# Supplemental materials

## Methods

The study linked state/territory health department data on HEU children to cancer registry data from participating sites in the HIV/AIDS Cancer Match Study (<https://hivmatch.cancer.gov/>). The study was approved by institutional review boards at these sites, as required.

We constructed a cohort of HEU children based on overlapping availability of HEU and cancer data in the following states/territories: Connecticut (calendar years of analysis: 2006-2017), Georgia (2005-2010), Louisiana (1990-2017), Michigan (1990-2017), Puerto Rico (1990-2016), and Texas (1999-2014). Follow-up started at birth and ended at the earlier of age 20, death, or end of cancer registry coverage. HEU data included demographic characteristics and maternal ARV use, although ARV data were inconsistently collected across sites.

Cancers were classified using the International Classification of Childhood Cancers [14] and grouped as leukemias, brain tumors, and other cancers. We also analyzed astrocytomas as a separate outcome [15]. We calculated standardized incidence ratios (SIRs) to measure cancer risk, by dividing the observed number of cancers among HEU children by the expected number. Expected counts were estimated by applying incidence rates from the general population based on sex, age (5-year categories), race/ethnicity, calendar year, and registry area.

We describe perinatal ARV medication exposure among children diagnosed with brain tumors. We also conducted a *post hoc* review of cancer registry records on children with brain tumors for evidence of inherited cancer syndromes.

## Results

The study cohort comprised 13,617 HEU children, most of whom were documented to be exposed to maternal ARVs during pregnancy and labor and delivery (Supplemental Table). Children were followed for a total of 133,667 person-years (median 9.3 years, interquartile range 4.4-15.2 years, with a maximum of 20 years). During this follow-up, 18 cancers were diagnosed, of which 6 were brain tumors (3 pilocytic astrocytomas, 1 oligoastrocytoma, 1 craniopharyngioma, 1 ependymoma), 5 leukemias (4 lymphoid leukemias, 1 chronic myeloproliferative disease), and 7 other cancers (1 fibrosarcoma, 4 nephroblastomas, 1 retinoblastoma, 1 gonadal germ cell tumor). Median age at cancer diagnosis was 2.5 years (interquartile range 1-7); 10 cases occurred among boys and 7 among girls.

Supplemental Table. Perinatal antiretroviral medication exposures among HIV-exposed uninfected children in the United States, 1990-2017.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Region | HEU children, N | Person-years of follow-up | *In utero* ARV  Exposure | | Labor and delivery ARV exposure | | Postnatal ARV  exposure | |
| Yes | Unknown/no | Yes | Unknown/no | Yes | Unknown/no |
| Connecticut | 414 | 2,584 | 97.6% | 2.4% | 83.2% | 16.8% | n/a | n/a |
| Georgia | 666 | 2,242 | 81.7% | 18.3% | 84.0% | 16.0% | n/a | n/a |
| Louisiana | 4,015 | 48,595 | 95.3% | 4.7% | 78.8% | 21.2% | 99.0% | 1.0% |
| Michigan | 1,428 | 20,867 | 50.6% | 49.4% | 38.7% | 61.3% | 57.9% | 42.1% |
| Puerto Rico | 124 | 1,752 | 13.8% | 86.2% | 12.2% | 87.8% | n/a | n/a |
| Texas | 6,970 | 61071 | 81.6% | 18.4% | 87.2% | 12.8% | 92.2% | 7.8% |
| Total | 13,617 | 133,667 | 81.2% | 18.8% | 75.7% | 24.3% | n/a | n/a |

HEU children were followed over the following calendar periods in 6 study regions: Connecticut (2006-2017), Georgia (2005-2010), Louisiana (1990-2017), Michigan (1990-2017), Puerto Rico (1990-2016), and Texas (1999-2017). HEU surveillance was complete in these regions over the periods indicated, except Georgia conducted only hospital-based surveillance in 7 centers, and Michigan had incomplete population-based HEU surveillance during 2013-2017. Postnatal ARV use was not routinely collected by all of the state health departments. Abbreviations: ARV antiretroviral, HEU HIV-exposed uninfected, n/a not available