Ageing with HIV: a longitudinal study of markers of resilience in young adults with perinatal exposure to HIV, with or without perinatally acquired HIV

Patricia A. Sirois1,§, Yanling Huo2, Molly L. Nozyce3, Patricia A. Garvie4, Lynnette L. Harris5, Kathleen Malee6, Robin McEvoy7, Claude A. Mellins8, Sharon L. Nichols9, Renee Smith10, Katherine Tassiopoulos11 and for the Pediatric HIV/AIDS Cohort Study

1§Corresponding author: Patricia A. Sirois, Department of Pediatrics, Tulane University School of Medicine, 1430 Tulane Avenue, Mail Code 8441, New Orleans, LA 70112, USA. (psirois@tulane.edu)

Abstract

Introduction: Medical challenges, including perinatally acquired HIV (PHIV), can be considered adversity with the potential to compromise individuals’ ability to meet societal expectations across the lifespan. Studies suggest that resilience, defined as positive adaptation in the context of adversity, helps individuals overcome challenges and improve their quality of life. Few longitudinal studies have examined resilience in young adults with perinatally acquired HIV (YAPHIV) or perinatal HIV exposure, uninfected (YAPHEU). We examined three young adult milestones, which can affect the life-long quality of life, as markers of resilience: high school graduation, postsecondary education and current employment.

Methods: Analyses included YAPHIV and YAPHEU, ages 19–27 years, followed in longitudinal cohort studies: Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol (AMP) (7–17 years) and AMP Up (≥18 years). Factors known to influence the attainment of milestones (outcomes) were examined: executive function, cognitive efficiency (working memory and processing speed), behavioural/social-emotional functioning, parent/caregiver mental/physical health and cumulative risk. HIV disease markers for YAPHIV were examined. The most recent AMP assessment was used for each factor; outcomes were measured at AMP Up 1-year follow-up. Separate robust Poisson regression models were used to assess associations of each factor with each outcome; PHIV status was explored as an effect modifier of each association.

Results: Participants (N = 315; YAPHIV = 228): 58% female, 67% Black and 27% Hispanic. Compared to YAPHEU, YAPHIV were older and from families with higher median income and fewer symptoms of parent/caregiver mental health/substance use disorders. Proportions of YAPHEU and YAPHEU, respectively, who achieved each milestone were comparable: 82% versus 78% for high school graduation (p = 0.49), 45% versus 51% for postsecondary education (p = 0.35) and 48% versus 54% for current employment (p = 0.32). Higher cognitive efficiency was positively associated with postsecondary education and current employment. Higher executive function, age-appropriate behavioural/social-emotional functioning and lower cumulative risk were associated with academic milestones. Among YAPHEU, positive associations were: higher current CD4 with postsecondary education and lower nadir CD4 with current employment. PHIV status did not modify any association.

Conclusions: YAPHEU and YAPHEU demonstrated resilience, attaining at least one young adult milestone. Cognitive, behavioural and social resources to support resilience in childhood and adolescence may provide the foundation for continued achievement throughout adulthood.

Keywords: resilience; young adults; perinatal HIV-exposed uninfected; perinatal HIV infection; milestones; lifespan development

Received 18 January 2022; Accepted 1 August 2022
Copyright © 2022 The Authors. Journal of the International AIDS Society published by John Wiley & Sons Ltd on behalf of the International AIDS Society. This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

1 INTRODUCTION

Resilience, defined as positive adaptation in the context of risk or adversity [1, 2], is instrumental to the quality of life and attainment of goals in young adulthood, particularly in the areas of work and vocational or higher education. Quality-of-life indicators in adulthood, such as financial stability, physical and mental health, and life expectancy, are improved with the attainment of high school and postsecondary education [3]. There is little information about high school graduation and higher education in the population with perinatal HIV exposure or perinatally acquired infection in the United States.
Therefore, we examined the attainment of three societal milestones known to contribute to the life-long quality of life: high school graduation, postsecondary education and employment.

Perinatal HIV exposure, with or without perinatally acquired HIV, can confer risks to development and well-being in childhood [4–10] and subsequently to quality of life in adulthood. Results from the Pediatric HIV/AIDS Cohort Study (PHACS) documented lowered performance in children and adolescents with perinatal HIV exposure compared to nationally representative test standardization samples on measures of key developmental domains. These include intellectual ability and academic achievement [11–13], language [14, 15], learning, memory, executive function [16–19] and adaptive behaviour [11, 18]. Children and adolescents with perinatally acquired HIV (PHIV) or with perinatal HIV exposure who are uninfected (PHEU) demonstrated higher rates of behavioural or emotional problems than their peers in the general population. These rates were not attributed solely to PHIV because children with PHEU showed similar or even higher rates of mental health problems [20–22]. Youth with PHIV or PHEU are often from vulnerable communities affected by poverty, racism and discrimination, familial stressors and health disparities that can affect development across multiple domains [7, 23–27]. Thus, it is critical to determine factors that might influence the attainment of young adult milestones as youth transition through the lifespan. This knowledge could form the basis for evidence-based interventions to benefit this population.

Many factors are known to influence adaptation to adversity: relationships with parents/caregivers and other adults; friends and romantic partners; intelligence and problem-solving skills; self-control, emotional regulation and planning; and self-efficacy and motivation [2]. Risks to optimal development include maternal education less than high school, parental divorce or death, single-parent family, perceived individual and structural racism and witnessing violence [2, 28]. Family socio-economic status (SES) is related to physical health and achievement of societal milestones, such as high school graduation, postsecondary education and sustained employment; thus, poverty and low SES, whether chronic or of recent onset, confer risks to development and are considered major stressors for children, adolescents and families [23, 29–32]. Medical illnesses present additional stressors related to disease and treatment. Regardless of the source of stress, increases in the cumulative number of stressors have been associated with increases in child maladaptation [2, 25–27]; Rutter [33] found child psychiatric problems increased substantially when any combination of four or more stressors was present in the family. Despite this knowledge base, there is a paucity of information about HIV and its effect on goal attainment as youth with PHIV or PHEU age into young adulthood.

This study draws from research in the fields of resilience and paediatric HIV to examine, from a lifespan developmental perspective, the influence of youth and parent/caregiver characteristics on the attainment of young adult milestones of high school graduation, enrolment in postsecondary education and entry into the workforce. These outcomes reflect the attainment of societal expectations for older adolescents and young adults in the United States [3]. The hypotheses were: (1) compared to young adults with PHEU (YAPHEU), a lower proportion of young adults with PHIV (YAPHIV) will earn a high school diploma or graduate equivalency degree (GED); enrol in postsecondary education, or become employed; (2) regardless of PHIV status, difficulties in youth cognitive and behavioural development and parent/caregiver mental and physical health will adversely affect the attainment of milestones; (3) regardless of PHIV status, higher cumulative risk, that is a greater number of individual, familial and life event risks, will adversely affect the attainment of these milestones; and (4) YAPHIV with better immune function will be more likely to attain one or more milestones than those with poorer immune function.

