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# Greater risk for viremia, immunosuppression, serious clinical events, and mortality with increasing age: the US perinatal HIV epidemic in its adolescence

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## Abstract

**Importance—**As perinatally HIV-infected youth (PHIVY) in the US grow older and more treatment-experienced, clinicians need updated information about the impact of age, CD4 count, viral load (VL), and antiretroviral drug (ARV) use on risks of opportunistic infections (OIs), key clinical events, and mortality in order to understand patient risks and improve care.

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**Cohort Registration:**

Pediatric HIV/AIDS Cohort Study (PHACS) Adolescent Master Protocol (AMP) (http://www.phacsstudy.org); NCT01418014 International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) P1074 (http://impaactnetwork.org); NCT01061164

**AUTHOR ROLES**

All authors contributed substantively to this manuscript in the following ways: Study design (AMN, KP, RVD, ALA, GRS III, ALC), data analysis (KP, BK), interpretation of results (all authors), drafting the manuscript (AMN, KP, BK, ALC), critical revision of the manuscript (all authors) and final approval of submitted version (all authors).

**Conflicts of Interest and Financial Disclosures**

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**Objective—**To determine the incidence or first occurrence during follow-up of key clinical events (including CDC-B and CDC-C events) and mortality among PHIVY stratified by age, CD4, and VL/ARV status.

**Design—**In the PHACS Adolescent Master Protocol (AMP) and IMPAACT P1074 multicenter cohort studies (2007–2015), we estimated event rates during person-time spent in key strata of age (7–12, 13–17, and 18–30 years), CD4 count (<200, 200–499, and ≥500 cells/μL), and VL/ARV status (< or ≥ 400 copies/mL; ARVs or no ARVs).

**Setting—**41 ambulatory sites in the US, including Puerto Rico.

**Participants—**1,562 participants in AMP and P1074 were eligible, 1446 PHIVY were included.

**Exposure(s) for observational studies—**Age, CD4 count, VL, ARV use.

**Main outcomes—**Clinical event rates stratified by person-time in age, CD4 count, and VL/ARV categories.

**Results—**During a mean follow-up of 4.9 years, higher incidences of CDC-B events, CDC-C events and mortality were observed as participants aged. Older PHIVY (13–17 and 18–30 year-olds) spent more time with VL ≥400 copies/mL and with CD4 <200/μL compared to 7–12 year-olds (30% and 44% vs. 22% of person-time with VL ≥400 copies/mL; 5% and 18% vs. 2% of person-time with CD4 <200/μL; p<0.01 for each comparison). We observed higher rates of CDC-B events, CDC-C events, bacterial infections, and mortality at lower CD4 counts, as expected. The mortality rate in older PHIVY was 6–12 times that of the general US population. Higher rates of sexually transmitted infections were also observed at lower CD4 counts, after adjusting for age.

**Conclusions and relevance—**Older PHIVY were at increased risk of viremia, immunosuppression, CDC-B events, CDC-C events, and mortality. Interventions to improve ART adherence and optimize models of care for PHIVY as they age are urgently needed to improve long-term outcomes among PHIVY.

### Keywords

Perinatal HIV infection; antiretroviral therapy; HIV viral load; CD4 count; adolescence; youth

## INTRODUCTION

Effective interventions to prevent mother-to-child HIV transmission and treat HIV-infected infants and children have shifted the US pediatric HIV epidemic; youth aged ≥13 years now represent the majority of perinatally HIV-infected youth (PHIVY) in the US.[1–3] Rates of viremia and immunosuppression have decreased among PHIVY in the US since the implementation of effective combination antiretroviral therapy (cART), but may remain higher for older PHIVY.[4,5] Compared to adults, PHIVY experience lower rates of HIV RNA viral load (VL) suppression and higher rates of loss to follow-up.[6–8] As youth age and transition to adult care, their risks of opportunistic infections (OI), other serious clinical events, and mortality are not well described.[9–14]

Understanding the frequency of important clinical events for PHIVY, as well as the consequences of being prescribed cART without a suppressed VL, will provide critical

information to design interventions for this group, who are at risk for severe illness, accumulation of resistance mutations, and secondary transmission.[15,16] Our objectives were to determine the frequency of viremia and immunosuppression among PHIVY and young adults aged 7–30 years engaged in care in two large national cohort studies and to analyze associations between age, CD4 count, viremia, ARV use, and risks of significant clinical events and mortality.

