## Supplemental Digital Content 1: Multivariable Models 2 & 3 Cohort Characteristics

SDC 1a. Table S1. Model 2 Cohort Characteristics

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| --- | --- | --- | --- |
| **Characteristics** | **HEU****N=411** | **HUU****N=1224** | **P-value** |
| **Maternal age**  | 29.9 ± 5.6 | 30.5 ± 5.6 | 0.056 |
| **Age at Follow Up**  | 8.4 ± 5.6 | 8.4 ± 5.6 | 0.90 |
| **Male Sex**  | 190 (46.2) | 573 (46.8) | 0.84 |
| **Gestational age (wks)**  | 37.7 ± 3.1 | 38.9 ± 1.8 | <0.0001 |
| **Gestational age <37 wks** | 83 (20.2) | 85 (6.9) | <0.0001 |
| **Birthweight (g)**  | 2985± 616 | 3384 ± 572 | <0.0001 |
| **Birthweight <2500g** | 68 (16.5) | 55 (4.5) | <0.0001 |
| **APGAR 1m**  | 7.9 ± 1.8 | 8.1 ± 1.5 | 0.32 |
| **APGAR 5m**  | 8.8 ± 1.3 | 9.1 ± 0.8 | <0.0001 |

Data shown as mean ± SD or N (%) p-value calculated from Pearson chi-squared test (proportions) or from Mann-Whitney U test (continuous variables).

*Abbreviations: HEU, HIV-exposed uninfected; HUU, HIV-unexposed uninfected; APGAR, appearance,*

*pulse, grimace, activity, respiration (scores at 1 minute and 5 minutes after birth)*

SDC 1b. Table S2. Model 3 Cohort Characteristics

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| --- | --- | --- | --- |
| **Characteristics** | **HEU****N=309** | **HUU****N=917** | **P-value** |
| **Maternal age**  | 30.2 ± 5.4 | 30.7 ± 5.6 | 0.083 |
| **Age at Follow Up**  | 5.9 ± 3.6 | 5.8 ± 3.6 | 0.79 |
| **Male Sex**  | 144 (46.6) | 432 (47.1) | 0.88 |
| **Gestational age (wks)**  | 37.7 ± 2.4 | 38.8 ± 1.8 | <0.0001 |
| **Gestational age <37 wks** | 61 (19.7) | 63 (6.9) | <0.0001 |
| **Birthweight (g)**  | 2993 ± 588 | 3379 ± 576 | <0.0001 |
| **Birthweight <2500g** | 48 (15.5) | 42 (4.6) | <0.0001 |
| **APGAR 1m**  | 7.9 ± 1.9 | 8.2 ± 1.5 | 0.34 |
| **APGAR 5m**  | 8.8 ± 1.2 | 9.1 ± 0.8 | <0.0001 |
| **Smoking (any)** | 107 (34.6) | 78 (8.5) | <0.0001 |
| **Alcohol use** **(identified as risk)** | 26 (8.4) | 12 (1.3) | <0.0001 |
| **Substance use (any)** | 111 (35.9) | 24 (2.6) | <0.0001 |

Data shown as mean ± SD or N (%) p-value calculated from Pearson chi-squared test (proportions) or from Mann-Whitney U test (continuous variables).

*Abbreviations: HEU, HIV-exposed uninfected; HUU, HIV-unexposed uninfected; APGAR, appearance,*

*pulse, grimace, activity, respiration (scores at 1 minute and 5 minutes after birth)*

## Supplemental Digital Content 2: Model 2 & 3 Covariates Included for Analysis, Crude and Adjusted Odds Ratios

SDC 2a. Table S3. Model 2 Covariates Included for Analysis

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Crude OR (CI)** | **Adjusted for** | **Adjusted OR (CI)** | **% Change** | **P****OR** | **P****LRT** | **P****Homogeneity OR** |
| **Any ND Diagnosis**  | 2.68(2.04, 3.53) | **Sex (M vs. F)** | 2.72 (2.06, 3.58) | + 1.5 | <0.0001 | <0.0001 | 0.44 |
| Age at Follow Up (i. 0-5, ii. 6-10, iii.11-15, iv.16-22) | 2.84 (2.13, 3.78) | + 6.0 | <0.0001 | <0.0001 | 0.18(p=0.16 test for interaction) |
| **Age at Follow Up (>11 yrs vs. ≤11 yrs)** | 2.74 (2.07, 3.61) | + 2.2 | <0.0001 | <0.0001 | 0.014 (p=0.011 test for interaction) |
| Maternal Age (i. <25, ii. 25-35, iii. >35) | 2.66 (2.02, 3.50) | - 0.7 | <0.0001 | 0.68 | 0.52(p= 0.40 test for interaction) |
| Maternal Age (>35 yrs vs. ≤35 yrs) | 2.69 (2.05, 3.54)  | + 0.4 | <0.0001 | 0.64 | 0.89 |
| **Preterm Birth****<37 weeks GA** | 2.36 (1.78, 3.13) | -12.0 | <0.0001 | <0.0001 | 0.85 |

HEU N=411, HUU N=1224. Interaction test p-value included for variables with multiple strata. Crude and adjusted odds ratios were calculated using Mantel-Haenszel method.