2 | METHODS

2.1 | Participants

The PHACS Adolescent Master Protocol (AMP) and PHACS AMP Up are prospective cohort studies of children, adolescents and young adults with PHIV or PHEU followed for long-term evaluation of cognitive, behavioural, social-emotional and physical health outcomes. In 2006, AMP began enrolling children and adolescents, age 7–15 years, at 15 sites in the United States and Puerto Rico, following them until their 18th birthday. AMP follow-up ended in 2021. In 2014, AMP Up began enrolment at 14 AMP sites for follow-up of AMP participants and other eligible YAPHIV age 18 and older. All YAPHIV and YAPHEU age 19 and older, who were previously followed in AMP and had completed the 1-year follow-up visit in AMP Up, were eligible for this analysis. Annual study visits in AMP included face-to-face testing with participants, interviews with participants and parents/caregivers and medical chart abstraction. Annual study visits in AMP Up include interviews with participants, web-based surveys and medical chart abstraction. Informed consent and assent were obtained from parents/caregivers and participants at the time of enrolment into AMP and from participants at enrolment into AMP Up. Both protocols were reviewed and approved by Institutional Review Boards at all participating sites and Harvard T.H. Chan School of Public Health.

2.2 | Milestone outcomes

Attainment of education and employment milestones was assessed by a web-based survey administered 1 year after entry into AMP Up. High school graduation was defined as receipt of a high school diploma or GED; participants reporting enrolment in postsecondary education without reporting receipt of a high school diploma or GED were counted as high school graduates. Postsecondary education included vocational or technical schools, 2-year associate degree or certification programmes, 4-year college bachelor programmes and graduate education. Employment was defined as current part-time or full-time work.

2.3 | Potential predictors

Several domains of functioning were evaluated as potentially associated with the attainment of the three outcomes
Figure 1. Compensatory (main effects) model of resilience in the AMP Up cohort of the Pediatric HIV/AIDS Cohort Study. Resilience was defined by participants' attainment of one or more young adult milestones. A measure of cumulative risk developed for this study assessed the total number of risks present across all domains. All measures were collected during AMP except for the PHQ-9 and CES-D-10 collected at entry into AMP Up. AMP, Adolescent Master Protocol; AMP Up, long-term follow-up of participants age 18 and older; BASC-2, Behavior Assessment System for Children, Second Ed. [37]; BRIEF, Behavior Rating Inventory of Executive Function [36]; BRI, Behavioral Regulation Index; CDC, Centers for Disease Control and Prevention; CES-D-10, Center for Epidemiological Studies Depression Scale [42]; MCI, Metacognition Index; PHQ-9, Patient Health Questionnaire [41]; Wechsler, Wechsler Intelligence Scale for Children, Fourth Ed. [34] or Wechsler Adult Intelligence Scale, Fourth Ed. [35]; YAPHIV, young adults with perinatally acquired HIV.

(Figure 1). Measures of each domain were administered on a regular schedule during AMP follow-up; not all measures were scheduled for the same visit. Measures selected for this analysis (Table 1) were obtained at the last AMP visit at which each measure was administered. Only those considered valid by internal test validity indices and/or examiner judgement were included. Data from AMP were used as predictors; AMP Up 1-year follow-up data were used for outcomes. Each measure was assessed individually to identify associations between predictors and outcomes. The measures were also combined...
Table 1. Potential predictors measured during AMP and included in the analysis

| Domain                                               | Measure                                                                 | Selected index/subtest score                          |
|-------------------------------------------------------|-------------------------------------------------------------------------|-------------------------------------------------------|
| Executive functioning                                 | Behavior Rating Inventory of Executive Function (BRIEF) [36], participant self-report and parent/caregiver report; administered as interviews | Behavioral Regulation Index (BRI) and Metacognition Index (MCI) |
| Cognitive efficiency                                  | Wechsler intelligence scales, child or adult version as appropriate for age [34, 35]; face-to-face testing with participant, using standardized administration procedures | Working Memory Index (WMI) and Processing Speed Index (PSI) |
| Behavioural and social-emotional functioninga         | Behavior Assessment System for Children, Second Edition (BASC-2) [37], participant self-report and parent/caregiver report; administered as interviews | Internalizing Problems, Emotional Symptoms and Personal Adjustment indices from the participant self-report; Externalizing Problems, Behavioral Symptoms and Adaptive Skills indices from the parent/caregiver report |
| Life events                                           | Life Events Checklist [38], participant self-report of potentially traumatic events; administered as interview | Average life events reported during AMP follow-upb    |
| HIV disease severity (YAPHIV only)                    | a) CD4 count (cells/mm³)                                                | a) Nadir and most recent                               |
|                                                      | a) Viral load (copies/ml)                                               | b) Peak and most recent                                |
|                                                      | c) Centers for Disease Control and Prevention (CDC) classification [39]; data obtained through medical chart abstraction | c) Class C (AIDS-defining diagnoses) versus non-Class C |
| Parent/caregiver characteristics                      | a) Client Diagnostic Questionnaire (CDQ) [40]; administered as interview | a) Number of positive screens for mental health and substance use disorders |
|                                                      | b) Caregiver health interviewd                                          | b) Number of functional limitations in physical health |
|                                                      | c) Caregiver quality of life interviewd                                 | c) Number of potentially traumatic life events during 12 months prior to interview |

Abbreviations: AMP, Adolescent Master Protocol; PHACS, Pediatric HIV/AIDS Cohort Study.

aDepending on time of entry into AMP Up, symptoms of depression were measured with one of two depression screening instruments: the Patient Health Questionnaire (PHQ-9) [41] or the Center for Epidemiological Studies Depression Scale (CES-D-10) [42]. Results are reported only for descriptive purposes. Total score ≥10 on either measure indicated a positive screen for symptoms of depression, not a diagnosis. Referrals for further clinical evaluation were provided as needed.

bA participant-reported screening measure for potentially traumatic life experiences (e.g. illness/death in family, witnessing violence and change in residence) during the 12 months prior to the interview. The average life events score (total events reported over AMP follow-up divided by total number of interviews completed in AMP) was used in the analysis to allow examination of chronic stress rather than recent stress.

cParent/caregiver self-report of symptoms of their own mental health and substance use. Positive scores indicated positive screens for disorders, not diagnoses.

dParent/caregiver self-reports developed for the Pediatric AIDS Clinical Trials Group and subsequently used in PHACS.

into a study-specific cumulative risk index, based on research indicating that cumulative stress is positively associated with adverse outcomes [2, 25–27, 33]. The index score reflected the total number of risks present across all domains. Risks were defined as follows: (1) performance greater than 1.0 standard deviation below the mean for age on the Wechsler [34, 35] Working Memory Index (WMI) and Processing Speed Index (PSI) or above cutoffs indicating clinically relevant concern on indices of the Behavior Rating Inventory of Executive Function (BRIEF) [36] and Behavior Assessment System for Children, Second Edition (BASC-2) [37] (Table 1); (2) number of parent/caregiver-reported symptoms of their own mental health, substance use and physical health problems >1; (3) average number of participant-reported life events >3; and (4) number of parent/caregiver-reported life events >3. The total score ranged from 0 to 13, determined by calculating the presence (1) or absence (0) of each risk.