## METHODS

### Study Population

We evaluated participants in the Pediatric HIV/AIDS Cohort Study (PHACS) Adolescent Master Protocol (AMP) and the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) P1074 cohort studies. AMP enrolled 451 PHIVY aged 7–16 years between March 2007 and November 2009 at 15 US sites; follow-up is ongoing.[2] P1074 enrolled 1,201 participants (87% PHIVY) with a mean age of 17.4 years (SD 5.4) between April 2009 and June 2013 at 40 US sites; follow-up was completed in June 2014.[17] For this analysis, AMP participants were eligible if they had ≥1 visits between March 2007 and April 2015, and ≥1 CD4 and VL recorded after baseline; P1074 participants were eligible if they were PHIVY and had ≥1 chart abstraction with CD4 count and VL data recorded after baseline. AMP baseline was defined as date of study entry; P1074 baseline was defined as 1 year prior to study entry. Simultaneous co-enrollment in AMP and P1074 was not permitted. Based on guidelines, practice patterns, and trial data, we defined cART regimens as one of three mutually exclusive types expected to be suppressive: (1) ≥3 drugs from ≥2 classes, or (2) a protease inhibitor (PI, excluding ritonavir alone) + 1 drug from another class, or (3) ≥3 nucleos(t)ide reverse transcriptase inhibitors.[2,18–22] We excluded person-time when patients had VL <400 copies/mL and were not prescribed ARVs and when patients had VL ≥400 copies/mL while being prescribed an ARV regimen other than cART. Although individual patient circumstances may have warranted these approaches, they are not expected to suppress VL and were not standard of care during the study period.[2,18–22] Lost to follow-up was defined as stopping data collection for any reason other than death, study completion, or site closure.

### Clinical and Laboratory Data

Participant consent and data collection methods have been described previously for both studies.[2,17] CD4 counts, VLs, ARV use, and clinical events were abstracted from medical records, and clinical events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 18 by Frontier Science Technology and Research Foundation.[23]

### Outcome Measures

Primary outcomes included mortality and first occurrence of CDC stage C/WHO stage 4 or CDC stage B/WHO stage 3 events during follow-up.[24–27] Secondary outcomes included: bacterial pneumonia; serious bacterial infections; presumptive pelvic inflammatory disease (PID); other sexually transmitted infections (STI); pregnancy; mental health and neurodevelopmental conditions; asthma, atopy or allergy conditions; gastrointestinal

conditions; cardiac conditions; anemia; pancreatitis or hepatitis; peripheral neuropathy; and metabolic or bone abnormalities, including renal conditions. Presumptive PID and pregnancy were limited to females aged ≥13; other STIs were limited to age ≥13 and stratified by sex due to sex-specific screening practices. Each MedDRA term was assigned a single diagnostic category, except for bacterial pneumonia and PID which were included in CDC-B/WHO-3 events, and also examined separately.

### Statistical Analyses

We estimated incidence rates of key clinical events, stratified by the combination of time-varying age (7–12, 13–17, and 18–30 years), CD4 count (<200, 200–499, and ≥500/μL), and VL/ARV status. VL/ARV status was categorized as: 1) *suppressive ARVs*: VL <400 copies/mL and prescribed any ARVs, 2) *non-suppressive cART*: VL ≥400 copies/mL and prescribed cART, and 3) *no ARVs*: VL ≥400 copies/mL and not prescribed any ARVs.

We estimated incidence rates and assessed trends by age, CD4 count, and VL/ARV categories using Poisson regression models, accounting for within-subject correlation with robust standard variance estimators. For selected individual events (STIs, pregnancy and cardiac events), incidence rates by CD4 counts were adjusted for age using inverse probability weighting because person-time contributing to each age category was unevenly distributed by CD4 category.[28–33] Only the first occurrence of each event after baseline for each participant was included.

To assign participants to baseline strata and calculate the total person-time contributed by all participants to each stratum, we used linear interpolation between adjacent CD4 and $\log_{10}$-transformed VL readings, and estimated dates when strata thresholds were crossed. The nearest CD4 and VL readings prior to baseline were used when available for interpolation, and last available CD4 count and VL were carried forward until the end of follow-up.

