**Supplemental Table 1. Final core models overall and for each domain evaluated**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Covariate** | **Domain (with sample sizes indicated for adjusted models)** | | | | | | |
| **Overall**  **N=2408** | **Neurologic**  **N=2348** | **ND**  **N=1165** | **Neurologic/ND**  **N=2349** | **Growth**  **N=1890** | **Language**  **N=1474** | **Metabolic**  **N=1524** |
| Born 2010 or later | 0.38 (0.31, 0.47)  <0.001 | 0.36 (0.22, 0.58)  <0.001 |  | 0.43 (0.29, 0.64)  <0.001 | 0.56 (0.35, 0.91)  0.019 |  | 0.11 (0.04, 0.35)  <0.001 |
| Black/Puerto Rican | 0.80 (0.70, 0.92)  0.002 |  |  |  |  |  |  |
| Low caregiver education | 1.10 (0.96, 1.27)  0.071 |  |  | 1.23 (0.93, 1.63)  0.14 |  | 1.25 (0.96, 1.62)  0.10 |  |
| 1st Trimester tobacco use | 1.19 (1.01, 1.40)  0.040 | 1.71 (1.121, 2.42)  0.003 |  | 1.53 (1.11, 2.09)  0.009 | 1.62 (1.13, 2.32)  0.009 |  |  |
| Pre-gestational diabetes |  | 1.95 (0.92, 4.12)  0.080 |  | 1.87 (0.94, 3.71)  0.072 |  |  | 1.94 (1.04, 3.61)  0.038 |
| Toxemia/pre-eclampsia |  | 1.95 (1.20, 3.18)  0.007 |  | 1.76 (1.12, 2.76)  0.014 |  |  |  |
| Low income level |  |  | 1.94 (1.02, 3.72)  0.045 |  |  |  |  |
| Maternal age <25yrs |  |  |  |  | 0.69 (0.47, 0.99)  0.046 |  |  |
| Female sex (child) |  |  |  |  |  | 0.54 (0.41, 0.72)  <0.001 |  |
| Latino |  |  |  |  |  |  | 1.46 (1.11, 1.92)  0.007 |
| Maternal gonorrhea |  |  |  |  |  |  | 1.82 (0.99, 3.32)  0.052 |
| Additionally included in sensitivity analyses | | | | | | | |
| Low birth weight | 1.42 (1.22, 1.65)  <0.001 | 2.49 (1.81, 3.43)  <0.001 | 2.23 (1.30, 3.81)  0.003 | 2.17 (1.63, 2.90)  <0.001 | 4.91 (3.44, 7.01)  <0.001 | 1.73 (1.30, 2.31)  <0.001 | (not associated with outcome) |
| Preterm birth |  |  |  |  | 0.46 (0.31, 0.71)  <0.001 |  |  |

Entries are relative risk, 95% confidence interval, and p-value from adjusted model including all covariates with estimates shown.