Based upon prior research [2, 28–33], the following participant and family characteristics were included in the multivariable models as confounding variables: participant age at the time of measurement of each potential predictor, sex, race/ethnicity, Wechsler [34, 35] Full-Scale Intelligence Quotient (FSIQ) and family SES, using annual household income and household density.
2.4 | Statistical analysis

Using chi-square or Fisher’s exact test, as appropriate, the proportions of participants who attained each of the three milestones were compared by PHIV status and age at outcome measurement. Each of the potential predictors, as well as proportions of participants who attained zero, one, two or all three milestones, were compared by PHIV status. Separate univariable and multivariable robust Poisson regression models were fit to evaluate the association of each measure with each milestone. Inverse probability of censoring weighting was used to adjust for potential selection bias due to loss to follow-up (censoring) of AMP participants who did not enrol into AMP Up. Weights were generated by fitting logistic regression models for 669 AMP participants (excluding five deaths and four with no visits after enrolment into AMP), with censoring as the outcome. Variables included as predictors of censoring were age, FSIQ and education at the most recent AMP visit, sex, race/ethnicity and research site, as well as the potential predictors of the milestone outcomes. The model for YAPHIV also included CD4 and viral load at the most recent AMP visit. The weights were then incorporated into the Poisson regression models. To evaluate whether any of the associations differed by PHIV status (effect modification), an interaction term between PHIV status and each measure was added to the univariable and multivariable models.

The multiple imputation approach was used to account for missing predictor and covariate measures. Fully conditional specification with discriminant function was used to impute missing data for categorical variables; the predictive mean matching method was used to impute missing data for continuous variables. Sensitivity analyses were conducted using the complete case analysis approach, excluding participants with incomplete data on any milestone. Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

3 | RESULTS

3.1 | Participant and parent/caregiver characteristics

AMP enrolled 678 participants. As of 1 January 2020, there were 712 participants enrolled in AMP Up, 411 of whom were previously enrolled in AMP (61%). Of the 411, 315 (228 YAPHIV and 87 YAPHEU) had completed the AMP Up Year 1 web-based survey and were included in the analysis. Table 2 summarizes participant and parent/caregiver characteristics for YAPHIV and YAPHEU and disease severity for YAPHIV. Compared to YAPHEU, YAPHIV were older (mean age 20.2 vs. 20.8 years, respectively, p = 0.002; range 19–27 years), more often from families with greater financial resources per person supported (p < 0.001) and with parents/caregivers less likely to screen positive for mental health or substance use disorders (p < 0.001 and p = 0.03, respectively). Measures of HIV disease severity indicated that 39% of YAPHIV had nadir CD4 <200 cells/mm³ and 28% had received a CDC Class C classification [39] at some time in their lives. For the majority of YAPHIV, the most recent CD4 count was ≥500 cells/mm³ (63%), and the most recent viral load was <400 copies/ml (64%). Primary caregivers included biological parents (43% YAPHIV vs. 77% YAPHEU); biological family members (24% vs. 14%, respectively); and non-biological family, such as adoptive and foster parents (32% vs. 9%, respectively). These data are presented for descriptive purposes and were not included in the analysis. A majority of parents/caregivers (68–72%) had a high school education or higher; 48–59% reported at least one limitation in physical health.

3.2 | Milestone outcomes

The proportions of YAPHIV and YAPHEU, respectively, who achieved each of the milestones were comparable: 82% versus 78% for high school graduation (p = 0.49), 45% versus 51% for postsecondary education (p = 0.35) and 48% versus 54% for current employment (p = 0.32). The proportions of YAPHIV and YAPHEU, respectively, who attained zero (11% vs. 16%), one (27% vs. 16%), two (37% vs. 37%) or all three milestones (24% vs. 31%) were also similar (p = 0.14). A small number of participants (n = 40; 13%) did not achieve any milestones (Table 3). This finding was associated with lower family SES and lower participant FSIQ, as well as lower cognitive efficiency and executive functioning (data not shown), which may be related to FSIQ. Among the 19-year-olds (n = 151), 72% had graduated high school by the AMP Up Year 1 follow-up visit; high school graduation rates were 93% for those age 22 and older (n = 59) (Table 3). There was greater variability across ages in the attainment of the other two milestones.

3.3 | Comparisons by PHIV status

3.3.1 | Executive functioning

On average, YAPHIV and YAPHEU were within age expectations on the Behavioral Regulation Index (BRI) and Metacognition Index (MCI) of the BRIEF, with no significant differences between the groups (Table 4).

3.3.2 | Cognitive efficiency

Compared to same-age peers in the Wechsler standardization samples, on average, YAPHIV and YAPHEU were within the Wechsler Low Average to Average range for age on the WMI and PSI and did not differ statistically from one another (Table 4). However, 9–10% of participants in both groups showed impairment in working memory (WMI <70); 6–7% showed impairment in processing speed (PSI <70).

3.3.3 | Behavioural and social-emotional functioning

According to the BASC-2 parent/caregiver reports, YAPHEU were more likely to show symptoms of externalizing behaviour problems than YAPHIV, although results for both groups, on average, were within age expectations. According to participant self-reports, there were no differences between the groups on any BASC-2 measures of behavioural and social-emotional functioning (Table 5); on average, both groups were within age expectations. Participants (18%) in both groups screened positive for symptoms of depression on the Patient Health Questionnaire (PHQ-9) [41] or Center for Epidemiological Studies Depression Scale (CES-D-10) [42] completed at AMP Up entry.
Table 2. Participant and parent/caregiver characteristics measured during AMP

| Perinatal HIV status | YAPHIV (n = 228) | YAPHEU (n = 87) | p-value |
|----------------------|------------------|-----------------|---------|
| **Participant characteristics** | | | |
| Age (years) at AMP Up Year 1 follow-up visit | Mean (SD) | 20.8 (1.6) | 20.2 (1.5) | 0.002<sup>a</sup> |
| | M | 93 (41%) | 39 (45%) | 0.52<sup>b</sup> |
| | F | 135 (59%) | 48 (55%) | 0.52<sup>b</sup> |
| Race/Ethnicity | Black, non-Hispanic | 160 (70%) | 50 (57%) | 0.13<sup>b</sup> |
| | White/other, non-Hispanic | 12 (5%) | 5 (6%) | 0.13<sup>b</sup> |
| | Hispanic | 55 (24%) | 30 (34%) | 0.13<sup>b</sup> |
| | Unknown | 1 (0%) | 2 (2%) | 0.13<sup>b</sup> |
| Family SES | Annual income per person supported, Mdn (Q1, Q3) | $8000 ($5000, $15,000) | $5000 ($3333, $7500) | <0.001<sup>a</sup> |
| Wechsler FSIQ | Mean (SD) | 84.2 (16.3) | 86.3 (15.4) | 0.30<sup>a</sup> |
| Nadir CD4 count, cells/mm<sup>3</sup> | $\geq$500 | 40 (18%) | n/a | |
| | 200–499 | 100 (44%) | n/a | |
| | $<200$ | 88 (39%) | n/a | |
| Most recent CD4 count, cells/mm<sup>3</sup> | $\geq$500 | 144 (63%) | n/a | |
| | 200–499 | 65 (29%) | n/a | |
| | $<200$ | 19 (8%) | n/a | |
| Peak viral load, copies/ml | $\leq$20,000 | 13 (6%) | n/a | |
| | $>20,000$ to $<100,000$ | 35 (15%) | n/a | |
| | $\geq$100,000 | 180 (79%) | n/a | |
| Most recent viral load, cells/mm<sup>3</sup> | $<400$ | 14.5 (64%) | n/a | |
| | 400 to $<1000$ | 14 (6%) | n/a | |
| | $\geq$1000 | 69 (30%) | n/a | |
| CDC Class C | Yes | 63 (28%) | n/a | |
| | No | 165 (72%) | n/a | |
| **Parent/caregiver characteristics** | | | |
| Education | High school or greater | 164 (72%) | 59 (68%) | 0.49<sup>b</sup> |
| | Less than high school | 62 (27%) | 27 (31%) | |
| | Unknown | 2 (1%) | 1 (1%) | |
| Limitations in physical health | Yes | 109 (48%) | 51 (59%) | 0.12<sup>b</sup> |
| | No | 106 (46%) | 33 (38%) | |
| Positive screen for mental health disorder | Yes | 46 (20%) | 38 (44%) | <0.001<sup>b</sup> |
| | No | 150 (66%) | 45 (52%) | |
| Positive screen for substance use disorder | Yes | 32 (14%) | 4 (5%) | |
| | No | 185 (81%) | 72 (83%) | |
| Life events in past year | 0–3 | 168 (74%) | 70 (80%) | 0.63<sup>b</sup> |
| | $>3$ | 24 (11%) | 12 (14%) | |
| | Unknown | 36 (16%) | 5 (6%) | |