We used weighted repeated measures generalized estimating equation (GEE) models with an independence working correlation, identity link, normal distribution and robust variance estimators to determine the association between: age and person-time with VL ≥400 copies/mL, age and person-time with CD4 <200/μL, and VL/ARV status and person-time with CD4 <200/μL. For these GEE analyses, we additionally sub-divided the older age stratum into 18–21, 22–25, and 26–30 years.

To compare mortality rates between PHIVY and youth in the general US population, we calculated standardized mortality ratios (SMRs) standardized to CDC age, sex and race distributions.[34] Confidence intervals (CI) for SMRs were calculated using the Boice-Monson method.

## RESULTS

### Characteristics of the study population

Of 1,467 PHIVY in AMP and/or P1074, we excluded 18 who did not have the combination of ARV, CD4 count and VL data at any point during follow-up, 1 who spent their entire person-time in the study with VL ≥400 while on a regimen other than cART, and 2 who

spent their entire person-time with VL <400 and off ARVs. We excluded 92.3 person-years (PY) (1.4% of overall person-time) while participants were viremic and on a regimen other than cART and 59.4 PY (0.9% of overall person-time) while participants had VL <400 copies/mL while off ARVs, from a total of 247 participants. Table 1 reports additional baseline and follow-up characteristics. Mean age at baseline was 14.6 years, with 52% female participants; 66% identified as black, and 26% identified as Hispanic. Notably, patients who were lost to follow-up differed significantly from retained patients only in baseline age (15.8 vs. 14.4 years).

## Distribution of person-time

Participants contributed 19% of person-time between ages 7–12, 38% between 13–17, and 43% between 18–30; only 2% of total person-time was between ages 26–30 (Table 2). The majority of person-time was spent with CD4 counts ≥500/μL (65% of person-time, compared to 24% at 200–499/μL and 10% at <200/μL), and on suppressive ARVs (66% of person-time, compared to 28% on non-suppressive cART and 7% on no ARVs). Person-years spent in older age strata (ages 13–17 and 18–30), compared to ages 7–12, were more likely to be spent with CD4 counts <200/μL (5% and 18% vs. 2%, p<0.001 for each pair-wise comparison). For older PHIVY (age ≥18), more person-time was also spent with VL ≥400 copies/mL (either non-suppressive cART or no ARVs, 30% and 44% vs. 22% of person-time, p<0.001 for both). When the older age stratum was further divided into 18–21, 22–25, and 26–30 years, proportions of time spent being viremic and with low CD4 counts remained substantially higher for each sub-stratum compared to younger ages (Table 3). Use of non-suppressive cART was not associated with having CD4 <200/μL, compared to use of no ARVs (25% vs. 24%, p=0.72).

## Mortality

Overall, there were 29 deaths (0.4/100PY) (eTables 1–4). Seventy-nine percent of deaths occurred at CD4 <200/μL (3.5/100PY). Eighty-three percent of deaths occurred while VL was ≥400 copies/mL, with mortality rates of 0.9/100PY for non-suppressive cART and 1.6/100PY for no ARVs (p<0.001 for trend). All but one death (97%) occurred in 18–30 year olds (1.0/100PY, p<0.001 for trend). PHIVY between ages 15–19 and 20–29 had 5.6-fold (95%CI: 2.8–11.1) and 12.3-fold (95%CI: 8.0–18.9) higher mortality rates than youth of the same age in the US general population, respectively.[34]

## First events during follow-up

**CDC-C/WHO-4 events—**There were 86 CDC-C/WHO-4 events (1.4/100PY; eTable 5). Higher rates of CDC-C/WHO-4 events were observed at lower CD4 counts (<200/μL: 9.6/100PY; 200–499/μL: 1.0/100PY; ≥500/μL: 0.4/100PY; p<0.001 for trend). Of 17 events that occurred at CD4 counts ≥500/μL (20% of total), only 2 were OIs (pulmonary tuberculosis and ocular toxoplasmosis); others were HIV-related kidney and cardiac disease. Higher rates of CDC-C/WHO-4 events occurred with higher VL (suppressive ARVs: 0.6/100PY; non-suppressive cART: 3.0/100PY; no ARVs: 2.4/100PY; p<0.001 for trend). Higher rates of CDC-C/WHO-4 events were also observed with older age (7–12: 0.7/100PY; 13–17: 0.9/100PY; 18–30: 2.1/100PY; p<0.001 for trend).