**Supplemental Table 2.**  **Association of Timing of the First ARV Use During Pregnancy with Overall Case Status**

| **ARV Exposure** | **First use during pregnancy** | **% in category** | **Case prevalence** | **Unadjusted Model** | | **Adjusted Model\*** | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **RR (95% CI)** | **P-value** | **RR (95% CI)** | **P-value** |
| **HAART** | Never exposed | 18.1 | 29.0 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 41.0 | 23.6 | **0.81 (0.68, 0.97)** | **0.02** | 0.98 (0.81, 1.18) | 0.83 |
|  | 2nd/3rd trimester | 40.9 | 25.1 | 0.87 (0.73, 1.03) | 0.11 | 0.97 (0.81, 1.17) | 0.76 |
| **NNRTIs** | Never exposed | 85.7 | 25.0 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 8.6 | 25.6 | 1.02 (0.81, 1.29) | 0.85 | 1.00 (0.79, 1.27) | 0.99 |
|  | 2nd/3rd trimester | 5.8 | 27.3 | 1.09 (0.83, 1.43) | 0.52 | 0.94 (0.71, 1.25) | 0.68 |
| **PIs** | Never exposed | 26.2 | 27.1 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 35.3 | 23.7 | 0.87 (0.74, 1.04) | 0.12 | 1.00 (0.84, 1.20) | 0.96 |
|  | 2nd/3rd trimester | 38.4 | 25.2 | 0.93 (0.79, 1.09) | 0.38 | 1.01 (0.85, 1.19) | 0.94 |
|  |  |  |  |  |  |  |  |
| ***Results for specific ARVs with p<0.10 in unadjusted or adjusted models*** | | | | | | | |
| **Stavudine (d4T)** | Never exposed | 96.0 | 24.9 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 2.6 | 36.8 | **1.47 (1.07, 2.03)** | **0.02** | 1.27 (0.92, 1.75) | 0.15 |
|  | 2nd/3rd trimester | 1.3 | 20.0 | 0.80 (0.41, 1.56) | 0.52 | 0.70 (0.36, 1.36) | 0.30 |
| **Emtricitabine (FTC)** | Never exposed | 74.9 | 26.9 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 15.5 | 17.8 | **0.66 (0.53, 0.83)** | **<0.001** | 0.86 (0.68, 1.08) | 0.20 |
|  | 2nd/3rd trimester | 9.6 | 24.0 | 0.89 (0.71, 1.13) | 0.34 | 1.19 (0.94, 1.49) | 0.15 |
| **Tenofovir (TDF)** | Never exposed | 70.8 | 26.8 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 17.8 | 19.4 | **0.73 (0.59, 0.89)** | **0.002** | 0.91 (0.74, 1.12) | 0.36 |
|  | 2nd/3rd trimester | 11.4 | 24.2 | 0.91 (0.73, 1.12) | 0.36 | 1.13 (0.91, 1.40) | 0.27 |
| **Zidovudine (ZDV)** | Never exposed | 26.1 | 20.4 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 28.2 | 27.1 | **1.33 (1.10, 1.60)** | **0.004** | 1.08 (0.89, 1.31) | 0.44 |
|  | 2nd/3rd trimester | 45.7 | 26.7 | **1.31 (1.10, 1.56)** | **0.003** | 1.05 (0.87, 1.25) | 0.63 |
| **Atazanavir (ATV)** | Never exposed | 84.7 | 26.0 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 9.0 | 23.5 | 0.91 (0.71, 1.15) | 0.42 | 1.12 (0.88, 1.41) | 0.37 |
|  | 2nd/3rd trimester | 6.3 | 17.1 | **0.66 (0.47, 0.93)** | **0.02** | 0.87 (0.62, 1.22) | 0.42 |
| **Fosamprenavir (FPV)** | Never exposed | 97.2 | 25.0 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 1.7 | 20.5 | 0.82 (0.46, 1.47) | 0.51 | 0.83 (0.45, 1.53) | 0.56 |
|  | 2nd/3rd trimester | 1.2 | 50.0 | **2.00 (1.39, 2.88)** | **<0.001** | **1.73 (1.23, 2.43)** | **0.002** |
| **Nelfinavir (NFV)** | Never exposed | 77.8 | 24.1 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 8.4 | 31.7 | **1.32 (1.07, 1.62)** | **0.01** | 1.11 (0.89, 1.37) | 0.35 |
|  | 2nd/3rd trimester | 13.8 | 27.6 | 1.15 (0.95, 1.38) | 0.15 | 0.94 (0.77, 1.14) | 0.53 |
| **Ritonavir (as booster)** | Never exposed | 46.7 | 27.8 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 25.4 | 20.8 | **0.75 (0.63, 0.89)** | **0.001** | 0.96 (0.80, 1.14) | 0.63 |
|  | 2nd/3rd trimester | 27.8 | 24.7 | 0.89 (0.76, 1.04) | 0.14 | 1.08 (0.92, 1.27) | 0.35 |
| **Darunavir (DRV)** | Never exposed | 94.9 | 25.7 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 2.4 | 8.1 | **0.31 (0.13, 0.73)** | **0.007** | 0.53 (0.23, 1.24) | 0.14 |
|  | 2nd/3rd trimester | 2.7 | 21.1 | 0.82 (0.52, 1.29) | 0.40 | 1.20 (0.77, 1.85) | 0.42 |
| **Saquinavir (SQV)** | Never exposed | 96.9 | 25.0 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 1.3 | 18.2 | 0.73 (0.35, 1.50) | 0.39 | 0.79 (0.39, 1.62) | 0.52 |
|  | 2nd/3rd trimester | 1.8 | 38.3 | **1.53 (1.06, 2.21)** | **0.02** | 1.33 (0.91, 1.93) | 0.14 |
| **Raltegravir (RAL)** | Never exposed | 96.7 | 25.5 | 1.00 (ref) |  | 1.00 (ref) |  |
|  | 1st trimester | 1.8 | 13.0 | 0.51 (0.24, 1.08) | 0.08 | 0.92 (0.44, 1.94) | 0.83 |
|  | 2nd/3rd trimester | 1.6 | 14.6 | 0.57 (0.27, 1.21) | 0.14 | 0.93 (0.45, 1.91) | 0.85 |