Abbreviations: AMP, Adolescent Master Protocol; AMP Up, Adolescent Master Protocol for Participants 18 Years of Age and Older; CDC, Centers for Disease Control and Prevention [39]; n/a, not applicable; SES, socio-economic status; Wechsler FSIQ, Wechsler Intelligence Scale for Children, Fourth Ed. [34] (ages 6–16) or Wechsler Adult Intelligence Scale, Fourth Ed. [35] (ages 17 and older) Full-Scale Intelligence Quotient; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.

<sup>a</sup>T-test with equal variance.

<sup>b</sup>Chi-square test.
3.3.4 | Cumulative risk

The average score on the cumulative risk index (Table 6) did not differ between YAPHIV and YAPHEU (3.1 vs. 3.2, respectively, \( p = 0.81 \)), but the frequency of individual risks in several domains was greater than expected. In executive functioning, 20% of YAPHIV demonstrated risk on BRI, and 26% demonstrated risk on MCI, according to parent/caregiver reports. In cognitive efficiency, 22-44% of participants met the criteria for the definition of risk in WM or PSI. In behavioural and social/emotional functioning, according to parent/caregiver reports, 21-23% of YAPHEU demonstrated behavioural problems, while 28-30% of both groups demonstrated lower-than-expected adaptive skills. Approximately 50% of YAPHIV and YAPHEU averaged more than three potentially traumatic life events per year during the course of AMP meeting one of the definitions of risk. Parents/caregivers of YAPHIV and YAPHEU (17% vs. 31%, respectively) reported one or more difficulties in their own mental health, physical health or substance use. Parents/caregivers in both groups (11-14%) reported three or more potentially traumatic life events occurring within the 12 months prior to the interview.

### Table 3. Distribution of milestones by age at AMP Up Year 1 follow-up visit

| Milestone                              | Total (N = 315) | Age (years) at AMP Up Year 1 follow-up visit | p-value<sup>2</sup> |
|----------------------------------------|-----------------|---------------------------------------------|---------------------|
|                                        |                 | 19 (n = 151) | 20 (n = 53) | 21 (n = 52) | ≥22 (n = 59) |
| High school graduation                 | Yes             | 254 (81%)   | 109 (72%) | 43 (81%)  | 47 (90%)  | 55 (93%) | 0.001 |
|                                        | No              | 61 (19%)    | 42 (28%)  | 10 (19%)  | 5 (10%)   | 4 (7%)   |
| Enrolment in postsecondary education   | Yes             | 146 (46%)   | 67 (44%)  | 32 (60%)  | 20 (38%)  | 27 (46%) | 0.12  |
|                                        | No              | 169 (54%)   | 84 (56%)  | 21 (40%)  | 32 (62%)  | 32 (54%) |
| Current employment                     | Yes             | 156 (50%)   | 63 (42%)  | 30 (57%)  | 27 (52%)  | 36 (61%) | 0.05  |
|                                        | No              | 159 (50%)   | 88 (58%)  | 23 (43%)  | 25 (48%)  | 23 (39%) |
| Number of milestones attained          | 0               | 40 (13%)    | 29 (19%)  | 4 (8%)    | 4 (8%)    | 3 (5%)   | 0.02  |
|                                        | 1               | 76 (24%)    | 36 (24%)  | 14 (26%)  | 13 (25%)  | 13 (22%) |
|                                        | 2               | 117 (37%)   | 55 (36%)  | 14 (26%)  | 24 (46%)  | 24 (41%) |
|                                        | 3               | 82 (26%)    | 31 (21%)  | 21 (40%)  | 11 (21%)  | 19 (32%) |

Abbreviation: AMP Up, Adolescent Master Protocol for Participants 18 Years of Age and Older.

High school graduation, high school diploma or graduate equivalency degree.

Enrolment in postsecondary education, enrolment in technical and trade schools, college (freshman to senior year), associate and bachelor degrees and graduate school.

Current employment, part-time or full-time employment at the time of the AMP Up Year 1 follow-up visit.

<sup>a</sup>Chi-square test.

3.4 | Predictors of attainment of young adult milestones

Higher cognitive efficiency was positively associated with enrolment into postsecondary education and current employment (Figure 2a). Higher executive function, per parent/caregiver report, and lower cumulative risk were associated with a greater likelihood of attaining both academic milestones (Figures 2a and b). Age-appropriate behaviour (BASC-2 parent/caregiver report) was positively associated with high school graduation, while age-appropriate adaptive skills (BASC-2 participant self-report and parent/caregiver report) and perceived lack of difficulty in emotional functioning (BASC-2 participant self-report Internalizing Problems and Emotional Symptoms indices) were positively associated with enrolment in postsecondary education. Lack of functional limitations in caregiver physical health was associated with a lower likelihood of employment (Figure 2b). For YAPHIV, positive associations were: higher current CD4 with postsecondary education and lower nadir CD4 with current employment (Figure 3). PHIV status did not modify any associations. The results of the complete case analysis approach were similar to those of the multiple imputation approach for missing data.

4 | DISCUSSION

Resilience among YAPHIV and YAPHEU participants was demonstrated by their attainment of one or more young adult milestones. Although PHIV is an important aspect of participants’ lives, it was not determinative of success in milestone attainment. Rather, success was influenced more by participants’ development during childhood and adolescence across the cognitive, behavioural and social/emotional domains examined.