**CDC B/WHO-3 events—**There were 193 CDC-B/WHO-3 events (3.2/100PY; Figures 1 and 2; eTable 6). Higher rates of CDC-B/WHO-3 events were observed at lower CD4 counts (<200/μL: 12.5/100PY; 200–499/μL: 3.8/100PY; ≥500/μL: 1.8/100PY; p<0.001 for trend). CDC-B/WHO-3 events were also more common at higher VL (suppressive ARVs: 2.0/100PY; non-suppressive cART: 5.5/100PY; no ARVs: 7.1/100PY; p<0.001 for trend). These event rates also increased as participants aged (7–12: 2.4/100PY; 13–17: 2.9/100PY; 18–30: 3.9/100PY; p=0.01 for trend). For bacterial pneumonia (CDC-B/WHO-3 event) and serious bacterial infections, higher event rates were also observed at lower CD4 counts and higher viral loads, but no trends were observed by age (eTables 7 and 8).

**Reproductive system events—**In female participants, higher rates of presumptive PID, other STIs, and pregnancies were observed with older age and with VL >400 copies/mL (eTables 9–11); higher rates of STIs (not including PID) and pregnancy were observed with lower CD4 counts. After adjusting for age, the association between increasing rates of pregnancies and lower CD4 counts no longer reached significance (<200/μL: 4.5/100PY; 200–499/μL: 4.8/100PY; ≥500/μL: 2.8/100PY; p=0.18); however, the trend of increased rates of first female STI at lower CD4 counts remained significant (<200/μL: 8.1/100PY; 200–499/μL: 5.9/100PY; ≥500/μL: 3.1/100PY; p<0.001). First STIs were infrequently reported in males (eTable 12).

**Other clinical events—**Mental health and neurodevelopmental conditions were among the most frequent conditions (4.0/100PY); no trends were observed by age, CD4 count, or VL/ARV strata (eTable 13). For asthma, atopy or allergy conditions, no trends were observed by age, CD4 count or VL/ARV strata (eTable 14). For gastrointestinal conditions, rates increased with lower CD4 counts (p<0.001); however, no trends were observed by age or VL/ARV strata (eTable 15). Higher rates of first non-AIDS-defining cardiac events were observed at lower CD4 counts (eTable 16), although this trend was no longer significant after adjusting for age (<200/μL: 2.1/100PY; 200–499/μL: 1.0/100PY; ≥500/μL: 0.7/100PY; p=0.08). Events potentially attributed to antiretroviral toxicity such as anemia (0.0/100PY), pancreatitis or hepatitis (0.4/100PY) and peripheral neuropathy (0.2/100PY) were among the least frequently reported events (eTables 17–19). Rates of first metabolic or bone abnormalities (1.5/100PY) showed no difference by age or CD4 count, but trended towards lower rates in patients with VL >400 copies/mL (suppressive ARVs: 1.7/100PY; non-suppressive cART: 1.1/100PY; no ARVs: 0.7/100PY; p=0.04) (eTable 20).

## DISCUSSION

We analyzed rates of clinical events and mortality during 6,548 person-years of follow-up from 1,446 PHIVY aged 7–30 years in the AMP and P1074 cohort studies, stratified by time-updated age, CD4 count, and VL/ARV status. There were three key findings from this work. First, older youth were at highest risk for viremia, low CD4 counts, and serious clinical events, including mortality, CDC-C/WHO-4, and CDC-B/WHO-3 events. Viral load monitoring remained consistent across age ranges, suggesting ongoing engagement in care; high overall rates of viremia in participants aged 18–30 years are likely therefore due to suboptimal medication adherence or acceptance, or accumulated HIV viral resistance. Older PHIVY had greater early exposure to mono- or dual-regimens compared to younger PHIVY;

the lack of viral suppression among those PHIVY prescribed cART is more likely related to poor medication adherence or acceptance, as resistance to newer ARVs, such as integrase inhibitors, is uncommon.[35] Older youth also spent more time with CD4 counts <200/μL. Data from PHIVY aged 6–17 suggest that having CD4 counts <200/μL is associated with lower quality of life, psychiatric symptoms, and poor cognitive, academic, and social functioning, and data from adults suggest high risks of OIs and death.[36,37] Our findings are consistent with a growing literature outlining the challenges to adhering to medications for PHIVY in adolescence, which intensify as PHIVY reach early adulthood[38–43]

