | RSV-Flu A | | | | RSV-Flu B | | | |
| HHS  region | variable | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection | No-interaction | Inhibition on co-infection | Cross protection | Co-infection and cross-protection |
| 10 | R01 | 1.4815 | 1.4804 | 1.2759 | **1.2721** | 1.4815 | 1.4845 | 1.2784 | **1.2664** |
| R02 | 1.6424 | 1.6093 | 1.6817 | **1.6810** | 1.1437 | 1.2009 | 1.5882 | **1.6268** |
| amplitude1 | 0.2926 | 0.3006 | 0.3361 | **0.3379** | 0.2925 | 0.2906 | 0.3523 | **0.3549** |
| amplitude2 | 0.1000 | 0.1055 | 0.1135 | **0.1135** | 0.0847 | 0.0860 | 0.1126 | **0.1106** |
| tpeak1 | 0.8907 | 0.8937 | 0.9109 | **0.9107** | 0.8907 | 0.8917 | 0.8729 | **0.8760** |
| tpeak2 | 0.2128 | 0.1891 | 0.2277 | **0.2276** | 0.1239 | 0.1246 | 0.3149 | **0.3272** |
| rho1 | 0.0005 | 0.0005 | 0.0010 | **0.0010** | 0.0005 | 0.0005 | 0.0010 | **0.0011** |
| rho2 | 0.0005 | 0.0005 | 0.0006 | **0.0006** | 0.0002 | 0.0002 | 0.0001 | **0.0001** |
| psi | 0.0000 | 0.7806 | 0.0000 | **0.0002** | 0.0000 | 0.7105 | 0.0000 | **0.2892** |
| chi | 0.0000 | 0.0000 | 0.5034 | **0.5046** | 0.0000 | 0.0000 | 0.8048 | **0.7347** |
| loglik | -5369.6862 | -5352.0236 | -5045.9053 | **-5046.5653** | -2821.1922 | -2820.2194 | -2311.6318 | **-2313.7381** |
| AIC | 10755.3724 | 10720.0473 | 10107.8106 | **10113.1306** | 5658.3843 | 5656.4389 | 4639.2637 | **4647.4761** |
| R2 | 0.3432 | 0.3448 | 0.3493 | **0.3492** | 0.4595 | 0.4590 | 0.4978 | **0.4967** |
| RMSE | 144.5390 | 144.4304 | 143.9212 | **143.9111** | 70.9281 | 70.9524 | 68.6912 | **68.6316** |