Despite well-documented early and sometimes ongoing risks for individuals affected by HIV, the proportions of young adults who attained each milestone did not differ by PHIV status, contrary to Hypothesis 1. Attainment of milestones was positively associated with higher participant executive functioning, cognitive efficiency and behavioural/social-emotional functioning, as well as fewer parent/caregiver risks and lower cumulative risk, supporting Hypotheses 2 and 3. For YAPHIV, higher current CD4 was positively associated with postsecondary education; the current viral load was not associated with any of the outcomes. Thus, Hypothesis 4 was partially supported. The finding that lower nadir CD4 was positively associated with current employment is counterintuitive; it is possible that residual or unmeasured confounding contributed to the observed association.
### Table 4. Measures of executive functioning and cognitive efficiency collected during AMP

| Domain and measures                      | Perinatal HIV status | YAPHIV (n = 228) | YAPHEU (n = 87) | p-value |
|------------------------------------------|----------------------|------------------|-----------------|---------|
| **Executive functioning**                |                      |                  |                 |         |
| BRIEF<sup>a</sup> Participant Self-Report|                      |                  |                 |         |
| Behavioral Regulation Index (BRI) Mean (SD) | 50.3 (12.1)          | 50.4 (11.4)      |                 | 0.95<sup>c</sup> |
| T ≥ 65: Yes                             | 29 (13%)             | 8 (9%)           |                 | 0.42<sup>d</sup> |
| No                                      | 170 (75%)            | 66 (76%)         |                 |         |
| Unknown                                  | 29 (13%)             | 13 (15%)         |                 |         |
| Metacognition Index (MCI) Mean (SD)      | 51.4 (11.4)          | 49.5 (11.4)      |                 | 0.23<sup>c</sup> |
| T ≥ 65: Yes                             | 29 (13%)             | 8 (9%)           |                 | 0.42<sup>d</sup> |
| No                                      | 170 (75%)            | 66 (76%)         |                 |         |
| Unknown                                  | 29 (13%)             | 13 (15%)         |                 |         |
| BRIEF Parent/Caregiver Report           |                      |                  |                 |         |
| Behavioral Regulation Index (BRI) Mean (SD) | 52.4 (11.6)          | 54.9 (12.9)      |                 | 0.13<sup>c</sup> |
| T ≥ 65: Yes                             | 23 (10%)             | 12 (14%)         |                 | 0.32<sup>d</sup> |
| No                                      | 169 (74%)            | 60 (69%)         |                 |         |
| Unknown                                  | 36 (16%)             | 15 (17%)         |                 |         |
| Metacognition Index (MCI) Mean (SD)      | 55.6 (12.5)          | 53.1 (12.1)      |                 | 0.14<sup>c</sup> |
| T ≥ 65: Yes                             | 46 (20%)             | 16 (18%)         |                 | 0.77<sup>d</sup> |
| No                                      | 146 (64%)            | 56 (64%)         |                 |         |
| Unknown                                  | 36 (16%)             | 15 (17%)         |                 |         |
| **Cognitive efficiency**                |                      |                  |                 |         |
| Wechsler<sup>b</sup> Working Memory Index (WMI) Mean (SD) | 86.8 (15.0)          | 90.2 (14.6)      |                 | 0.08<sup>c</sup> |
| WMI > 115                                | 7 (3%)               | 4 (5%)           |                 | 0.34<sup>d</sup> |
| WMI = 85–115                             | 113 (50%)            | 53 (61%)         |                 |         |
| WMI = 70–84                              | 77 (34%)             | 22 (25%)         |                 |         |
| WMI < 70                                 | 23 (10%)             | 8 (9%)           |                 |         |
| Wechsler<sup>b</sup> Processing Speed Index (PSI) Mean (SD) | 90.6 (16.4)          | 94.2 (14.7)      |                 | 0.07<sup>c</sup> |
| PSI > 115                                | 16 (7%)              | 7 (8%)           |                 | 0.34<sup>d</sup> |
| PSI = 85–115                             | 133 (58%)            | 61 (70%)         |                 |         |
| PSI = 70–84                              | 55 (24%)             | 14 (16%)         |                 |         |
| PSI < 70                                 | 16 (7%)              | 5 (6%)           |                 |         |

Abbreviations: AMP, Adolescent Master Protocol; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.

<sup>a</sup>BRIEF, Behavior Rating Inventory of Executive Function [36], reported as T-scores with Mean = 50, SD = 10. T ≥ 65 is considered clinically significant.

<sup>b</sup>Wechsler, Wechsler Intelligence Scale for Children, Fourth Ed. [34] (ages 6–16) or Wechsler Adult Intelligence Scale, Fourth Ed. [35] (ages 17 and older), reported as standard scores with Mean = 100, SD = 15. WMI/PSI < 70 indicates impaired performance.

<sup>c</sup>T-test with equal variance.

<sup>d</sup>Chi-square test.

The National Center for Education Statistics (NCES) [43] reports public high school graduation rates for young adults who complete high school within 4 years of entering ninth grade. In 2019, the rates were 86% for the United States general population and 80%, 82% and 89% for Black, Hispanic and White students, respectively. In our study, 81% of the total sample (N = 315) met the high school graduation/GED milestone, and graduation rates increased steadily from 72% for 19-year-olds to 93% for those age 22 and older. The comparison between NCES data and the present study is not equal because the NCES report does not reference student age, only timely graduation, and our sample of graduates included participants who attained a GED, while the NCES sample does not. While the total high school graduation rate in our sample is consistent with NCES data for Black and Hispanic students, the relatively low proportion among 19-year-olds (72%) indicates the presence of difficulties that may have impeded their academic progress. Developmental delays and subsequent difficulties in cognition, executive functioning and language [8, 9, 11–19], and possibly school absences due to medical complications, were present throughout the lives of many PHACS participants and may contribute to the slower-than-expected graduation rate.

Regarding mental health, 18% of 19-year-olds in each group screened positive for depression, comparable to a sample of 18- to 29-year-olds in the general population who
Table 5. Measures of behavioural and social-emotional functioning collected during AMP

| Measure | YAPHIV (n = 228) | YAPHEU (n = 87) | p-value |
|---------|------------------|-----------------|---------|
| **BASC-2\textsuperscript{a} Participant Self-Report** | | | |
| Internalizing Problems | Mean (SD) | 48.4 (10.3) | 47.0 (10.5) | 0.28\textsuperscript{c} |
| Clinically significant | T ≥ 70 | 8 (4%) | 3 (3%) | 0.92\textsuperscript{d} |
| At risk | T = 60–69 | 21 (9%) | 7 (8%) | |
| Average | T < 60 | 189 (83%) | 76 (87%) | |
| Unknown | 10 (4%) | 1 (1%) | |
| Emotional Symptoms Index | Mean (SD) | 48.4 (10.4) | 47.1 (10.1) | 0.30\textsuperscript{c} |
| Clinically significant | T ≥ 70 | 10 (4%) | 2 (2%) | 0.46\textsuperscript{d} |
| At risk | T = 60–69 | 16 (7%) | 9 (10%) | |
| Average | T < 60 | 192 (84%) | 75 (86%) | |
| Unknown | 10 (4%) | 1 (1%) | |
| Personal Adjustment | Mean (SD) | 50.5 (9.7) | 51.2 (9.9) | 0.59\textsuperscript{c} |
| Clinically significant | T ≤ 30 | 8 (4%) | 2 (2%) | 0.75\textsuperscript{d} |
| At risk | T = 31–40 | 21 (9%) | 10 (11%) | |
| Average | T ≥ 41 | 189 (83%) | 74 (85%) | |
| Unknown | 10 (4%) | 1 (1%) | |
| **BASC-2 Parent/Caregiver Report** | | | |
| Externalizing Problems | Mean (SD) | 48.6 (10.1) | 52.4 (10.5) | 0.003\textsuperscript{c} |
| Clinically significant | T ≥ 70 | 9 (4%) | 9 (10%) | 0.07\textsuperscript{d} |
| At risk | T = 60–69 | 17 (7%) | 9 (10%) | |
| Average | T < 60 | 194 (85%) | 69 (79%) | |
| Unknown | 8 (4%) | 0 (0%) | |
| Behavioral Symptoms Index | Mean (SD) | 49.5 (10.7) | 52.3 (10.5) | 0.04\textsuperscript{c} |
| Clinically significant | T ≥ 70 | 13 (6%) | 7 (8%) | 0.29\textsuperscript{d} |
| At risk | T = 60–69 | 21 (9%) | 13 (15%) | |
| Average | T < 60 | 186 (82%) | 67 (77%) | |
| Unknown | 8 (4%) | 0 (0%) | |
| Adaptive Skills | Mean (SD) | 47.8 (11.4) | 47.9 (11.1) | 0.94\textsuperscript{c} |
| Clinically significant | T ≤ 30 | 15 (7%) | 7 (8%) | 0.63\textsuperscript{d} |
| At risk | T = 31–40 | 54 (24%) | 17 (20%) | |
| Average | T ≥ 41 | 151 (66%) | 63 (72%) | |
| Unknown | 8 (4%) | 0 (0%) | |
| **PHQ-9\textsuperscript{b} or CES-D-10\textsuperscript{b}, Total ≥ 10** | Yes | 42 (18%) | 16 (18%) | 0.96\textsuperscript{d} |
| No | 183 (80%) | 71 (82%) | |
| Unknown | 3 (1%) | 0 (0%) | |