Second, we observed relatively few clinical events and deaths during the follow-up period, during which cART was standard of care. These results add to prior reports of clinical events in AMP and P1074 by stratifying clinical event rates by time-updated age, CD4, and VL/ARV status.[1,17] Our results are similar to other cohort studies of PHIVY in the US, UK and Ireland.[9,13,44] For example, our observed incidence rates of mortality (0.4/100 PY), CDC-C/WHO-4 events (1.4/100 PY), CDC-B/WHO-3 events (3.2/100 PY), and bacterial pneumonia (1.4/100 PY) were comparable to those reported in the PACTG 219c cohort in 2006, 10 years into the cART-era (mortality: 0.5–0.8/100 PY; CDC-C: 1.5/100 PY; CDC-B: 5.0/100 PY; bacterial pneumonia 2.2/100 PY).[5,12,44] However, the mortality rate in older adolescent (ages 15–19) and young adult (ages 20–29) PHIVY remained 6 and 12 times that of the US general population, respectively, after accounting for age, sex, and race. STIs among female participants and mental health and neurodevelopmental diagnoses were among the most commonly documented conditions. Higher STI rates (excluding PID) among female participants were associated with lower CD4 counts after adjusting for age. This finding has been previously reported, as well as the association of lower CD4 with herpes simplex virus reactivation and lack of human papilloma virus clearance.[28–30,45–49] These data suggest a potential biological effect of immunosuppression; additionally, more frequent risk behavior among patients incompletely adherent to cART may contribute to higher STI rates.[8,30] Pregnancy rates overall (3.5/100PY) and at older ages (13–17 years: 2.0/100PY and 18–30 years: 4.9/100PY) were similar to the general population (range for 15–29 years: 3.95–16.30/100PY).[50] Pregnancy rates were higher among those with lower CD4 counts, although the strength of this relationship decreased after age adjustment. Complications potentially related to long-term antiretroviral therapy, including anemia, pancreatitis, hepatitis, peripheral neuropathy, and metabolic and bone abnormalities, were documented infrequently, likely reflecting use of less toxic ARVs over time.[35,51]

Finally, our person-time results add a valuable dimension to the literature base of cross-sectional and longitudinal studies on viremia in PHIVY. In the AMP and P1074 cohorts described here, 66% of person-time was spent with VL <400 copies/mL, similar to that observed in the HIV Research Network (63% of PHIVY aged 12–21 with VL <400 copies/mL from 2009–2012). However, viral suppression is higher than reported in the Adolescent Trials Network (ATN, 37% of PHIVY with VL below the lower level of detection) and in a recent meta-analysis (pooled North America estimate of youth with suppressed VL: 53% (range: 28–75%) of youth aged 12–24 years from 1990–2013).[4,8,52] While lower suppression rates in the meta-analysis cohorts may reflect the inclusion of non-perinatally HIV-infected youth, lower suppression rates for PHIVY in the ATN cohort may reflect older age in that cohort (17.9 years versus 14.6 years). In contrast to data from adults,

we found that having VL ≥400 copies/mL while being prescribed cART did not improve immunosuppression compared to having VL ≥400 copies/mL while taking no ARVs at all.[53–61] The 35% of person-time spent with VL ≥400 copies/mL in our study raises critical concerns not only for individual patient outcomes, but also for the HIV epidemic among US youth.[30,35,62] Youth who are viremic despite being engaged in care are more likely to have resistant virus and to report lower condom use than non-viremic youth, and thus are at risk of secondary horizontal or vertical transmission.[63–65]