\*Adjusted model includes black race or Puerto Rican origin, low caregiver education (< high school), 1st trimester maternal tobacco use, and birth cohort (2010+ vs <2010)

**Supplemental Table 3. Association of *in utero* ARV exposure with Overall Case Status: Sensitivity Analysis Restricted to the Dynamic Cohort**

|  | | **Percent Exposed** | **Percent of Cases** | | **Unadjusted Model**  **(N=1446)** | | **Adjusted Model\***  **(N=1446)** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposed** | **Unexposed** | **RR (95% CI)** | **P-value** | **RR (95% CI)** | **P-value** |
| **By ARV Drug Class or Regimen** | | | | | | | |  |
|  | HAART | 88.9 | 19.8 | 18.6 | 1.06 (0.75, 1.49) | 0.73 | 1.20 (0.86, 1.68) | 0.29 |
|  | NNRTIs | 10.9 | 20.9 | 19.5 | 1.07 (0.78, 1.48) | 0.67 | 1.07 (0.78, 1.46) | 0.67 |
|  | PIs | 82.6 | 20.0 | 17.9 | 1.12 (0.84, 1.49) | 0.46 | 1.14 (0.86, 1.51) | 0.36 |
| **Nucleoside Reverse Transcriptase Inhibitors (NRTIs)** | | | | | | | | |
|  | Lamivudine (3TC) | 66.9 | 21.0 | 16.9 | 1.24 (0.98, 1.57) | 0.07 | 1.02 (0.81, 1.28) | 0.90 |
|  | Abacavir (ABC) | 21.1 | 19.7 | 19.6 | 1.00 (0.78, 1.29) | 0.99 | 0.88 (0.68, 1.13) | 0.31 |
|  | Stavudine (d4T) | 0.8 | 27.3 | 19.6 | 1.39 (0.53, 3.68) | 0.50 | 1.13 (0.43, 2.94) | 0.80 |
|  | Didanosine (ddI) | 1.6 | 34.8 | 19.4 | **1.79 (1.01, 3.17)** | **0.04** | 1.53 (0.88, 2.67) | 0.13 |
|  | Emtricitabine (FTC) | 39.8 | 17.6 | 21.0 | 0.84 (0.67, 1.04) | 0.11 | 0.99 (0.79, 1.22) | 0.90 |
|  | Tenofovir (TDF) | 42.4 | 17.9 | 20.9 | 0.86 (0.69, 1.06) | 0.17 | 1.01 (0.81, 1.24) | 0.96 |
|  | Zidovudine (ZDV) | 65.8 | 21.1 | 16.8 | **1.26 (1.00, 1.59)** | **0.05** | 1.05 (0.83, 1.31) | 0.70 |
|  | ZDV + 3TC | 62.7 | 21.3 | 16.9 | **1.26 (1.01, 1.58)** | **0.04** | 1.06 (0.85, 1.32) | 0.61 |
| **Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)** | | | | | | | | |
|  | Efavirenz (EFV) | 5.5 | 17.7 | 19.8 | 0.90 (0.55, 1.46) | 0.66 | 0.86 (0.53, 1.38) | 0.53 |
|  | Nevirapine (NVP) | 4.2 | 26.2 | 19.4 | 1.36 (0.88, 2.09) | 0.17 | 1.26 (0.83, 1.92) | 0.28 |
| **Fusion Inhibitors/Integrase Inhibitors** | | | | | | | | |
|  | Raltegravir (RAL) | 6.0 | 13.8 | 20.0 | 0.69 (0.40, 1.18) | 0.17 | 0.92 (0.54, 1.56) | 0.75 |
| **Protease Inhibitors (PIs)** | | | | | | | | |
|  | Atazanavir (ATV) | 24.1 | 18.1 | 20.1 | 0.90 (0.70, 1.16) | 0.41 | 0.98 (0.77, 1.25) | 0.86 |
|  | Darunavir (DRV) | 9.1 | 15.3 | 20.1 | 0.76 (0.50, 1.15) | 0.20 | 1.00 (0.66, 1.50) | 0.99 |
|  | Fosamprenavir (FPV) | 4.1 | 28.8 | 19.3 | 1.50 (0.99, 2.27) | 0.06 | 1.34 (0.89, 2.00) | 0.16 |
|  | Lopinavir (LPV) | 44.5 | 21.6 | 18.1 | 1.20 (0.97, 1.47) | 0.09 | 1.09 (0.89, 1.34) | 0.39 |
|  | Nelfinavir (NFV) | 9.3 | 21.6 | 19.4 | 1.11 (0.79, 1.57) | 0.54 | 0.99 (0.71, 1.38) | 0.94 |
|  | Ritonavir (as booster) | 75.7 | 20.1 | 18.2 | 1.11 (0.86, 1.42) | 0.43 | 1.16 (0.91, 1.48) | 0.25 |
|  | Saquinavir (SQV) | 2.1 | 20.0 | 19.6 | 1.02 (0.49, 2.10) | 0.96 | 0.84 (0.41, 1.72) | 0.64 |