Abbreviations: AMP, Adolescent Master Protocol; YAPHEU, young adults with perinatal HIV exposure, uninfected; YAPHIV, young adults with perinatally acquired HIV.

\textsuperscript{a}BASC-2, Behavior Assessment System for Children, Second Ed. [37], reported as T-scores, Mean = 50, SD = 10.

\textsuperscript{b}PHQ-9, Patient Health Questionnaire [41]; CES-D-10, Center for Epidemiological Studies Depression Scale [42]. Depending on time of entry into AMP Up, symptoms of depression were measured with one of two depression screening instruments. Results are reported only for descriptive purposes. Total score ≥ 10 on either measure indicated a positive screen for symptoms of depression, not a diagnosis. Referrals for further clinical evaluation were provided as needed.

\textsuperscript{c}T-test with equal variance.

\textsuperscript{d}Chi-square test.

completed a similar screener [44]. In addition, participants in our sample reported symptoms of depression and anxiety at a level commensurate with their peers in a national standardization sample [37].

To our knowledge, there are only two reports examining similar milestones in longitudinal studies of YAPHIV and YAPHEU. In the Bellevue pediatric cohort study (birth years 1977–1978) conducted in New York City, 57% of YAPHIV, age 19 and older, had graduated high school or earned a GED [45]; YAPHEU were not included, thus limiting comparisons with the present study. Investigators with the Child and Adolescent Self-Awareness and Health Study (CASAH; enrolment in 2003–2008) [46] reported on the attainment of young adult milestones among YAPHIV and YAPHEU, age...
Table 6. Risk index: frequency of participant and parent/caregiver risks by perinatal HIV status

| Perinatal HIV status | YAPHIV (n = 228) | YAPHEU (n = 87) |
|----------------------|------------------|-----------------|
| Risk present (n, %)  |                  |                 |
| **Participant risks**|                  |                 |
| Performance discrepant from age expectations<sup>a</sup> on measures of: |                  |                 |
| Executive functioning (BRIEF)<sup>b</sup> |                  |                 |
| Participant or parent/caregiver report, BRI ≥ 65 | 45 (20%) | 19 (22%) |
| Participant or parent/caregiver report, MCI ≥ 65 | 60 (26%) | 20 (22%) |
| Cognitive efficiency (Wechsler) |                  |                 |
| WMI < 85 | 100 (44%) | 30 (34%) |
| PSI < 85 | 71 (31%) | 19 (22%) |
| Behavioral/social-emotional functioning (BASC-2) |                  |                 |
| Participant self-report, Internalizing Problems > 60 | 29 (13%) | 10 (11%) |
| Participant self-report, Emotional Symptoms > 60 | 26 (11%) | 11 (13%) |
| Participant self-report, Personal Adjustment < 40 | 29 (13%) | 12 (14%) |
| Parent/caregiver report, Externalizing Problems > 60 | 26 (11%) | 18 (21%) |
| Parent/caregiver report, Behavioral Symptoms Index > 60 | 34 (15%) | 20 (23%) |
| Parent/caregiver report, Adaptive Skills Index < 40 | 69 (30%) | 24 (28%) |
| Number of participant-reported life events > 3, averaged over all life event interviews completed in AMP | 110 (48%) | 47 (54%) |
| **Parent/caregiver risks** |                  |                 |
| Number of parent/caregiver mental health, substance use and physical health problems > 1<sup>c</sup> | 38 (17%) | 27 (31%) |
| Number of parent/caregiver-reported life events > 3 in 12 months prior to interview | 24 (11%) | 12 (14%) |
| Mean Index Score<sup>d</sup> | 3.1 (2.6) | 3.2 (2.9) |

Abbreviations: AMP, Adolescent Master Protocol of the Pediatric HIV/AIDS Cohort Study (PHACS); BRIEF, Behavior Rating Inventory of Executive Function [36]; BRI, Behavioral Regulation Index; MCI, Metacognition Index; PSI, Processing Speed Index; Wechsler, Wechsler Intelligence Scale for Children, Fourth Ed. [34] (ages 6–16) or Wechsler Adult Intelligence Scale, Fourth Ed. [35] (ages 17 and older); WMI, Working Memory Index; YAPHEU, young adults with perinatally acquired HIV; YAPHIV, young adults with perinatal HIV exposure, uninfected; YAPHEU, young adults with perinatally acquired HIV.

<sup>a</sup>Defined as T-scores or standard scores greater than 1.0 standard deviation from the population mean.

<sup>b</sup>For the BRIEF, when the participant self-report and parent/caregiver report were both available (n = 225), the report with the higher score (indicating greater difficulty) was used in the analysis.

<sup>c</sup>Only parents/caregivers with available data for all three measures were included in the calculation.

<sup>d</sup>Each variable was assigned a score of 0 or 1 depending on the absence (0) or presence (1) of the variable. The total score for each participant ranged from 0 to 13; higher scores indicated greater total adversity.

18–28 years, living in New York City: 67% graduated high school or earned a GED, 19% were in college, 42% were employed; 38% were neither in school nor working. Milestone attainment was higher in AMP Up than in CASAH, but both studies found no differences in attainment between YAPHIV and YAPHEU. Important differences between the study samples might have contributed to discrepancies in results. CASAH was recruited from four sites in New York City versus 14 sites across the United States, and participants in CASAH were older than those in AMP Up at the time milestone attainment was assessed.

Attainment of academic and employment milestones is not the only way to define resilience; however, these milestones are important in United States society and predictive of success in adulthood [3]. Understanding of HIV disease and appropriate treatment has improved substantially since the early days of the epidemic, resulting in reduced morbidity and mortality. Because of these advances, our participants were likely better able to participate in social and educational activities available to their peers, possibly contributing to the attainment of young adult milestones. It is important to note that data included in this analysis were obtained prior to the COVID-19 pandemic. Results of future studies may differ for youth who missed social, educational and psychotherapeutic opportunities or access to comprehensive medical care due to pandemic-related restrictions in 2020–2022.