This analysis of PHIVY in two large cohort studies had several limitations. First, the smallest proportion of person-time (19%) was spent at ages 7–12; nevertheless, we had adequate power for all statistical comparisons. Next, data collection protocols in the two cohorts may have impacted incidence rate estimates for specific events: 1) because we analyzed first events, we could not identify "recurrent bacterial pneumonia," potentially underestimating CDC-C events; 2) STI screening was not performed at study-specific intervals but per local care practice; 3) care sought by participants at non-study healthcare facilities was recorded only if reported to study staff. Additionally, P1074 recorded only events deemed "clinically significant" by healthcare providers, whereas AMP recorded all events; we addressed this limitation by including only events that met the reporting threshold for both studies (e.g. laboratory-value diagnoses were excluded). Furthermore, PHIVY least engaged in care and at highest risk for adverse outcomes may not have been included. Conversely, to permit consistent coding of events between the AMP and P1074 studies, we excluded events prior to baseline, which may have led to overestimation of some first event rates. Finally, adherence data were not included in the analysis, because adherence measures were collected only in one study (AMP). Despite these counterbalancing possibilities, this analysis provides the most recent, detailed data available about clinical risks in US PHIVY over time. This information will be critical information for US policy makers as research and programmatic funding shifts for pediatric HIV in the US.[66]

In summary, we find that serious clinical events, including OIs and death, are rare in PHIVY receiving suppressive ART, but viremia, lower CD4 counts, and rates of serious clinical events and mortality increase throughout adolescence and young adulthood. Interventions to improve ART adherence and optimize models of care as perinatally HIV-infected youth age are urgently needed to improve long-term outcomes among this growing and vulnerable population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**PHACS**

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**IMPAACT**

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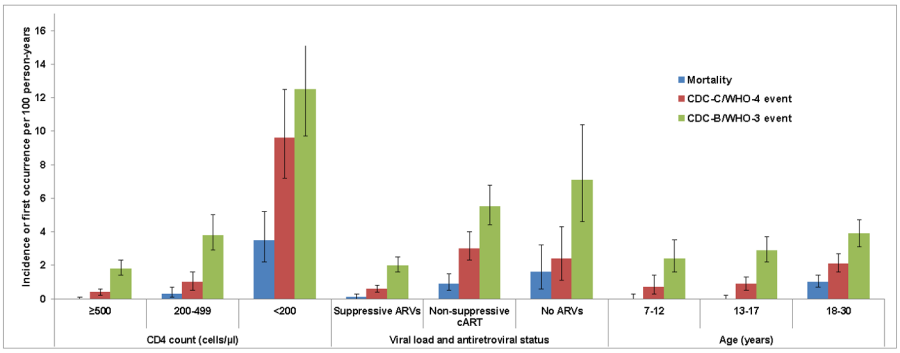


**Figure 1.**

Incidence of mortality and first occurrence of CDC-C/WHO-4 and CDC-B/WHO-3 events by CD4 count, viral load and antiretroviral status and age in AMP and P1074

VL: viral load; ARV: antiretroviral; cART: combination antiretroviral therapy

Exact Poisson 95% confidence intervals are presented in the error bars.