*Abbreviations: HEU, HIV-exposed uninfected; HUU, HIV-unexposed uninfected; ND,*

*neurodevelopmental disorder; OR, odds ratio; CI, confidence interval; LRT, likelihood ratio test*

SDC 2b. Table S4. Model 3 Covariates Included for Analysis

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Crude OR (CI)** | **Adjusted for** | **Adjusted OR (CI)** | **% Change** | **P****OR** | **P****LRT** | **P****Homogeneity OR** |
| **Any ND Diagnosis**  | 2.25(1.61, 3.15) | **Sex (M vs. F)** | 2.27 (1.6, 3.17) | + 0.9 | <0.0001 | 0.002 | 0.23 |
| **Age at Follow Up (>6 yrs vs. ≤6 yrs)** | 2.34 (1.7, 3.31) | + 4.0 | <0.0001 | <0.0001 | 0.567 |
| Maternal Age (i. <25, ii. 25-35, iii. >35) | 2.24 (1.6, 3.13) | - 0.4 | <0.0001 | 0.44 | 0.18(p=0.17 test for interaction) |
| Maternal Age (>35 yrs vs. ≤35 yrs) | 2.26 (1.6, 3.31) | + 0.4 | <0.0001 | 0.77 | 0.24 |
| **Preterm Birth****(<37 weeks GA)** | 1.92 (1.41, 2.7) | - 15.0 | 0.0002 | <0.0001 | 0.62 |
| Smoking (any) | 1.94 (1.35, 2.79) | - 14.0 | 0.0003 | 0.006 | 0.31 |
| Alcohol (identified as risk) | 2.26 (1.6, 3.19) | + 0.44 | <0.0001 | 0.83 | 0.15 |
| Drug/Substance Use | 1.46 (0.96, 2.21) | - 35 | 0.073 | <0.0001 | 0.11 |
| **Drug/Substance Use + Smoking** | 1.58 (1.06, 2.21) | - 30.0 | 0.025 | <0.0001 | 0.21 |

HEU N=309, HUU N=917. Interaction test p-value included for variables with multiple strata and/or for variables with p<0.1 homogeneity odds ratio test. Smoking and Drug/substance use tested positive for collinearity and were combined into a trichotomised variable and included in the multivariable logistic regression. Crude and adjusted odds ratios were calculated using Mantel-Haenszel method.

*Abbreviations: HEU, HIV-exposed uninfected; HUU, HIV-unexposed uninfected; ND,*

*neurodevelopmental disorder; OR, odds ratio; CI, confidence interval; LRT, likelihood ratio test*

**Supplemental Digital Content 3: British Columbia Antiretroviral Regimens, Any Neurodevelopmental Disorder Diagnoses & HIV-Exposed Uninfected Births Over Study Period, & Antiretroviral Exposure Durations**

**SDC 3a. Figure S1. ARV Regimens, ND Diagnoses & HEU Births (N=446)**

*Abbreviations: ARV, antiretroviral; ND, neurodevelopmental disorder; HEU, HIV-exposed uninfected;*

*NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase*

*inhibitor; PI, protease inhibitor*

**SDC 3b. Figure S2. HEU ARV Exposure Durations (N=446)**

*Abbreviations: HEU, HIV-exposed uninfected; ARV, antiretroviral*

## Supplemental Digital Content 4: Antiretroviral Drugs Used in Pregnancy for Women Living with HIV in BC

SDC 4. Table S5. Antiretroviral Drugs Used During Pregnancy for Mothers Living with HIV in British Columbia (1990-2012)

|  |  |
| --- | --- |
| **Nucleoside Reverse Transcriptase Inhibitors (NRTIs):** | **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):** |
| Zidovudine (AZT) | Nevirapine (NVP) |
| Didanosine (ddI) | Efavirenz (EFV) |
| Zalcitabine (ddC) | Etravirine (ETR) |
| Stavudine (d4T) |  |
| Lamivudine (3TC) | **Protease Inhibitors (PIs):** |
| Abacavir (ABC) | Indinavir (IDV) |
| Tenofovir (TVF) | Ritonavir (RTV) alone or as a booster  |
| Emtricitabine (FTC) | Saquinavir (SQV) |
|  | Nelfinavir (NFV) |
| **Integrase Inhibitors (IIs):** | Lopinavir (LPV) |
| Raltegravir (RAL)  | Darunavir (DRV) |

(Data obtained from medical chart information from The Oak Tree Clinic, Vancouver, BC, Canada)