This study has several strengths, including a large number of participants, longitudinal follow-up through childhood and into young adulthood, and the use of standardized, well-researched measures of functioning. Some limitations were noted. The sample might not be representative of the general population of YAPHIV or YAPHEU since all participants
Figure 2. (a) Adjusted associations between predictors and attainment of young adult milestones. The association between each predictor and outcome is presented as follows: the solid diamond represents the prevalence ratio, and the horizontal line represents the 95% confidence interval. In addition, the dotted vertical line represents the null value (prevalence ratio = 1.0). The adjusted prevalence ratio for the attainment of a specific milestone compared participants with a specific predictor versus a reference group. Each model adjusted for sex, race/ethnicity, Wechsler FSIQ (except the model for cognitive efficiency due to potential overcorrection), family socioeconomic status (an index including annual income and household density) and age at the time of measurement of each predictor. *Indicates lower frequency or intensity of problems. (b) Adjusted associations between predictors and attainment of young adult milestones. The association between each predictor and outcome is presented as follows: the solid diamond represents the prevalence ratio, and the horizontal line represents the 95% confidence interval. In addition, the dotted vertical line represents the null value (prevalence ratio = 1.0). The adjusted prevalence ratio for the attainment of a specific milestone compared participants with a specific predictor versus a reference group. Each model adjusted for sex, race/ethnicity, Wechsler FSIQ, family socioeconomic status (an index including annual income and household density), and age at the time of measurement of each predictor. BASC-2, Behavior Assessment System for Children, Second Ed. [37]; BRIEF, Behavior Rating Inventory of Executive Function [36]; Risk index, a study-specific summary of risks; Wechsler FSIQ, Wechsler Intelligence Scale for Children, Fourth Ed. [34] or Wechsler Adult Intelligence Scale, Fourth Ed. [35] Full-Scale Intelligence Quotient.
Figure 3. Adjusted associations between measures of HIV disease severity and attainment of young adult milestones in YAPHIV. The association between each predictor and outcome is presented as follows: the solid diamond represents the prevalence ratio, and the horizontal line represents the 95% confidence interval. In addition, the dotted vertical line represents the null value (prevalence ratio = 1.0). The adjusted prevalence ratio for the attainment of a specific milestone compared YAPHIV participants with a specific measure of HIV disease severity (predictor) versus a reference group. Each model adjusted for sex, race/ethnicity, Wechsler FSIQ (except the models for nadir CD4 and peak viral load), family socio-economic status (an index including annual income and household density) and age at the time of measurement of each predictor. Wechsler FSIQ, Wechsler Intelligence Scale for Children, Fourth Ed. [34] or Wechsler Adult Intelligence Scale, Fourth Ed. [35] Full-Scale Intelligence Quotient; YAPHIV, young adults with perinatally acquired HIV.
5 | CONCLUSIONS

Future studies of resilience in youth with PHIV and PHEU should examine additional milestones typically involved in the transition to adulthood, such as sustained employment, financial independence, romantic and committed partner/marital relationships and parenthood. Our findings suggest it is important to maintain developmental surveillance and interventions, including access to medical care and age-appropriate multidisciplinary supports, throughout the lifespan. With targeted and timely support, we can strengthen cognitive and behavioral/social-emotional functioning to promote resilience and thereby increase rates of education, employment and medical wellbeing among YAPHIV and YAPHEU.

AUTHORS’ AFFILIATIONS

1Department of Pediatrics, Tulane University School of Medicine, New Orleans, Louisiana, USA; 2Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA; 3Department of Pediatrics, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA; 4Research Department, Children’s Diagnostic & Treatment Center, Fort Lauderdale, Florida, USA; 5Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA; 6Departments of Infectious Diseases and Psychiatry and Behavioral Science, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; 7Department of Pediatrics, Infectious Diseases, University of Colorado School of Medicine, Children’s Hospital Colorado, Aurora, Colorado, USA; 8HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute, and Departments of Psychiatry and Sociomedical Sciences, Columbia University, New York City, New York, USA; 9Department of Neurosciences, University of California, San Diego, La Jolla, California, USA; 10Department of Pediatrics, University of Illinois at Chicago, Chicago, Illinois, USA; 11Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

COMPETING INTERESTS

The authors have no competing interests to disclose.

AUTHORS’ CONTRIBUTIONS

PAS and MLN conceived the idea for the study and wrote the first draft of the manuscript. YH and KT designed the statistical method and analysed the data. PAS, YH, MLN, PAG, LLH, KM, RMCE, CAM, SLN, RS and KT contributed to the study design, provided critical reviews and edited the manuscript for content. All authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

We thank the participants, caregivers and families for their participation in the Pediatric HIV/AIDS Cohort Study (PHACS) and the individuals and institutions involved in the conduct of PHACS. We also thank Laticria Conley and Brandon Montanez, members of the PHACS Peers United Group, for their contributions to this project. This research was presented as a Science Spotlight presentation at the virtual Conference on Retroviruses and Opportunistic Infections (vCROI), March 6–10, 2021.

The following institutions, clinical site investigators and staff participated in conducting PHACS AMP and AMP Up in 2019, in alphabetical order: Ann & Robert H. Lurie Children’s Hospital of Chicago: Ellen Chadwick, Margaret Ann Sanders, Kathleen Malee, Yoonsun Pyun; Baylor College of Medicine: Mary Paul, Sheldon Buschur, Chivon McMullen-Jackson, Lynnette Harris; Bronx Lebanon Hospital Center: Munir Purswani, Mahboobullah Mirza Baig, Alma Villegas; Children’s Diagnostic & Treatment Center: Lisa Gaye Robinson, Sandra Navarro, Patricia A. Garvie; Boston Children’s Hospital: Sandra K. Burchett, Rebecca Pinskey, Adam R. Cassidy; Jacobi Medical Center: Andrew Winiwa, Marlene Burey, Ray Shaw, Molly L. Nozyce; Rutgers–New Jersey Medical School: Arrie Dieudonne, Linda Bettica, Juliette Johnson, Karen Surowiec; St. Christopher’s Hospital for Children: Janet S. Chen, Taesha White, Mitzi Grant; St. Jude Children’s Research Hospital: Katherine Knapp, Jamie Russell-Bell, Megan Wilkins, Erick Odero; San Juan Hospital Research Unit/Department of Pediatrics, San Juan, Puerto Rico: Mideola Acevedo-Flores, Heidi Rios, Vivian Olivera; Tulane University School of Medicine: Margarita Silio, Medea Gabriel, Patricia Sirols; University of California, San Diego: Stephen A. Spector, Megan Loughran, Veronica Figueroa, Sharon Nichols; University of Colorado Denver Health Sciences Center: Elizabeth McFarland, Carrie Chambers, Emily Barr, Mary Gildeen; University of Miami: Gwendolyn Scott, Grace Alvarez, Juan Caffroni, Anai Cuadra.

FUNDING

The study was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development with co-funding from the National Institute on Drug Abuse, the National Institute of Allergy and Infectious Diseases, the National Institute of Mental Health, the National Institute of Neurological Disorders and Stroke, the National Institute on Deafness and Other Communication Disorders, the National Institute of Dental and Craniofacial Research, the National Cancer Institute, the National Institute on Alcohol Abuse and Alcoholism, the Office of AIDS Research and the National Heart, Lung, and Blood Institute through cooperative agreements with the Harvard T.H. Chan School of Public Health (HD052102) (Principal Investigator: George R. Seage III; Programme Director: Liz Salomon) and the Tulane University School of Medicine (HD052104) (Principal Investigator: Russell Van Dyke; Co-Principal Investigator: Ellen Chadwick; Project Director: Patrick Davis). Data management services were provided by Frontier Science and Technology Research Foundation (PI: Suzanne Siminski), and regulatory services and logistical support were provided by Westat, Inc (PI: Julie Davidson).