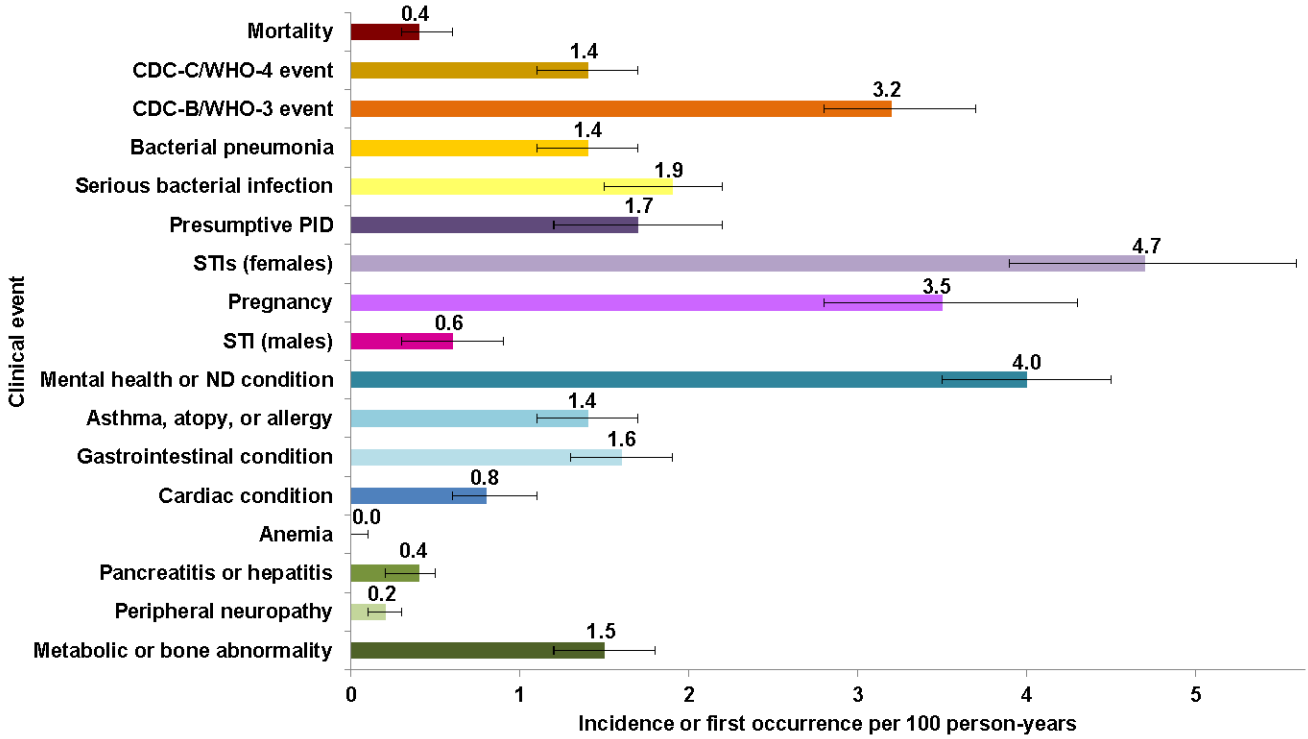


**Figure 2.**

Incidence of mortality and first occurrence of all clinical outcomes in AMP and P1074

PID: pelvic inflammatory disease; STI: sexually transmitted infection; ND: neurodevelopmental

Exact Poisson 95% confidence intervals are presented in the error bars.

## Table 1

Characteristics of PHACS AMP and IMPAACT P1074 participants at baseline

| Study | Participants, n (%) |
|---|---|
| AMP | 421 (29%) |
| P1074 | 1,008 (70%) |
| Both | 17 (1%) |
| **Demographic characteristics** | **Total participants (n=1,446)** |
| Age at baseline, years, mean (SD) | 14.6 (4.6) |
| Female sex, n (%) | 759 (52%) |
| Year of birth, mean (SD) | 1994 (4.6) |
| Race | |
| Black/African-American, n (%) | 953 (66%) |
| White/other, n (%) | 470 (33%) |
| Not reported, n (%) | 23 (2%) |
| Hispanic ethnicity, n (%) | 370 (26%) |
| Not reported, n (%) | 1 (0%) |
| **Clinical characteristics** | |
| CD4 count at baseline, cells/μL, mean (SD) | 712 (422) |
| Viral load <400 copies/mL at baseline, n (%) | 934 (65%) |
| Prescribed cART at baseline, n (%) | 1,330 (92%) |
| Prescribed ARVS but not cART at baseline, n (%) | 68 (5%) |
| No ARVs at baseline, n (%) | 48 (3%) |
| CD4 counts per person per year during follow-up, mean (SD) | 3.6 (9.6) |
| Viral loads per person per year during follow-up, mean (SD) | 3.6 (9.6) |
| Total ARV regimens per person, mean (SD) [a] | 2.4 (1.6) |
| Years of follow-up under study protocols, mean (SD) | 4.9 (1.3) |
| Cumulative loss to follow-up, n (%) | 171 (12%) |

Data are presented as number (%), or mean (SD).

[a]Regimen change was defined as a change in any single drug.

ARV, antiretroviral; cART, combination antiretroviral therapy; IMPAACT, International Maternal Pediatric Adolescent AIDS Clinical Trials Network; PHACS AMP, Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol; VL, viral load.