\*Adjusted model includes black race or Puerto Rican origin and birth cohort (2010+ vs <2010)

**Supplemental Table 4. Association of *in utero* ARV exposure with Incidence Rates for Case Status in Specific Domains Evaluated at Every Study Visit, for exposures with p<0.10 in either unadjusted or adjusted analysis**

| **Domain/ARV Exposure** | | **Percent Exposed** | | **Incidence Rates (per 100 person-years)** | | **Unadjusted Model** | | **Adjusted Model\*** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Exposed** | **Unexposed** | **IRR (95% CI)** | **P-value** | **aIRR (95% CI)** | **P-value** |
| **Metabolic Abnormality (N=1640 in unadjusted model, N=1524 in adjusted model)** | | | | | | | | | |
|  | HAART | | 79.0 | 5.23 | 7.27 | **0.72 (0.52, 0.99)** | **0.041** | **0.64 (0.46, 0.89)** | **0.007** |
|  | PIs | | 70.2 | 5.33 | 6.46 | 0.82 (0.61, 1.11) | 0.20 | 0.76 (0.56, 1.04) | 0.088 |
|  | Zidovudine (ZDV) | | 79.6 | 6.10 | 3.88 | **1.57 (1.01, 2.46)** | **0.046** | **1.61 (1.01, 2.58)** | **0.047** |
|  | Lopinavir (LPV) | | 28.5 | 3.96 | 6.18 | **0.64 (0.43, 0.96)** | **0.033** | 0.66 (0.44, 1.00) | 0.052 |
|  | Atazanavir (ATV) | | 10.5 | 8.57 | 5.52 | 1.55 (0.94, 2.56) | 0.084 | 1.55 (0.92, 2.60) | 0.096 |
|  | Zidovudine (1st trimester) | | 31.2 | 6.55 | 5.29 | 1.24 (0.92, 1.67) | 0.16 | 1.24 (0.92, 1.69) | 0.16 |
|  | Lopinavir (1st trimester) | | 11.4 | 3.03 | 5.98 | **0.51 (0.26, 0.99)** | **0.047** | **0.47 (0.23, 0.95)** | **0.036** |
| **Impaired Growth (N=2062 in unadjusted model, N=1890 in adjusted model)** | | | | | | | | | |
|  | NRTIs | | 97.0 | 2.62 | 5.28 | **0.50 (0.25, 0.98)** | **0.042** | **0.43 (0.20, 0.91)** | **0.029** |
|  | Lopinavir (LPV) | | 30.9 | 3.29 | 2.46 | 1.34 (0.96, 1.86) | 0.083 | 1.32 (0.93, 1.87) | 0.12 |
|  | Nelfinavir (NFV) | | 25.2 | 2.01 | 2.97 | **0.68 (0.46, 1.00)** | **0.050** | 0.69 (0.45, 1.05) | 0.081 |
| **Neurologic (N=2582 in unadjusted model, N=2348 in adjusted model)** | | | | | | | | | |
|  | NNRTIs | | 14.4 | 3.66 | 2.73 | 1.34 (0.91, 1.98) | 0.14 | 1.40 (0.93, 2.10) | 0.11 |
|  | Efavirenz | | 4.7 | 4.89 | 2.78 | 1.76 (0.98, 3.17) | 0.060 | 1.77 (0.96, 3.28) | 0.069 |
|  | Didanosine (1st trimester) | | 2.0 | 5.05 | 2.82 | 1.79 (0.84, 3.82) | 0.13 | 1.95 (0.86, 4.43) | 0.11 |

IRR=incidence rate ratio comparing exposed to unexposed; aIRR=adjusted IRR

\*Adjusted model includes the following covariates for each domain:

**Metabolic**: pre-gestational diabetes, Latino ethnicity, maternal gonorrhea, and birth cohort (2010+ vs <2010)

**Growth**: maternal tobacco use during pregnancy, young maternal age (<25 yrs) at delivery, and birth cohort (2010+ vs <2010)

**Neurologic**: 1st trimester maternal tobacco use, pre-gestational diabetes, toxemia/pre-eclampsia, and birth cohort (2010+ vs <2010)