DISCLAIMER

The conclusions and opinions expressed in this article are those of the authors and do not necessarily reflect those of the National Institutes of Health or the U.S. Department of Health and Human Services.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

REFERENCES

1. Hillard ME, McQuaid EL, Nabors L, Hood KK. Resilience in youth and families living with pediatric health and developmental conditions: introduction to the special issue on resilience. J Pediatr Psychol. 2015;40(9):835–9.
2. Masten AS. Ordinary magic: resilience in development. New York: Guilford Press; 2014.
3. IOM (Institute of Medicine) and NRC (National Research Council). Investing in the health and well-being of young adults. Washington, DC: National Academies Press; 2015.
4. Betancourt TS, Meyers-Olhi SE, Charrow A, Hansen N. Annual research review: mental health and resilience in HIV/AIDS-affected children – a review of the literature and recommendations for future research. J Child Psychol Psychiatry. 2013;54(4):423–44.
5. Li X, Chi P, Sherr L, Stanton B. Psychological resilience among children affected by parental HIV/AIDS: a conceptual framework. Health Psychol Behav Med. 2015;3(1):217–35.
6. Funk-Brentano I, Assoumou L, Veber F, Moshouss D, Frange P, Blanche S. Resilience and life expectations of perinatally HIV-1 infected adolescents in France. Open AIDS J. 2016;10:209–24.
7. Harrison S, Li X. Toward an enhanced understanding of resilience for youth HIV populations. AIDS Care. 2018;30(SUP4):1–4.
8. Laughton B, Cornell M, Bolvin M, Van Rie A. Neurodevelopment in perinatally HIV-1 infected children: a concern for adolescence. J Int AIDS Soc. 2013;16(1):18603.
9. Smith R, Wilkins M. Perinatally acquired HIV infection: long-term neuropsychological consequences and challenges ahead. Child Neuropsychol. 2015;21(2):234–68.
10. Slogrove AL. It is a question of equity: time to talk about children who are HIV-exposed and “HIV-free.” J Int AIDS Soc. 2021;24(11):e25850.
11. Smith R, Chernoff M, Williams PL, Malee KM, Sirols PA, Kammerer B, et al. Impact of HIV severity on cognitive and adaptive functioning during childhood and adolescence. Pediatr Infect Dis J. 2012;31(6):592–9.
12. Garvie PA, Zeldow B, Malee K, Nichols SL, Smith RA, Wilkins ML, et al. Discordance of cognitive and academic achievement outcomes in youth with perinatal HIV exposure. Pediatr Infect Dis J. 2014;33(9):e232–8.
13. Nozyce ML, Hsu Y, Williams PL, Kapetanovic S, Hazra R, Nichols S, et al. Safety of in utero and neonatal antiretroviral exposure: cognitive and academic outcomes in HIV-exposed, uninfected children 5–13 years of age. Pediatr Infect Dis J. 2014;33(11):1128–33.

14. Rice ML, Buchanan AL, Siberry GK, Malek KM, Zeldow B, Frederick T, et al. Language impairment in children perinatally infected with HIV compared to children who were HIV-exposed and uninfected. J Dev Behav Pediatr. 2012;33(2):112–23.

15. Redmond SM, Yao T-J, Russell JS, Rice ML, Hoffman HJ, Siberry GK, et al. Longitudinal evaluation of language impairment in youth with perinatally acquired human immunodeficiency virus (HIV) and youth with perinatal HIV exposure. J Pediatr Infect Dis Soc. 2016;6(suppl 1):S33–40.

16. Nichols SL, Chernoff MC, Malek K, Sirois PA, Williams PL, Figueroa V, et al. Learning and memory in children and adolescents with perinatal HIV infection and perinatal HIV exposure. Pediatr Infect Dis J. 2016;35(6):649–54.

17. Nichols SL, Chernoff MC, Malek KM, Sirois PA, Woods SP, Williams PL, et al. Executive functioning in children and adolescents with perinatal HIV infection and perinatal HIV exposure. J Pediatr Infect Dis Soc. 2016;6(suppl 1):S15–23.

18. Sirois PA, Chernoff MC, Malek KM, Garvie PA, Harris LL, Williams PL, et al. Associations of memory and executive functioning with academic and adaptive functioning among youth with perinatal HIV exposure and/or infection. J Pediatr Infect Dis Soc. 2016;6(suppl 1):S24–32.

19. Malek KM, Chernoff MC, Sirois PA, Williams PL, Garvie PA, Cammerer BL, et al. Impact of perinatally acquired HIV disease upon longitudinal changes in memory and executive functioning. J Acquir Immune Defic Syndr. 2017;75(4):455–64.

20. Malek KM, Tassiopoulou K, Hsu Y, Siberry G, Williams PL, Hazra R, et al. Mental health functioning among children and adolescents with perinatal HIV infection and perinatal HIV exposure. AIDS Care. 2011;23(12):1533–44.

21. Mellenis CA, Tassiopoulou K, Malek K, Moscicki AB, Patton D, Smith R, et al. Behavioral health risks in perinatally HIV-exposed youth: co-occurrence of sexual and drug use behaviors, mental health problems, and nonadherence to antiretroviral treatment. AIDS Patient Care STDs. 2011;25(7):413–22.

22. Smith R, Hsu Y, Tassiopoulou K, Rutstein R, Kapetanovic S, Mellenis C, et al. Mental health diagnoses, symptoms, and service utilization in US youth with perinatal HIV infection or HIV exposure. AIDS Patient Care STDs. 2019;33(1):1–13.

23. Metzler M, Merrick MT, Klevens J, Ports KA, Ford DC. Adverse childhood experiences and perinatal HIV infection or HIV exposure. AIDS Patient Care STDS. 2012;26(8):499–507.

24. Brown DW, Anda RF, Tiemeier H, Felitti VJ, Edwards VJ, Croft JB, et al. Adverse childhood experiences and life opportunities: shifting the narrative. Child Youth Serv Rev. 2017;72:141–49.

25. Brown DW, Anda RF, Tiemeier H, Felitti VJ, Edwards VJ, Croft JB, et al. Adverse childhood experiences and the risk of premature mortality. Am J Prev Med. 2009;37(5):389–96.

26. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health. 2017;2(8):e356–66.

27. Meeker EC, O’Connor BC, Kelly LM, Hodgeman DD, Scheel-Jones AH, Berbery C. The impact of adverse childhood experiences on adolescent health risk indicators in a community sample. Psychol Trauma. 2021;13(3):302–12.

28. Balistreri KS, Alvira-Hammond M. Adverse childhood experiences, family functioning and adolescent health and emotional well-being. Public Health. 2016;136:72–8.

29. Trent M, Dooley DG, Dougé J, SECTION ON ADOLESCENT HEALTH; COUNCIL ON COMMUNITY PEDIATRICS; COMMITTEE ON ADOLESCENCE. The impact of racism on child and adolescent health. Pediatrics. 2019;144(2):e20191765.