## Table 2

Distribution of person-time stratified by age, CD4 count and viral load and antiretroviral status

| Distribution of person-time during follow-up | Participants, n (%) [a] | Person-time, years (%) [b] |
|---|---|---|
| Age (years) | | |
| 7–12 | 504 (35) | 1,243 (19) |
| 13–17 | 921 (64) | 2,459 (38) |
| 18–30 | 967 (67) | 2,846 (43) |
| 18–21 | 871 (60) | 1,887 (29) |
| 22–25 | 428 (30) | 806 (12) |
| 26–30 | 87 (6) | 153 (2) |
| CD4 count (cells/μL) | | |
| ≥500 | 1,211 (84) | 4,286 (65) |
| 200–499 | 850 (59) | 1,597 (24) |
| <200 | 318 (22) | 664 (10) |
| VL/ARV status | | |
| Suppressive ARVs | 1,328 (92) | 4,292 (66) |
| Non-suppressive cART | 941 (65) | 1,810 (28) |
| No ARVs | 346 (24) | 445 (7) |

[a] Number of participants contributing person-time towards a given stratum.

[b] Participants may contribute person-time to more than one stratum.

ARV, antiretroviral; cART, combination antiretroviral therapy; VL, viral load.

**Table 3**

Person-time: Association between age, CD4 count and viral load and antiretroviral status

| | CD4 count, cells/μL [a] | | | Viral load / ARV status [b] | | |
|---|---|---|---|---|---|---|
| | **<200** | **200–499** | **≥500** | **Suppressive ARVs** | **Non-suppressive cART** | **No ARVs** |
| Age, years | | | | | | |
| 7–12 | 19.2 (2%) | 139.8 (11%) | 1084.1 (87%) | 958.6 (77%) | 239.5 (19%) | 45.1 (4%) |
| 13–17 | 129.3 (5%) | 558.9 (23%) | 1,770.4 (72%) | 1,726.1 (70%) | 587.3 (24%) | 145.2 (6%) |
| 18–30 | 515.7 (18%) | 898.5 (32%) | 1,431.7 (50%) | 1,607.3(56%) | 983.6 (35%) | 255.0 (9%) |
| 18–21 | 276.7 (15%) | 592.4 (31%) | 1,018.1 (54%) | 1,087.0 (58%) | 648.6 (34%) | 151.6 (8%) |
| 22–25 | 202.3 (25%) | 263.0 (33%) | 340.8 (42%) | 426.2 (53%) | 291.0 (36%) | 89.1 (11%) |
| 26–30 | 36.6 (24%) | 43.1 (28%) | 72.8 (48%) | 94.2 (62%) | 44.1 (29%) | 14.3 (9%) |
| Viral load/ARV status [c] | | | | | | |
| Suppressive ARVs | 95.4 (2%) | 699.2 (16%) | 3,497.4 (81%) | | | |
| Non-suppressive cART | 460.4 (25%) | 704.7 (39%) | 645.3 (36%) | | | |
| No ARVs | 108.5 (24%) | 193.3 (43%) | 143.5 (32%) | | | |

Row percents are presented.

[a] Proportion of person-time with CD4 count <200 cells/μL according to age: Relative difference (95% confidence interval): 13–17 vs. 7–12 years: 4% (2 – 5%); 18–21 vs. 7–12 years: 13% (10 – 16%); 22–25 vs. 7–12 years: 24% (19 – 28%); 26–30 vs. 7–12 years: 22% (13 – 31%); p<0.001 for all comparisons.

[b] Proportion of person-time with VL ≥400 copies/mL according to age: Relative difference (95% confidence interval): 13–17 vs. 7–12 years: 7% (3 – 11%); 18–21 vs. 7–12 years: 20% (15 – 24%); 22–25 vs. 7–12 years: 24% (18 – 30%); 26–30 vs. 7–12 years: 15% (5 – 25%); p<0.01 for all comparisons. The median frequency of HIV RNA measurements during follow-up for subjects while aged 7–12, 13–17, 18–21, 22–25, and 26–30 years was every 3.6, 3.5, 3.9, 4.3, and 4.3 months, respectively.

[c] Proportion of person-time with CD4 count <200 cells/μL according to VL/ARV status: Relative difference (95% confidence interval): suppressive ARVs vs. no ARVs: −22% (−28 – −17%), p<0.001, non-suppressive cART vs. no ARVs: 1% (−5 – 7%), p=0.72. (Similar results were seen for the outcome of CD4 count <500/μL.)

ARV, antiretroviral; cART, combination antiretroviral therapy